CHEMICAL REVIEWS

Volume 99, Number 8 August 1999

Chemistry of Acyl Radicals

Chryssostomos Chatgilialoglu*

I.Co.C.E.A., Consiglio Nazionale delle Ricerche, Via P. Gobetti 101, 40129 Bologna, Italy

David Crich*

Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, Illinois 60607-7061

Mitsuo Komatsu and Ilhyong Ryu*

Department of Applied Chemistry, Graduate School of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

Received November 17, 1998

Contents

10.1021/cr9601425 CCC: $35.00
Published on Web 06/24/1999

Chryssostomos Chatgilialoglu was born in Nikea, Greece, in 1952. He received his doctorate degree in Chemistry from the University of Bologna, Italy, in 1976. He was a postdoctoral fellow at the University of York, England, from 1977 to 1979, and from 1979 to 1982 he worked at the National Research Council of Canada (Ottawa) as a research associate. In 1983 he returned to Italy at the Consiglio Nazionale delle Ricerche, Bologna, where he has been the director of research since 1991. His research focuses on free-radical chemistry in solution. He has developed several radical-based reagents for organic synthesis, including tris(trimethylsilyl)silane for which he was winner of the Reagent of the Year 1990 (Fluka Prize). His current research interests span from design of new synthetic strategies to polymer applications and mechanistic studies of biological processes.

David Crich was born in Chesterfield, England (1959), and graduated with his BSc in Chemistry and French from the University of Surrey in 1981. He obtained his doctorate (Docteur ès Sciences) from the Université de Paris XI in 1984 under the direction of D. H. R. Barton and stayed in France, at the Institut de Chimie des Substances Naturelles in Gif sur Yvette, for a one-year postdoctoral study with Professors D. H. R. Barton and P. Potier. He spent five years at University College London as a Lecturer in the Chemistry Department before moving, as Associate Professor in 1990, to the University of Illinois at Chicago where he is now Full Professor. He is a recipient of the Franco-British prize of the French Academy of Sciences and the Corday-Morgan and Tate and Lyle medals of the Royal Society of Chemistry and has been a Fellow of the A. P. Sloan Foundation and a University of Scholar of the University of Illinois at Chicago. His main interests are in the chemistry of free radicals, asymmetric synthesis, and carbohydrate chemistry.

I. Introduction

The chemistry of acyl radicals has a long history which can be traced back to the early part of this century. Nevertheless, the application of acyl radicals in fine organic synthesis has, until relatively recently, lagged behind that of simple alkyl and even vinyl radicals. In part, this must be due to the early, confusing, and often contradictory results from different laboratories on the regiochemistry of cyclization reactions and the unpredictable and variable yields observed when using acyl chlorides in conjunction with Kuivila's popular tin hydrides[1] as sources of acyl radicals. However, in just over a decade the field has expanded enormously. Many new and versatile acyl radical precursors have been introduced, most notably the acyl selenides, and old ones reexamined, particularly the previously maligned carbonylation of alkyl radicals.[2] These new methods have, in turn, enabled the complexities of regiochemistry to be examined and understood. These practical advances in the generation and reactions of acyl radicals have been shadowed by a vastly increased

Mitsuo Komatsu received his doctorate of Engineering degree in 1974 from Osaka University under the supervision of Professor Toshio Agawa. From 1975 to 1976, he worked with the late Professor Gerrit L'abbé as a postdoctoral fellow at Catholic University of Leuven. He received the Progress Award in Synthetic Organic Chemistry, Japan, in 1983. His professional career started in 1969 by joining the faculty of Engineering at Osaka University as Assistant Professor. After being promoted to Associate Professor, he became Full Professor in 1994 at the same university, where he belongs to the Department of Applied Chemistry, Graduate School of Engineering, since 1995. His major research fields cover heterocyclic chemistry, heteroatom chemistry, and radical chemistry. His current interests are focused on development of new methodology for synthesis of heterocyclic compounds and application of heterocycles to organic synthesis and functional materials.

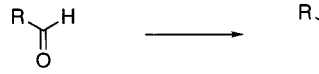
Ilhyong Ryu grew up in the suburbs of Nagoya. He received his B.S. in 1973 from Nagoya University and his Ph.D from Osaka University working with Professor Noboru Sonoda in 1978. After spending some years as a JSPS postdoctoral fellow and a research associate at Osaka University, he became Assistant Professor at Osaka University in 1987 and was promoted to Assiociate Professor of the Graduate School of Engineering, Osaka University, in 1995. He was a visiting scientist at the University of Ottawa with Professor Howard Alper (1991–1992). He has been the recipient of the Progress Award in Synthetic Organic Chemistry, Japan (1990), and the Daicel Chemical Award in Synthetic Organic Chemistry (1989). He has been a Fellow of the Sumitomo Foundation (1996). His research interests include the development of new synthetic methodologies based on free-radical species, catalytic synthetic transformations, concise synthetic reactions, and automated synthesis.

comprehension of their reaction rates. This expanded database of kinetic information, when added to the existing horlogeries,[3a−c] permits the confident prediction of the outcome of new radical chain sequences involving acyl radicals. The synthetic organic chemist, as well as the spectroscopist, should now be able to find a precursor suitable to almost any common conditions and substrate type. Coupled with the many other recent advances in the general area of free-radical chemistry,[3d−i] stereoselectivity,[3j,k] and tandem processes[3l−o] and applications to synthesis,[3p] these developments in acyl radical chemistry should remove any remaining barriers to their widespread application in organic chemistry. Excellent coverage of the early work on acyl radicals was given in reviews by Nikishin[4a] and Minisci[4b] in the 1970s. However, with the exception of more limited personal accounts by Boger[5] and Crich,[6] there has been no attempt to bring together all of the recent developments which have served to make acyl radical chemistry into the dynamic, vibrant field it currently is. This article seeks to fill that void.

II. Structural Properties

A. Thermodynamic Data

Bond strengths in polyatomic molecules are notoriously difficult to measure accurately. Bond dissociation enthalpies of aldehydes, $D°$[RC(O)−H], defined as the enthalpy changes in eq 1, are directly related to the heats of formation of acyl radicals, $\Delta H_f°$[RC(O)•]. Therefore, $D°$ measurements are "equivalent" to $\Delta H_f°$ measurements for radicals and vice versa (eq 2). Since both quantities are important, not only in

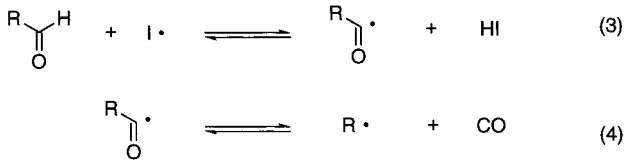


(1)

$$D°[RC(O)—H] = \Delta H_f°(\dot{R}CO) + \Delta H_f°(H\bullet) - \Delta H_f°[RC(O)H] \quad (2)$$

the thermochemistry but also in the kinetics and mechanisms of reactions involving acyl radicals, we will briefly consider some pertinent works of interest.

In the 1970s and 1980s, the most important reference regarding the thermochemistry of acyl radicals was either work based on iodination methods (eq 3) or on studies of the dissociation/recombination equilibria of acyl radicals (eq 4).[7,8] In the latter experi-



(3)

(4)

ments, the heats of formation of radical R•, $\Delta H_f°(R\bullet)$, were also previously obtained by the iodination method.

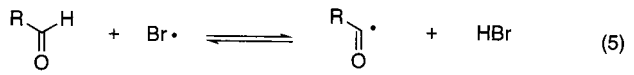
A striking feature of aldehydes such as $CH_3C(O)H$,[7,9] $CH_3CH_2C(O)H$,[10] $CH_2{=}CHC(O)H$,[11] and $PhC(O)H$[12] was the almost constant C(O)−H bond strength values, i.e., 86.0, 87.4, 87.1, and 86.9 kcal mol^{-1}, respectively. The error limits were ±1 kcal mol^{-1}.[8] The heats of formation determined by the iodination method combine the measured activation energies for the forward reaction of eq 3 and the assumed activation energies of the reverse reaction of eq 3. However, recent work from Gutman and co-workers has shown that the activation energy for the reaction of alkyl radicals with HI is slightly negative, in contrast to the previous assumption that it was slightly positive.[13]

Table 1. Bond Dissociation Enthalpies of RC(O)−H, Heats of Formation, and Standard Potentials of RC(O)• Radicals

RC(O)•	$\Delta H_f°$(RC(O)•) (kcal mol^{-1})	$D°$[RC(O)−H] (kcal mol^{-1})	$E°_{RC(O)•}$ (V)
$CH_3C(O)•$	-2.3 ± 0.3[a]	89.3 ± 0.4[a]	−1.75[c]
$CH_3CH_2C(O)•$	−7.7[b]	89.5[b]	−1.75[c]
$CH_2{=}CHC(O)•$	15.3[b]	89.1[b]	
$PhC(O)•$	24.1[b]	88.9[b]	−1.13[c]

[a] Reference 15. [b] See text. [c] Reference 20.

At the beginning of the 1990s, Nicovich and co-workers[14] addressed the forward reaction of eq 5 while Gutman and co-workers[15] studied the reverse reaction. $D°$[$CH_3C(O)$−H] and $\Delta H_f°$[$CH_3C(O)•$] were



(5)

determined with good accuracy to be 89.3 ± 0.4 and -2.4 ± 0.3 kcal mol^{-1}, respectively. In addition, the heat of formation of the $CH_3C(O)•$ radical was also estimated to be -2.2 ± 0.7 kcal mol^{-1} at 298 K using an isodesmic reaction at the G2(MP2) level of theory.[16] Therefore, $D°$[$CH_3C(O)$−H] and $\Delta H_f°$[$CH_3C(O)•$] are 3.3 kcal mol^{-1} higher and 3.3 kcal mol^{-1} lower, respectively, than the previous values.

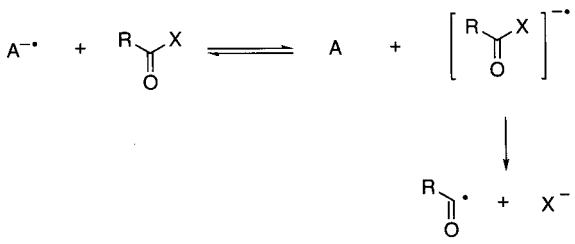
On the basis of $\Delta H_f°$[$CH_3C(O)•$] and taking into account the currently accepted heats of formation of R• radicals[13] and of molecules $CH_3C(O)R$,[17] the bond dissociation enthalpies of $CH_3C(O)$−R compounds were evaluated to be 84.4 (R = Me), 83.0 (R = Et), 81.6 (R = *i*-Pr), and 78.7 kcal mol^{-1} (R = *t*-Bu). Similarly, taking the heats of formation of Cl[18] and $CH_3C(O)Cl$,[19] $D°$[$CH_3C(O)$−Cl] was evaluated to be 84.6 kcal mol^{-1}. These values are also considerably higher than those previously reported.[17]

Thermodynamic data for other acyl radicals are poor, with uncertainties mainly derived from assumptions without experimental comparison. However, some important information is available. The $\Delta H_f°$ of the $CH_3CH_2C(O)•$ radical and the $D°$ of the corresponding aldehyde can be revised (see Table 1) by taking into account the currently accepted heats of formation of the ethyl radical[21] and of propanal.[22] Since the reverse reaction of eq 3 is still more rapid than that of eq 5, the likelihood exists that the former reactions also have significantly negative activation energies. With the assumption that in the reverse reaction (eq 3) for $CH_2{=}CHC(O)H$ and $PhC(O)H$ the activation energies are −1 kcal mol^{-1}, we recalculate $D°$ and $\Delta H_f°$ of the corresponding acyl radicals from the original work (see Table 1).[11,12]

Acyl radicals have been shown by EPR spectroscopy to be σ-type radicals (section II.B). Since in such σ-radicals there can be little or no delocalization of the unpaired electron; even when there is a neighboring vinyl or aromatic ring, the bond strengths of the parent aldehydes, $D°$[RC(O)−H], should be virtually independent of the nature of the R group. The $D°$ values reported in Table 1 are consistent with this observation.

The redox properties of acyl radicals have recently been reported.[20] Acyl radicals were generated by indirect electrochemical reduction of acyl chlorides and anhydrides [RC(O)X] by aromatic radical anion ($A^{-•}$) (eq 6). The standard potentials, $E°_{RC(O)•}$, of alkyl-substituted acyl radicals are between −1.68 and −1.75 V vs SCE.

On the other hand, the $E°_{RC(O)•}$ of the aryl-substituted radicals are between −1.07 and −1.16 V (Table 1). Furthermore, in all cases the self-exchange reorganization energy $\lambda_{RC(O)•}(0)$ was found to be 30 kcal mol^{-1}. The acetyl radical as well as the acetyl and benzoyl anions were the subject of theoretical calculations.[23,24] Interestingly, ∠CCO in the acetyl radical is ca. 130° whereas in acetyl and benzoyl anions it is ca. 113° and 169°, respectively. The 600−700 mV difference between alkyl- and aryl-substituted acyl radicals could be interpreted by considering the stability of the aromatic acyl anion due to extensive delocalization of the charge on the aryl group. On the other hand, the large reorganization energy could reflect a substantial decrease or increase of ∠CCO in the transformation of the acyl radical into the corresponding alkyl- or aryl-substituted acyl anion, respectively.



(6)

From the photoelectron spectrum of $CH_3C(O)^-$, the electron affinity, EA, of the acetyl radical was found to be 10.45 ± 0.85 kcal mol^{-1}.[23] The bond dissociation enthalpies of C(O)−H in aldehydes are connected to the EAs of the corresponding acyl radicals via the thermochemical cycle in eq 7. The data allow the gas-

$$D°[CH_3C(O)-H] = \Delta H°[CH_3CHO \rightarrow CH_3C(O)^- + H^+] + EA[CH_3C(O)•] - IP(H•) \quad (7)$$

phase acidity of acetaldehyde to be calculated as 392.3 ± 1.3 kcal mol^{-1}.

The ionization potentials of the acetyl and propanoyl radicals were estimated to be 6.4 ± 0.1 and 6.8 ± 0.1 eV, respectively,[25] by using the values of appearance potentials[26,27] of $CH_3C(O)^+$ and of $CH_3CH_2C(O)^+$ from the parent aldehydes and the heats of formation of acetyl and propanoyl radicals from Table 1.

B. Electron Paramagnetic Resonance (EPR) Spectra

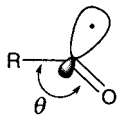
The Landolt−Börnstein compilations of organic radicals include ca. 140 entries for the EPR parameters of α-substituted acyl radicals up to the beginning of 1986.[28,29] After this period, very little has been added to this subject, although some theoretical work has allowed for a better understanding of the relationship between experimental data and structure. However, it is well established by both experiment and theory that the radical center in acyl radicals is bent (structure **1**) and that the unpaired electron

Table 2. Experimental ^{13}C hfs Constants Together with Theoretical θ Bond Angles and ^{13}C hfs Constants for XC(O)• Radicals

X	experiment $a(^{13}C)$, G	theory[f] θ/deg	theory[g] $a(^{13}C)$, G
H	133.9[a]	126.6	127.2
CH_3	124.6[b]	129.4	123.0
NH_2	170.0[c]	130.8	167.3
$OC(CH_3)_3$	183.5[d]	128.6	183.2
F	286.6[e]	128.1	271.6

[a] Reference 30. [b] Reference 31. [c] Reference 32. [d] Reference 33. [e] Reference 34. [f] UHF/6-311G** level of theory; reference 35. [g] UMP2/DZP//UHF/6-311G**; reference 35.

occupies an orbital with substantial 2s character, and therefore this species can be considered a σ-type radical.

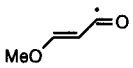
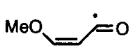
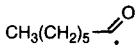
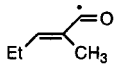
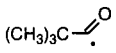
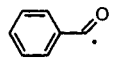
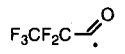
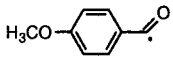
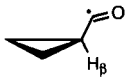
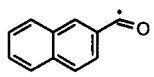
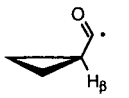
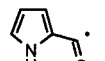
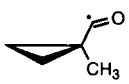
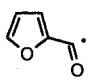
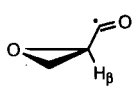
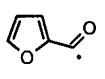
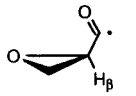
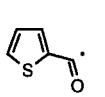


1

Generally, the EPR spectra of acyl radicals contain a central set of lines due to ^1H coupling constants with satellites due to coupling with ^{13}C ($I = {}^1/_2$, 1.1% natural abundance). ^{13}C hyperfine splitting (hfs) constants, which can be used as a guide to the distribution of unpaired electron density, are not easy to interpret. It has been found that the nature of the substituent in the radical center enormously influences EPR parameters; the ^{13}C hfs constants in acyl radicals increase along the series R = CH_3 < NH_2 < OBu^t < F (Table 2). These large variations in ^{13}C hfs constants in acyl radicals have been correlated to changes in geometry at the radical center. It was suggested that by increasing the electronegativity of the α-substituents, the geometry at the radical center becomes more bent, which would also mean a higher percentage of 2s character in the singly occupied molecular orbital (SOMO) and therefore an increase in the ^{13}C hfs.

In a theoretical study (ab initio calculations at the UMP2/DZP//UHF/6-311G** level of theory),[35] it has recently been noted by Guerra that for a variety of α-substituted acyl radicals [XC(O)•, where X = H,

Table 3. Electron Paramagnetic Resonance (EPR) Parameters for a Variety of α-Substituted Acyl Radicals

acyl radicals	T, K	hfs, G	*g* factor	ref(s)	acyl radicals	T, K	hfs, G	*g* factor	ref(s)
	170	131.75 (1 H_α)	2.0003	36		153	18.50 (1 H_β)	2.0008	40
	170	4.0 (3 H_β)	2.0005	36		153	19.63 (1 H_β)	2.0008	40
	221	2.18 (2 H_β)	2.0005	37		154	1.10 (3 H_γ)	2.0005	37,40
	178		2.0008	36,37		183	1.18 (2 *m*-H), 0.21 (2 *o*-H)	2.0008	43
	149	4.44 (2 F_β), 16.1 (1 F_γ)	2.0008	38		223 143	1.15 (2 *m*-H) 2.3 (1 *m*-H), 0.4 (1 *o*-H)	2.0008	44
	172	18.2 (1 H_β), 0.2 (2 H_γ), 120.5(1 ^{13}C)	2.0009	39		218	2.0 (1 H), 0.4 (1 H)	2.0008	45
	172	0.5 (1 H_β), 0.95 (2 H_γ), 0.6 (2 H_γ), 123.6(1 ^{13}C)	2.0008	39		173	2.75 (3 H), 0.75 (1 H) 4.25 (1 N)	2.0011	46
	163	0.85 (3 H_γ)	2.0009	39		173	2.65 (1 H), 0.20 (2 H)	2.0011	46
	148	14.2 (1 H_β)	2.0005	39		173	2.30 (1 H), 0.40 (1 H)	2.0008	46
	148	1.6 (1 H_β), 3.2 (1 H_γ)	2.0004	39		173	3.65 (1 H), 0.30 (1 H)	2.0020	46

CH_3, NH_2, OH, and F] the θ angle is essentially constant at 128°, i.e., slightly larger than that expected for sp^2 hybridized carbons (Table 2). According to this study, the large variations observed experimentally in ^{13}C hfs constants as the electronegativity of the α-substituent increase are due to the electronic influence of the substituent. In fact, there is a large breakdown in the orbital following the SOMO which strongly depends on the electronegativity of the α-substituents.

The EPR data for acyl radicals presented in Table 3 were selected to illustrate the effect of a variety of different substituents. In addition, isotropic hyperfine splitting and *g* factors obtained directly from solution are reported. The low *g* values are typical of σ-type radicals.

Aliphatic acyl radicals have hfs constants derived from the interaction of the unpaired electron with the β-protons. Davies and Sutcliffe[37] found that the conformational behavior of these acyl radicals parallels that of the parent aldehydes. For example, both a_H in $CH_3C(O)^\bullet$ and $^3J_{CHCHO}$ in CH_3CHO show a similar type of angular dependence. Furthermore, the two constants are linearly related for a variety of substituents on the carbonyl moiety. Perfluoroalkyl-substituted acyl radicals have also been reported.[38] The EPR spectra of the $CF_3C(O)^\bullet$ radical at low temperatures reveal three equivalent fluorine hfs constants, i.e., $a_F = 11.54$ G (3 F). Interestingly, the EPR spectra of the $CF_3CF_2C(O)^\bullet$ radical were found to be temperature dependent due to restricted rotation of both C−C bonds, and therefore, hfs interaction from only one γ-fluorine nucleus is observed (Table 3).

Vinyl acyl radicals have large hfs constants of ca. 20 G derived from the β-hydrogens.[37,40] On the basis of INDO calculations, it was suggested that these radicals adopt an *s-trans* conformation, i.e., the conformation in which the hydrogen is eclipsed by the carbonyl group and is antiperiplanar to the SOMO, and so their conformation is determined from that of the parent aldehydes. However, both *s-trans* and *s-cis* rotamers of (*E*)-^{t}BuCH=CHC(O)$^\bullet$ radicals have been observed upon photolysis of bis[(*E*)-4,4-dimethylpent-2-enoyl]peroxide.[41]

A series of three-membered ring-substituted acyl radicals have also been reported.[39] The prototype cyclopropylacyl radical exists at 172 K in both *s-cis* and *s-trans* conformations of approximately equal stability (see Table 3), in which the plane of the acyl group bisects the ring (as in the parent aldehyde). Furthermore, the EPR spectra display alternating line-width effects which are temperature dependent. Computer simulation of the spectra allows the barrier to interconversion of these conformers to be calculated as 4.2 kcal mol^{-1}, which is ca. 1 kcal mol^{-1} lower than in the parent aldehyde.[42] On the other hand, the β-methyl-substituted analogue was found to be in a single conformation. Similar to the case of EtCH=C(Me)C(O)$^\bullet$ radical (see Table 3), a trans arrangement of the singly occupied orbital with respect to the methyl group was suggested based on the large hfs of the methyl group. Oxiranylacyl radicals (Table 3) behave like cyclopropylacyl radicals, however with a rather lower barrier to rotation. The prototype cyclobutylacyl radical exists at 143 K in both the *s-cis* and *s-trans* conformations, with the *s-trans* rotamer having the larger β-hydrogen hfs (3.95 vs 1.13 G) present in a slightly larger amount.[41]

The EPR spectra of aryl- and heteroaryl-substituted acyl radicals contain some peculiar features. Initially, it was shown using deuterated compounds that the major hydrogen hfs constants are due to the meta hydrogens.[43] In fact, today there are many σ-type radicals in which the largest hfs are assigned to the positions corresponding to one end of a zigzag (or W-relationship) chain bond with the orbital of the unpaired electron at the other end (eq 8, structure **2**). The fact that two *m*-Hs are equivalent in the

(8)

2

benzoyl radical (Table 3) means that the C−C(O)$^\bullet$ bond rotates freely.

In the case of the *p*-methoxybenzoyl radical, the C−C(O)$^\bullet$ rotation is rapid on the EPR time scale above 223 K and the spectrum shows two equivalent *m*-Hs. However, at lower temperatures (143 K) there is a hfs from only one *m*-H, indicating a freeze of rotation.[44] Computer simulation of the observed alternating line-width effects allows the free energy of activation to be calculated as 4.2 kcal mol^{-1}. Some other para-substituted acyl radicals have been studied, and the free energies of activation ($\Delta G^\ddagger$) for rotation about the Ar−CO bond of *p*-X−$C_6H_4C(O)^\bullet$, where X = H, Me, MeO, and Me_2N, were found to be 2.8, 3.3, 4.2, and 5.7 kcal mol^{-1}, respectively. It is worth pointing out that these barriers for acyl radicals are about 5 kcal mol^{-1} lower than the $\Delta G^\ddagger$ values observed by NMR for the corresponding aldehydes. In the case of naphthyl-substituted acyl radicals, the 1-naphthoyl radical shows two rotamers, with a conformational ratio apparently different from that of the parent aldehyde, whereas the 2-naphthoyl radical behaves like the benzoyl radical (Table 3).[45] On the other hand, the spectra of a number of furoyl, thienoyl, and pyrroyl radicals whose parent aldehydes have relatively high rotational barriers decay faster than they interconvert, and so their conformational ratio is mainly determined by that of the parent aldehydes.[46] The larger hfs in these heteroaromatic-substituted acyl radicals is due to the hydrogen which adopts a W-relationship with respect to the SOMO.

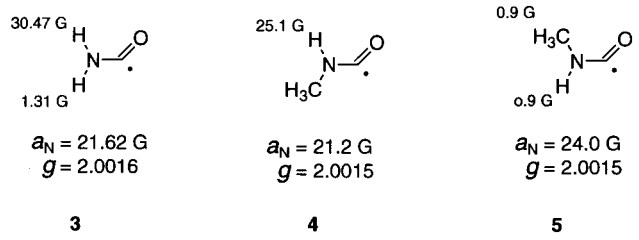
A few studies dealing with carbamoyl[47−50] and alkoxycarbonyl radicals[33,48,51] have also been carried out in solution (section XI). The EPR spectrum of carbamoyl radical **3** contains hfs constants from two different Hs, indicating a frozen conformation.[47,48] This is in agreement with the fact that the barriers to internal rotation in amides are very high. In fact, *N*-alkylformamides exist in a mixture of trans and cis conformations, and the reaction with photogenerated *tert*-butoxyl radicals gives an isomeric mixture

Table 4. Calculated Total Atomic Electron Densities ρ in the SOMO for XC(O)• Radicals[a,b]

X	ρ_C	ρ_O	ρ_X
H	0.53	0.36	0.11
CH_3	0.53	0.29	0.18
NH_2	0.56	0.34	0.10
$OC(CH_3)_3$	0.52	0.28	0.20
F	0.54	0.36	0.10

[a] Taken from ref 35. [b] UHF/6-311G** level of theory.

of carbamoyl radicals **4** and **5** in approximately the same ratio.[49a] The hydrogen located trans to the



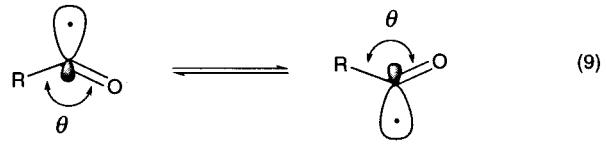
3 **4** **5**

orbital containing the unpaired electron has the larger hfs.

Addition of RO• radicals to phosphorus(III) isocyanates, followed by isomerization, allows for the formation of $(RO)_3P{=}NC(O)$• radicals and their characterization by EPR spectroscopy.[50] Moreover, the EPR spectra of a variety of alkoxycarbonyl radicals, generated by reaction of alkoxyl radicals with the corresponding alkyl formates, have been recorded. For example, the parameters for MeOC(O)• radicals are $g = 2.0013$, $a_H = 1.23$ G (3 H).[48]

It is also interesting to note that in a few cases the $a(^{17}O)$ constant has been measured by using ^{17}O-labeled compounds. Values of −15.1, 16.1, and 16.5 G were reported for $HC(^{17}O)$•, $PhH_2C(^{17}O)$•, and $PhC(^{17}O)$•, respectively,[30,52] and suggest a substantial delocalization of the unpaired electron on the carbonyl moiety. The local spin electron densities of the SOMO on carbon (ρ_C), oxygen (ρ_O), and X-substituents (ρ_X) have been calculated by Guerra for a variety of substituted acyl and related radicals and are given in Table 4.[35]

Acyl and related carbonyl radicals are also expected to show an inversion barrier, as illustrated in eq 9, although no experimental data are available. Al-



(9)

though the θ angle is essentially constant (see Table 2) and the total spin density changes only slightly (see Table 4) along the series X = H, CH_3, NH_2, OH, F, the computed inversion barriers increase substantially with increased electronegativity and parallel the changes in ^{13}C hfs, i.e., the s character of the SOMO.[35] Thus, calculated values are ca. 30 and 80 kcal mol^{-1} for CH_3 and F substituents, respectively.

The EPR spectra of a variety of acyl radicals adducts to spin traps such as $PhCH{=}N(O)Bu^t$ and $Me_3CN{=}O$ were also reported.[53a,b] In the nitrone spin adducts, the β-H hfs range from 2.71 to 5.93 G and are characteristic of the particular acyl fragment. Evidence that 4-nitrosobutanoyl and 5-nitrosopentanoyl radicals cyclize in the exo mode to give the corresponding nitroxide radicals has been obtained by EPR spectroscopy upon photolysis of alicyclic nitrites.[53c,d]

Table 5. C=O Stretch Frequencies of RC(O)• Radicals and Corresponding Aldehydes

R	$\nu_{C=O}$[RC(O)•][a]	$\nu_{C=O}$(RCHO)[a]	ref
CH_3	1864	1736	55
CH_3CH_2	1859	1742	55
$(CH_3)_2CH$	1853	1743	55
$(CH_3)_3C$	1848	1733	55
C_6H_5	1828	1713	55
4-$MeOC_6H_4$	1813	1703	55
4-BrC_4H_4	1832	1714	55
4-NCC_4H_4	1824	1716	55
mesityl	1805	1742	155

[a] In cm^{-1}.

C. Infrared and Electronic Absorption Spectra

In recent years, Ingold and co-workers have reported the IR spectra of a variety of acyl radicals in solution.[54,55,155] Prior to this work, IR data on related species were limited to the solid matrixes for $CH_3C(O)$• [56] and HOC(O)• [57] radicals.[58] Ingold and coworkers, in particular, reported the data collected in Table 5 referring to C=O stretch frequencies.[55] The acyl radicals were generated either by photolysis of appropriate ketones or by the reaction of photogenerated *tert*-butoxyl radicals with the corresponding aldehydes and detected by time-resolved infrared spectroscopy. Table 5 also contains the C=O stretch frequencies of the corresponding aldehydes for comparison.

The higher frequencies of the C=O stretch for acyl radicals compared to aldehydes (ca. 120 cm^{-1} for the same substituent) have been attributed to delocalization of the unpaired electron into the carbonyl moiety, which causes an increase in the carbonyl bond order. On the other hand, the monotonic reduction of the carbonyl stretch frequencies by 16 cm^{-1} along the alkyl-substituted series has been attributed to sterically induced changes in the ∠CCO angle. Furthermore, the lower C=O stretch frequencies of aryl-substituted acyl radicals with respect to alkyl-substituted ones have been attributed to the interaction of the C=O π-bond with aromatic π-electrons, which causes a small reduction in the carbonyl bond order. It is also worth mentioning that the matrix IR absorption spectra of $CH_3C(O)$• show C=O stretch and methyl deformation frequencies at 1844 and 607 cm^{-1}.[56]

Acetyl radicals [$CH_3C(O)$•], which have been characterized in the range of 195−280 nm in the gas phase, show a broad band in the region 200−240 nm with $\lambda_{max} = 216$ nm and $\epsilon_{max} \approx 10^4$ M^{-1} cm^{-1}.[59] The pivaloyl radical in hexane exhibits similar features, i.e., $\epsilon_{230\ nm} = 2000$ M^{-1} cm^{-1}, and does not absorb at $\lambda > 240$ nm.[60] The absorption of the phenylacetyl radical [$PhCH_2C(O)$•] is red-shifted ($\lambda_{max} \approx 275$ nm), and this effect has been attributed to conjugation

Table 6. Electronic Absortion Spectra of XC(O)• Radicals

X	phase or solvent	λ_{max} (nm)	ϵ_{max} (M^{-1} cm^{-1})	ref
CH_3	gas	216	10 000	59
	2-Me-THF−glass	540, 500, 340		61
PhCH=CH	2-Me-THF−glass	550, 500, 400		61
$PhCH_2$	hexane	275		60
Ph	3-Me-3-pentanol	368, 460	*a*	62, 63
$(RO)_3P=N$	isooctane	415	125	64

[a] $\epsilon_{368} \approx 200$ M^{-1} cm^{-1} has been estimated.

between the phenyl ring and the carbonyl group since AM1 calculations revealed a coplanarity of these groups in energy-minimized conformations with C=O in the cis and trans arrangements to the phenyl ring.[60] However, acyl radicals, being σ-type species, are expected to show a weak band in the visible region resulting from a $\pi \rightarrow$ n excitation. In fact, this weak band has been observed in the solid phase (see Table 6).[61]

The optical absorption spectrum of the benzoyl radical has been obtained by photolysis of PhC(O)R, where R is a variety of trisubstituted carbon atoms.[62,63] To avoid absorption overlap with the alkyl moiety, the spectra were considered at wavelengths higher than 320 nm. The continuous absorption from 320 to 650 nm shows two bands with maxima at 368 and ca. 460 nm (Table 6).

The absorption spectrum of the $(RO)_3P=N-C(O)^•$ radical obtained by the addition of a *t*-BuO• radical to $(EtO)_2P-N=C=O$ followed by an unimolecular rearrangement shows a weak broad band between 350 and 480 nm with $\lambda_{max} = 410$ nm (Table 6).[64]

III. Carbonylation–Decarbonylation Equilibria

The most well-known reactions involving acyl radicals are the addition of an alkyl radical to carbon monoxide (carbonylation) and its reversal, i.e., decarbonylation, as shown in eq 10. Kinetic information

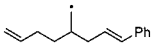
$$R^• + CO \underset{k_d}{\overset{k_{CO}}{\rightleftharpoons}} R\text{-}C(=O)^• \qquad (10)$$

on these reversible reactions is of fundamental importance in order to understand and plan free-radical processes based on acyl radicals. Although several kinetic studies regarding eq 10 have been published in the past few years, a lot remains to be done in order to fully understand these processes.

A. Carbonylation

Kinetic studies regarding the carbonylation of alkyl radicals are limited to a few cases which are shown in Table 7. All these reactions were studied in competition with other processes, and therefore, their kinetic data depend on the reported literature values for the reference reaction (see notes in Table 7). The gas-phase reactions of the methyl and ethyl radicals with CO were reported in the early 1970s.[9,10] The preexponential factors (Table 7) for the two cases are similar and fall within the expected range for bimolecular processes.[68] On the basis of the heats of formation of $CH_3C(O)^•$ and $CH_3CH_2C(O)^•$ radicals

Table 7. Kinetic Data for the Carbonylation of Alkyl Radicals

alkyl radicals	phase or solvent	log(A/M^{-1} s^{-1})	E_{CO},[a] kcal mol^{-1}	k_{CO}, $M^{-1}s^{-1}$	ref
$CH_3^•$	gas	8.2 [b]	6.0 [b]	$k_{25}=6.3 \times 10^3$	9
	H_2O		(3.0)	$k_{25}=2.0 \times 10^6$ [c]	65
$CH_3CH_2^•$	gas	8.2 [b]	4.8 [b]	$k_{80}=1.7 \times 10^5$	10
	C_6H_6		(4.4)	$k_{80}=6.3 \times 10^5$ [d]	66
	*c*-C_6H_{12}		(4.9)	$k_{50}=1.2 \times 10^5$ [e]	67

[a] The activation energies in parentheses are derived by assuming log(A/M^{-1} s^{-1}) = 8.5 and taking the reported experimental rate constant. [b] Depends on the Arrhenius parameters for the alkyl radicals recombination. [c] Depends on the rate constant for the reaction of the methyl radical with a cobalt complex. [d] Depends on the literature value for the 2-methyl-hex-5-enyl radical rearrangement. [e] Depends on the rate constant for the reaction of the cyclohexyl radical with CCl_4.

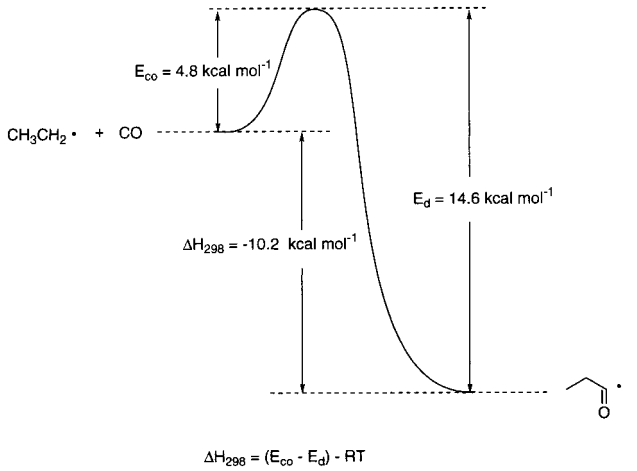


Figure 1.

reported in Table 1, both reactions are exothermic by 10−11 kcal mol^{-1}, which matches reasonably well with the difference in activation energies for the forward and reverse reactions of eq 10. For example, Figure 1 shows the activation energies for the forward and reverse reactions of the ethyl radical with CO which are related to the enthalpy change. It can be seen that the value $\Delta H_{298} = -10.2$ kcal mol^{-1} is in agreement with $\Delta E - RT = -10.4$ kcal mol^{-1} at 298 K.

The rate constant for the addition of a primary alkyl radical to CO with benzene as the solvent has been recently found to be 6.3×10^5 M^{-1} s^{-1} at 80 °C, which is in agreement with the gas-phase value for the ethyl radical at the same temperature (see Table 7).[66] Furthermore, the rate constant for the reaction of cyclohexyl radical with CO in cyclohexane has been found to be 1.2×10^5 M^{-1} s^{-1} at 50 °C.[67] Assuming a "normal" preexponential factor, i.e., log(*A*/M^{-1} s^{-1}) = 8.5,[68] the two experiments in nonpolar organic solvents give activation energies of 4.4 and 4.9 kcal mol^{-1}, respectively, in agreement with the gas-phase value of 4.8 kcal mol^{-1}.[10] Interestingly, Ryu and co-

workers did not find any solvent effect on replacing benzene by *tert*-butyl alcohol.[66]

The rate constant for the reaction of the methyl radical with CO in aqueous solution was found to be 2.0×10^6 M^{-1} s^{-1} at 25 °C.[65] This value is 2−3 orders of magnitude larger than the gas-phase rate constant (Table 7). This large increase on going from the gas phase to aqueous solution was related to the stabilization of the acetyl radical by dipolar interactions with the solvent.[65] Although this effect is operative, it is expected to be less than 1 order of magnitude for the reverse reaction (section III.B). Therefore, the huge change in the rate constant for methyl radical addition to CO is either a particular effect associated with the acetyl radical or presumably due to the errors arising from the gas-phase measurements. Comparison of $\Delta H_{298} = -10.8$ kcal mol^{-1} with $\Delta E - RT = -11.8$ kcal mol^{-1} at 298 K for the reaction of the methyl radical with CO indeed reveals a discrepancy of 1 kcal mol^{-1}.

B. Decarbonylation

Kinetic studies for this class of reactions are numerous, and the first estimated E_d of acetyl radical decarbonylation is dated 1939.[69,70] Since the first estimation, several Arrhenius parameters for the reverse process of eq 10 have been reported.

In 1987, Fischer and Paul collected and analyzed all the data available in the literature concerning the decarbonylation reaction.[71,72] The rate constants which depend strongly on the nature of substituent R, at room temperature, cover over 15 orders of magnitude. However, most of the activation parameters were obtained either in a relatively narrow temperature range or in competition with some reactions where the rate constants were assumed and, therefore, the data scatter considerably. For example, the reported preexponential factors for the endothermic decarbonylations scatter between 10^{10} and 4×10^{14} s^{-1}. It is also worth mentioning that the average value is found to be $\log(A/s^{-1}) = 13$, i.e., similar to the expected value of 13.2 for such unimolecular processes.[68] A plot of log k_d vs D[R−C(O)•] revealed a linear correlation, although several points deviated markedly from the straight line. Although some of the thermodynamic data used by Fischer and Paul have changed substantially, e.g., the latest D[Me−C(O)•] = 10.78 kcal mol^{-1} is 3.8 kcal mol^{-1} lower,[15] the general trends and considerations are still correct as we will see below.

Table 8 shows the collected kinetic data which we recommend for decarbonylation of a variety of acyl radicals. Arrhenius expressions for the acetyl and propanoyl radicals refer to the gas phase. Furthermore, the data for the $CH_3CH_2C(O)$• radical have been obtained by averaging the data of two independent measurements.[10,73]

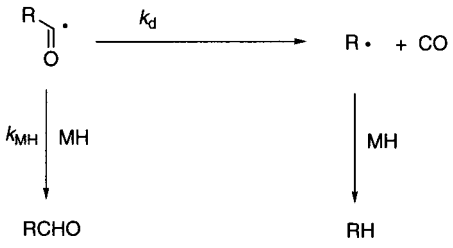
Recently, the kinetics of decarbonylation of primary, secondary, and tertiary alkyl-substituted acyl radicals in competition with hydrogen abstraction from Bu_3SnH or $(TMS)_3SiH$ have been measured (Scheme 1).[74,75] The relative preexponential factors are essentially independent of the nature of the acyl radical and the hydride; i.e., $\log(A_d/A_{MH}) = 4.8$.[75] On the other hand, the relative activation energies, i.e., $E_d - E_{MH}$, decrease by ca. 2 kcal mol^{-1} on going from primary to secondary and also on going from secondary to tertiary substituents at the carbonyl moiety for a particular hydride.[75] When going from Bu_3SnH to $(TMS)_3SiH$ for a particular acyl radical, the $E_d - E_{MH}$ also decreases by ca. 2 kcal mol^{-1}. Assuming that the rate of hydrogen abstraction for a particular reducing agent by the RC(O)• radical is independent of the nature of the alkyl substituent R, those results indicate that the entropy changes on the approach to the transition state are negligible and that the large variation in rates is caused by changes in the activation energies. A combination of the relative kinetic data with the Arrhenius parameters for the propanoyl radical decarbonylation allows the corresponding data for the decarbonylation of secondary and tertiary alkyl-substituted acyl radicals to be obtained (Table 8) as well as the activation param-

Table 8. Kinetic Data for the Decarbonylation of a Variety of Acyl Radicals

acyl radicals	phase or solvent	log(A/s^{-1})	E_d, kcal mol^{-1}	k_d at 296 K, s^{-1}	ref
$H_3C\dot{C}{=}O$	gas	13.2	17.2	4.0	9
$CH_3CH_2\dot{C}{=}O$	gas	13.1[a]	14.6[a]	2.1×10^2	10,73
$CH_3CH_2CH_2CH(CH_3CH_2)\dot{C}{=}O$	toluene	13.0[b]	12.0[b]	1.4×10^4	75
	hexane	13.1[b]	10.0[b]	5.2×10^5	75
$(CH_3)_3C\dot{C}{=}O$	hexane			8.3×10^5	60
	hexane			6.7×10^5	55
$PhCH_2\dot{C}{=}O$	isooctane	12.0	6.9	8.1×10^6	79
$PhMeCH\dot{C}{=}O$	isooctane	12.2[c]	6.2[c]	4.2×10^7	80
$PhMe_2C\dot{C}{=}O$	isooctane	11.2[c]	4.1[c]	1.5×10^8	80

[a] The Arrhenius expression is derived by averaging the following data for the decarbonylation: $\log(k_d/s^{-1}) = 12.8 - 14.4/\theta$ and $\log(k_d/s^{-1}) = 13.3 - 14.7/\theta$, where $\theta = 2.3RT$ kcal mol^{-1}. [b] Depends on the Arrhenius parameters for the decarbonylation of the propanoyl radical from this table and on the assumption that the hydrogen donation from Bu_3SnH or $(TMS)_3SiH$ toward RC(O)• is essentially independent of the nature of the alkyl substituent R. [c] Arrhenius expression obtained in a small range of temperatures (less than 30°).

Scheme 1



MH = Bu_3SnH:
$\log (k_{MH}/M^{-1}s^{-1}) = 8.2 - 3.5/\theta$; where $\theta = 2.3RT$ kcal mol^{-1}
k_{MH}(23 °C) = 4.1×10^5 $M^{-1}s^{-1}$

MH = $(TMS)_3SiH$:
$\log (k_{MH}/M^{-1}s^{-1}) = 8.2 - 5.4/\theta$; where $\theta = 2.3RT$ kcal mol^{-1}
k_{MH}(23 °C) = 1.6×10^4 $M^{-1}s^{-1}$

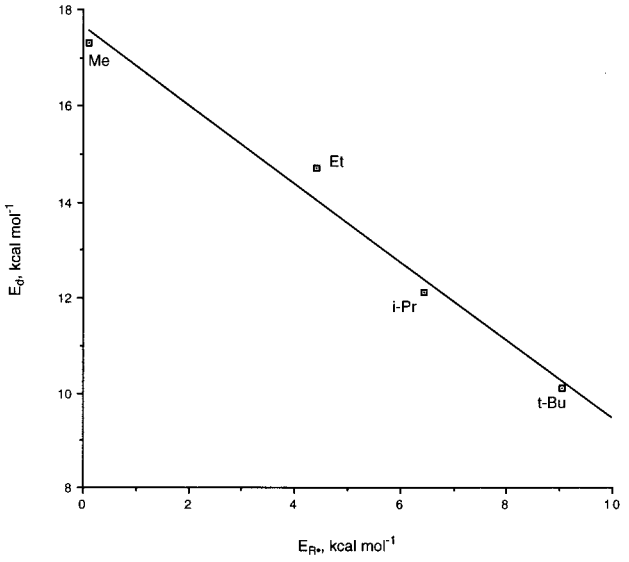


Figure 2.

eters for the reaction of acyl radicals with Bu_3SnH and $(TMS)_3SiH$ (Scheme 1).[75] In this respect, the absolute rate constant for the reaction of the propanoyl radical with Bu_3SnD was found to be 3.0×10^5 M^{-1} s^{-1} at 23 °C.[55] On the basis of the kinetic data in Scheme 1, we calculate a deuterium kinetic isotope effect of 1.4.

It is worth mentioning that the relative rates for the decarbonylation and the chlorine abstraction from tetrachloromethane have been determined by competitive methods.[76,77] By combining these data with the recent values of the absolute rate constants for chlorine atom abstraction from CCl_4 (Table 10, vide infra), more data for decarbonylation rate constants can be obtained.

Recent laser flash photolysis studies either by UV[60] or IR[56] detection allowed the rate constant of the decarbonylation of pivaloyl radical to be measured directly at room temperature (Table 8). It is worth pointing out that these values are in good agreement with the rate constant estimated from the Arrhenius expression of tertiary alkyl-substituted acyl radicals (Table 8).

The activation energies (E_d) of these endothermic decarbonylations (cf. Figure 1) can be correlated to the degree of stabilization of the resulting alkyl radicals ($E_{R\bullet}$)[13] by an Evans−Polanyi relationship similar to the one previously reported.[71,72] Figure 2 shows such a simple plot which can be described by the relation $E_d = 17.5 - 0.82\ E_{R\bullet}$. The slope is close to the value 0.75 proposed for endothermic reactions,[78] and the intercept is close to the stabilization energy of the benzyl radical, which is found to be slightly exothermic.

Table 8 also contains some representative decarbonylation data for phenylacetyl and analogous radicals.[79,80] These unimolecular processes which are found to be slightly exothermic have lower preexponential factors, which has been explained in terms of partial freezing of one internal rotation in the transition state.

The effect of solvent on decarbonylation has also been studied in some detail. Initially, Ingold and co-workers noticed that the decarbonylation of the $PhCH_2C(O)^\bullet$ radical is slightly influenced by the polarity of the solvent, i.e., at 296 K the rate constant was 8.1×10^6, $\sim 7 \times 10^6$, and 4.1×10^6 s^{-1} in isooctane, tetrahydrofuran, and methanol, respectively.[79] Using the same technique, others found a value of 5.0×10^6 and 6.2×10^6 s^{-1} in isooctane[80] and 1:1 acetonitrile−water,[81] respectively, for the same reaction and temperature. However, these rate constants were calculated from the corresponding Arrhenius expressions, and some of them may be associated with large errors since a small temperature range was employed. Later, Scaiano and co-workers found a rate constant of $\sim 3.5 \times 10^6$ s^{-1} in 0.1 M SDS micellar solution.[82] More recently, Fischer and co-workers studied the solvent effect on the decarbonylation of acyl radicals in more detail.[60] In fact, the phenylacetyl radical dissociates with k_d of 6.0, 3.1, and 1.7×10^6 s^{-1} in cyclohexane, propan-2-ol, and acetonitrile, respectively. Similarly, the pivaloyl radical decarbonylates with k_d of 8.3, 4.2, and 1.4×10^5 s^{-1} in hexane, methanol, and acetonitrile, respectively. On the other hand, viscosity effects in the decarbonylation reaction were found to be marginal. Since acyl radicals have an appreciable dipolar moment, they should be stabilized with increasing solvent polarity, and therefore, the rate constants are decreased by increasing the activation energy.

Other endothermic decarbonylations have been studied, and Arrhenius expressions are available. The dissociation of the $PhC(O)^\bullet$ radical is unimportant at ordinary temperatures. In fact, the Arrhenius expression $\log(k_d/s^{-1}) = 14.6 - 29.4/\theta$, where $\theta = 2.3RT$ kcal mol^{-1}, obtained in the gas phase, indicates a rate constant of 7.8×10^{-8} s^{-1} at 296 K.[12] Furthermore, the gas-phase data for the decarbonylation of the $CF_3C(O)^\bullet$ radical were found by Kerr and Wright to be $\log(k_d/s^{-1}) = 13.3 - 19.8/\theta$, which gives a rate constant of 4.7×10^{-2} s^{-1} at 296 K.[83] However, the last temperature-dependent function was criticized on the basis of ab initio calculations and gas-phase kinetics, suggesting an activation energy as low as 12.4 kcal mol^{-1}.[84,85] The rates of decarbonylation of $HOCH_2C(O)^\bullet$ and $HOC(CH_3)_2C(O)^\bullet$ radicals as a function of temperature were studied in acetonitrile by EPR spectroscopy and found to be $\log(k_d/s^{-1}) = 11.0 - 8.8/\theta$ and $\log(k_d/s^{-1}) = 11.4 - 7.4/\theta$, respectively.[72,86] From these Arrhenius expressions, k_d values of 3.2×10^4 and 4.3×10^5 s^{-1} at 296 K have been calculated, respectively. Therefore, a β-hydroxyl substituent on acyl radicals considerably increases the rate of decarbonylation by further stabilizing the resulting alkyl radical. It is worth mentioning that in the above-reported Evans−Polanyi relationship (Figure 2) if we take into consideration the data of $CF_3C(O)^\bullet$ ($E_d = 19.80$, $E_{R\bullet} = -1.89$), $HOCH_2C(O)^\bullet$ ($E_d = 8.84$, $E_{R\bullet} = 10.87$), and $HOC(CH_3)_2C(O)^\bullet$ ($E_d = 7.41$, $E_{R\bullet} = 13.74$), a good straight line is obtained which is described by the relationship $E_d = 17.75 - 0.80\ E_{R\bullet}$, i.e., very similar to the one reported in Figure 2. However, the relatively narrow temperature range used in the EPR experiments, the reevaluation of E_d in the $CF_3C(O)^\bullet$ radical, and, presumably, the solvent effect suggests that this analysis should

be regarded with caution.

IV. Acyl Radical Precursors: Methods for the Generation of Acyl Radicals

Conceptually three different methods may be envisaged for the generation of acyl radicals. The first and most obvious of these is the homolytic rupture of a RC(O)−X bond. The second involves carbonylation of a carbon-centered radical (R•) with CO, and the third fragmentation of a C−C bond as, for example, in loss of CO_2 from an α-ketocarboxyl radical or the cleavage of a CO−C bond in the Norrish-type I photocleavage. Of the three methods, the first has been by far the most widely applied but, in recent years, the second has gained considerable prominence. The third is of importance in generating acyl radicals for spectroscopic and mechanistic studies.

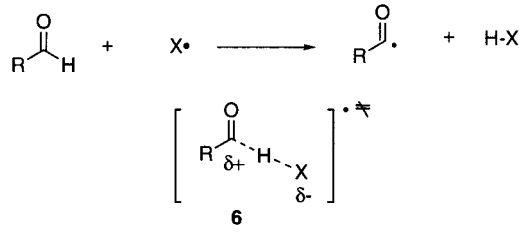
A. Generation of Acyl Radicals from RCO–X

In this method, the group X may be any group susceptible to homolytic rupture of the C−X bond, namely hydrogen, halogen, chalcogen, and various metals. Thus, a considerable range of acyl radical precursors are available which exhibit homolytic chemistry under a wide range of conditions, meaning that one or the other will be suitable for most synthetic applications.

1. Acyl Radicals from Aldehydes (RCO–H)

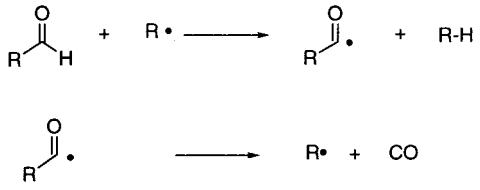
The homolytic scission of the aldehyde C(O)−H bond leads to the generation of acyl radicals (Scheme 2). When the abstracting radical, X•, is electrophilic,

Scheme 2



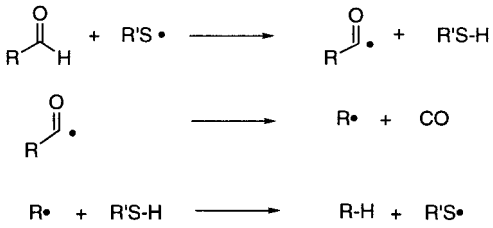
this is readily achieved. However, when the abstracting radical is a nucleophilic alkyl radical, this step is relatively slow, suggestive of a polarized transition state (**6**) for this reaction. This effect is readily seen in the simple peroxide-induced decarbonylation of aldehydes. Thus, thermal, peroxide-initiated decarbonylation of aldehydes (Scheme 3) is a relatively

Scheme 3



inefficient process owing primarily to the poor chain transfer step of aldehydic hydrogen abstraction by the alkyl radical resulting from decarbonylation. However, as initially demonstrated by Harris and Waters[87,88] and investigated in detail later by others,[89] the reaction is catalyzed by thiols. Here, an inefficient, two propagation step sequence (Scheme 3) is replaced by a much more efficient three-step one (Scheme 4), with the electrophilic thiyl radical serv-

Scheme 4

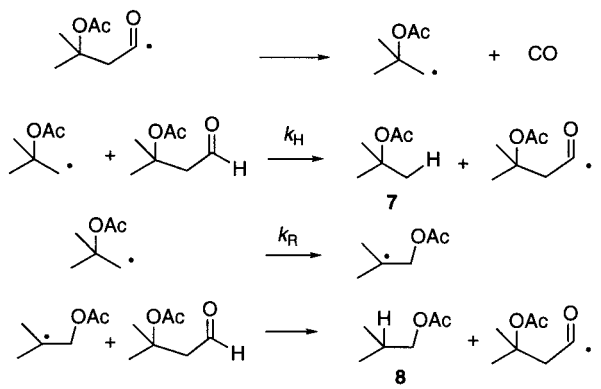


ing to abstract the aldehydic hydrogen atom (N. B. this step is itself reversible, e.g., see Schemes 18 and 28).

This problem of inefficient chain transfer bedevilled much of the early work in the area on inter- and intramolecular addition of aldehyde-derived acyl radicals wherein the abstraction of the aldehydic hydrogen atom by an alkyl radical is a necessary propagation step. This had several consequences but most notably the need for high concentrations of aldehyde. Indeed, in intermolecular processes the aldehyde was usually employed as solvent, which clearly limits the scope. In cyclization reactions, the slow chain transfer meant that what are now recognized as thermodynamic products predominated. For example Julia found only cyclohexanone on the benzoyl peroxide initiated cyclization of 5-hexenal in cyclohexane at 81 °C (cf. section VII.A.1).[90,91]

A measure of the rate of abstraction of the aldehydic hydrogen by alkyl radicals can be gleaned from the pioneering work of Tanner on the β-(acyloxy)alkyl radical rearrangement. In this work, the benzoyl peroxide initiated decarbonylation of 3-acetoxy-3-methylbutyraldehyde was studied in benzene at 75 °C. Considerable amounts of *iso*-butyl acetate (**8**) were observed in addition to the anticipated *tert*-butyl acetate (**7**). The rearranged product arose from an acyloxy migration successfully competing with the abstraction of hydrogen from the aldehyde by the decarbonylated radical (Scheme 5).[92] The rate con-

Scheme 5

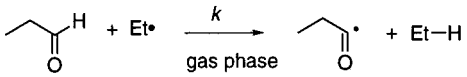


stant (k_R) for this particular rearrangment was later found, by Ingold and co-workers, to be 4.5×10^2 s^{-1}

at 75 °C in similar solvents,[93] from which, using the product ratios and concentrations in Tanner's paper, it can be deduced that the rate constant (k_H) for the abstraction of the aldehydic hydrogen by a primary alkyl radical is approximately 5×10^3 M^{-1} s^{-1} at 75 °C.

Arrhenius parameters for the abstraction of aldehydic hydrogen by alkyl radicals do not appear to have been determined in solution. However, Trotman-Dickenson has determined the relationship for several alkyl radicals and aldehydes in the gas phase, one of which is presented below, together with the calculated rate constant at 25 °C (Scheme 6).[94] It is

Scheme 6

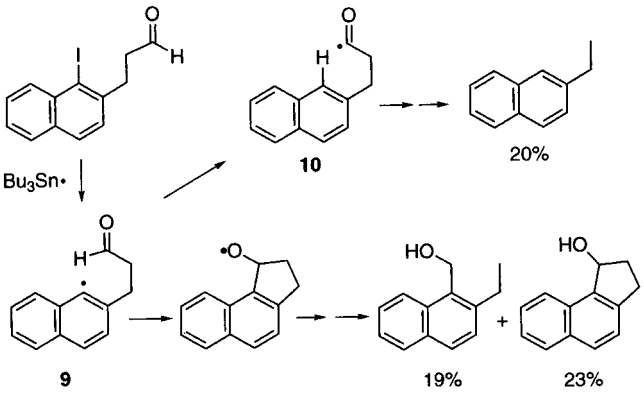


log (k) = 8.1 - 5.9/θ; where θ = 2.3 RT kcal mol^{-1}; k = 5.9 × 10^3 M^{-1} s^{-1} at 25 °C

stressed that these are gas-phase numbers and that they should only be extrapolated to the solution phase with caution. Rate constants for the intramolecular abstraction of aldehydic hydrogen by alkyl radicals, through six-membered cyclic transition states, vary between 1.5×10^5 and 1.4×10^7 s^{-1} for the simple 4-formylbutyl radical and its 3-*tert*-butyl analogue, respectively, both at 80 °C in benzene.[95]

Aryl radicals, within the limits imposed by polar effects, are typically more reactive than simple alkyl radicals in hydrogen abstraction reactions, and it is to be expected that such radicals will abstract aldehydic hydrogens with reasonable efficiency. One example of such a process is given in Scheme 7. Here,

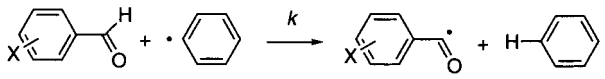
Scheme 7



the authors generated an aryl radical **9** from an aryl iodide with a stannane. Intramolecular hydrogen abstraction, through a six-membered cyclic transition state, to give an acyl radical **10** competed effectively with closure onto the carbonyl group.[96] A comparable but less effective abstraction was also seen with the one-carbon homolog, now via a seven-membered cyclic transition state.

Kinetic data for the intermolecular abstraction of aldehydic hydrogen by phenyl radicals are scarce. The relative rates for the abstraction of hydrogen and chlorine from substituted benzaldehydes and tetrachloromethane, respectively, have been determined by competition methods.[97] Combining these with recent data on the absolute rate constants for chlorine-atom abstraction from tetrachloromethane, as determined by Scaiano and co-workers,[98] we arrive at the following rate constants for hydrogen abstraction (Scheme 8) which, it will be noted, are 3−4 orders of

Scheme 8



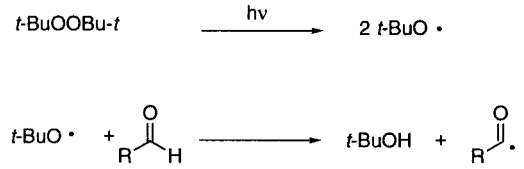
X = H: k = 1.0 x 10^7 M^{-1}s^{-1} at 30 °C
X = *m*-NO$_2$: k = 1.6 x 10^7 M^{-1}s^{-1} at 30 °C
X = *p*-NO$_2$: k = 2.0 x 10^7 M^{-1}s^{-1} at 30 °C

magnitude higher than the corresponding abstractions by alkyl radicals.

With more electrophilic radicals, as in the catalytic cycle of Waters (Scheme 4), hydrogen-atom abstraction proceeds smoothly and fewer problems are encountered. Thus, bromine atoms, and/or succinimidyl radicals, abstract aldehydic hydrogen atoms efficiently, such that the reaction of aldehydes with *N*-bromosuccinimide is an efficient preparation of acyl bromides (section VI.A.2).[99]

Hydrogen abstraction from aldehydes by oxygen-centered radicals is the cleanest method of generation of acyl radicals for EPR spectroscopic studies. For example, the reactions of photogenerated *tert*-butoxyl radicals with a variety of aldehydes (Scheme 9) have

Scheme 9



been used extensively in EPR spectroscopy. Furthermore, hydrogen abstraction by oxygen-centered radicals is a fundamental step in any auto-oxidation sequence (section IX.A.1).

Rate constants for reactions of a variety of oxygen-centered radicals with aldehydes in the liquid phase are collected in Table 9. The absolute rate constants for hydrogen abstraction by *t*-BuO• were measured directly by means of laser flash photolytic techniques.[46] The k values for propionaldehyde, benzaldehyde, 2-furancarbaldehyde, and 2-thiophenecarbaldehyde are similar, as expected based on the similarity of the bond strengths of some of the parent aldehydes and on the localization of the unpaired electron in the forming radicals. However, the rates are drastically affected by replacing the alkyl or aryl substituent with an amino or an alkoxy group as in formamide and formate, respectively. The Arrhenius expression for the hydrogen abstraction from PhCHO by *tert*-butoxyl radicals was found to be $\log(k/M^{-1}\ s^{-1}) = 8.8 - 1.3/\theta$, where $\theta = 2.3RT$ kcal mol^{-1}.[46] Relative rate constants for H-atom abstraction from substituted benzaldehydes (*p*-Me, *m*-Me, *p*-Cl, *m*-Cl, *p*-Br, *m*-F, *m*-CF_3, and *m*-CN) have also been reported, and a ρ^+ value of −0.32 was rationalized in terms of a polar contribution to the transition state.[101,102]

Some rate constants for the reaction of HOO•, RC(O)OO•, and ROO• radicals with a variety of

Table 9. Absolute Rate Constants for the Reaction of Oxygen-Centered Radicals with RCHO

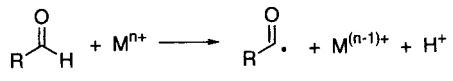
RCHO	radical	solvent	T, °C	k, M^{-1} s^{-1}	ref
CH_3CHO	*t*-BuO•	C_6H_6	0	7.0×10^7 [a]	46, 100
	t-BuOO•	heptane	0	4.8[c]	106
	$CH_3C(O)OO$•	C_6H_5Cl	0	2.7×10^3	105
CH_3CH_2CHO	*t*-BuO•	(*t*-BuO)$_2$/C_6H_6	24	8.9×10^7	46
n-$C_6H_{13}CHO$	HOO•	C_6H_5Cl	0	50	105
	n-$C_6H_{13}C(O)OO$•	C_6H_5Cl	0	3.1×10^3	105
c-$C_6H_{11}CHO$	HOO•	C_6H_5Cl	0	1.9×10^2	105
	c-$C_6H_{11}C(O)OO$•	C_6H_5Cl	0	1.1×10^3	105
t-BuCHO	HOO•	C_6H_5Cl	0	2.3×10^2	105
	t-BuC(O)OO•	C_6H_5Cl	0	2.6×10^3	105
C_6H_5CHO	*t*-BuO•	(*t*-BuO)$_2$/C_6H_6	24	6.8×10^7	46
	HOO•	C_6H_5Cl	0	17	105
	t-BuOO•	C_6H_5Cl	30	0.85	104
	ROO• [b]	heptane	30	5.4[c]	106
	$C_6H_5C(O)OO$•	C_6H_5Cl	40	20	103
		C_6H_5Cl	0	1.2×10^4	105
		C_6H_5Cl	30	3.3×10^4	104
		C_6H_5Cl	40	1.5×10^4	103
C_6D_5CDO	*t*-BuO•	(*t*-BuO)$_2$/C_6H_6	24	3.7×10^7	46
2-furaldehyde	*t*-BuO•	(*t*-BuO)$_2$/C_6H_6	24	3.9×10^7	46
2-thienyl aldehyde	*t*-BuO•	(*t*-BuO)$_2$/C_6H_6	24	7.5×10^7	46
Me_2NCHO	*t*-BuO•	(*t*-BuO)$_2$/C_6H_6	24	1.0×10^7	46
EtOCHO	*t*-BuO•	(*t*-BuO)$_2$/C_6H_6	24	5.1×10^5	46

[a] Calculated using the relative kinetic data with PhCHO (ref 100) and the absolute rate constant of *t*-BuO• with PhCHO at 0 °C (see text). [b] R = 1,2,3,4-tetranaphthalen-1-yl. [c] Calculated from the Arrhenius expression (see text).

aldehydes have been obtained from studies on the oxidation of aldehydes.[103−105] The reactivities of the aldehydes toward a HOO• radical decrease by 1 order of magnitude along the series *t*-BuCHO > *c*-C_6H_{11}-CHO > *n*-$C_6H_{13}CHO$ > C_6H_5CHO, and this trend has been attributed to the inductive effect of the R group attached to the CHO moiety.[105] The rate constants for the reaction of aldehydes with acylperoxyl radicals are 3−4 orders of magnitude higher than for the analogous reactions of alkylperoxyl radicals.[103−105] Table 9 shows this behavior for benzaldehyde. The differences in reactivity between the various acylperoxyl radicals are small and have been rationalized in terms of polar effects.[105] Arrhenius parameters were recently determined for the reaction of aldehydes with the *tert*-butylperoxy radical in heptane solution using the kinetic EPR method.[106] For example, in the respective cases of benzaldehyde and acetaldehyde, the following Arrhenius expressions were determined: $\log(k/M^{-1}\ s^{-1}) = 5.2 - 6.2/\theta$ and $4.2 - 4.4/\theta$ where $\theta = 2.3RT$ kcal mol^{-1}. A primary kinetic isotope effect of $k_H/k_D = 7.8 \pm 1.8$ was additionally determined for hydrogen abstraction from benzaldehyde by *t*-BuOO•.[106]

There is extensive literature on the oxidation of aldehydes by transition-metal ions leading to the formation of acyl radicals (Scheme 10) which has

Scheme 10



been reviewed.[107,108] As discussed in section IX.A.1, most often the reaction is conducted with catalytic metal salts and under an atmosphere of oxygen, when the acyl radical is trapped to give, initially, an acylperoxy radical. Such chemistry forms the basis for the industrial synthesis of acetic acid, acetic anhydride, and peroxyacetic acid from acetaldehyde.[107]

2. Acyl Radicals from Acyl Chlorides (RCO–Cl)

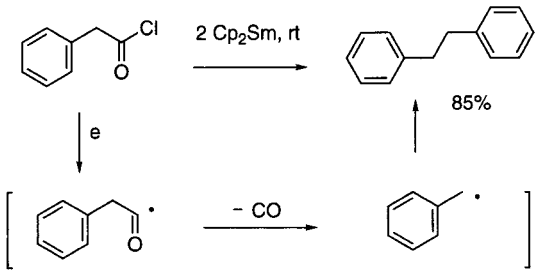
The stannane-mediated reduction of acyl chlorides to aldehydes via acyl radicals is plagued by the formation of byproducts, typically esters, which may even become the major products depending on the conditions. Thus, early workers studying the reduction of benzoyl chloride noted the formation of benzyl benzoate and, under certain conditions, its exclusive nature.[109−114] There was much discussion about the mechanism of ester formation[109−114] until Ingold and co-workers convincingly demonstrated it to involve over-reduction of the aldehyde by a polar mechanism and reaction of a stannyl alkoxide with the acyl chloride.[190,115] In light of these complications, as is evident from sections VII and VIII, studies on the use of acyl radicals generated from acyl chlorides in synthesis are quite limited.

Jackson reported on the decarbonylation of acyl chlorides using triisopropylsilane and peroxide initiation but found it necessary to use temperatures around 170 °C in order to obtain good yields.[187] Oka and co-workers reported the reductive decarbonylation of acyl chlorides with trichlorosilane on initiation with γ-irradiation at room temperature, but the major product was that of over-reduction to the trichlorosilyl alkoxide.[188] On the other hand, $(TMS)_3SiH$ does not react spontaneously with acyl chlorides and smoothly reduces these substrates in the presence of radical initiators.[189] The rate constant for reaction of the $(TMS)_3Si$• radical with acyl chlorides is estimated to be 7×10^5 M^{-1} s^{-1} at 80 °C.[75]

Kagan and co-workers studied the reaction of acyl chlorides with samarium diiodide and dicyclopentadienylsamarium.[116,117] When phenylacetyl chloride was exposed to dicyclopentadienylsamarium at room

temperature, an 85% yield of dibenzyl was obtained (Scheme 11), which strongly supports the notion that acyl radicals are intermediates in this chemistry (see section IX.B.1). A similar reaction is obtained on dropping samarium diiodide into this acid chloride.

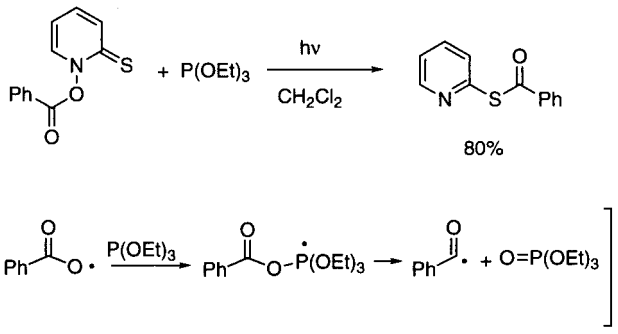
Scheme 11



3. Acyl Radicals from Carboxylic Acids via Carboxyl Radicals (RCO–OH)

Barton and co-workers have shown that benzoyloxy radicals generated from an *O*-benzoyl thiohydroxamate may be trapped with phosphines and phosphites to give an acyloxyphosphoranyl radical which then undergoes fragmentation to generate the benzoyl radical (Scheme 12).[118] In this reaction system the

Scheme 12



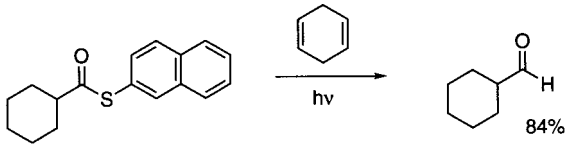
benzoyl radical was trapped by the *O*-benzoyl thiohydroxamate in a chain sequence to give *S*-(2-pyridyl) thiobenzoate as the ultimate product.

Ohmori and co-workers reported that reduction of α-amino acids to α-amino aldehydes took place in high yield without loss of the chirality by anodic oxidation in the presence of triphenylphosphine at −30 °C.[119] However, since decarbonylation of α-aminoacyl radicals is a facile process (section V.A), it is uncertain whether the reaction involves cathodic reduction of *free* acyl radicals to acyl anions.

4. Acyl Radicals from Thioesters and Related Species (RCO–SR′)

Following preliminary reports on the successful photochemical and thermal homolytic cleavage of the acyl−SPh bond in *S*-phenyl thiobenzoate,[120−122] Penn and Liu introduced the *S*-(2-naphthyl) thioesters as convenient photochemical sources of acyl radicals.[123] White light photolysis of these readily prepared substances, in the presence of cyclohexa-1,4-diene as a hydrogen donor, resulted in excellent yields of the corresponding aldehydes for a range of aromatic, primary, secondary, and tertiary acid derivatives (Scheme 13). With α,β-unsaturated *S*-(2-naphthyl)

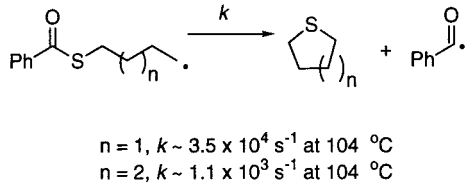
Scheme 13



thio esters, reduction of the alkene was a serious competing process. Unfortunately, the quantum yields of these processes were low, resulting in long reaction times ($\phi = 0.01$, 43 h irradiation at 300 nm for 96% conversion in the example shown).

As noted by both the Boger[124] and Crich[125] groups, simple *S*-phenyl thioesters are unreactive toward $Bu_3Sn^{\bullet}$ radicals, which essentially precludes their use as acyl radical precursors in stannane-mediated chain sequences. This lack of reactivity may be nicely circumvented by the addition of an extra propagation step, rendering the homolytic displacement at sulfur intramolecular. Beckwith and Duggan determined the rate constant for cyclization of an alkyl radical onto a thioester with expulsion of an acyl radical, and formation of a tetrahydrothiophene, to be 3.5×10^4 s^{-1} at 104 °C (Scheme 14),[126] which is at the lower

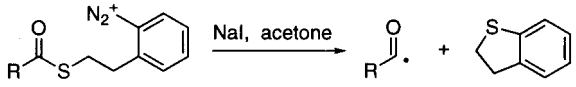
Scheme 14



limit for preparatively useful radical rearrangements. Tada and Nakagiri have described a closely related process in which an alkyl radical, generated from alkylcobaloxime, cyclizes onto a thioester with expulsion of a pivaloyl radical and formation of a tetrahydrothiophene in good yield.[127]

Crich and Yao adapted this chemistry to the use of the more reactive phenyl radicals and have made good use of this chemistry in the generation of acyl radicals for use in cyclizations (section VII).[198] This chemistry, in conjunction with decarbonylation, has subsequently been applied by the same authors to the generation of nucleotide C4′ radicals, which is noted in section V.A.[201] Subsequently, Crich and Hao adapted this chemistry to nonreducing conditions. This modification makes use of aryl radical generation from diazonium salts using suitable electron donors such as iodide (Scheme 15).[128] Applications

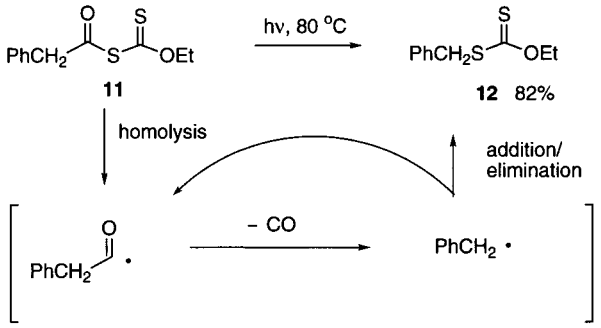
Scheme 15



are shown later in Schemes 89, 108, and 118.

An alternative solution to the lack of reactivity of simple thioesters toward homolytic cleavage has been devised by Zard and co-workers using the *S*-acyl xanthates. This chemistry had its genesis in Barton's early observation that white light photolysis of *S*-phenylacetyl *O*-ethyl dithiocarbonate, **11**, resulted in

Scheme 16



the formation of *S*-benzyl *O*-ethyl dithiocarbonate, **12**, through a process initially thought to involve homolytic cleavage of the phenylacetyl−*S* bond and, following decarbonylation of the phenylacetyl radical, recombination to the product (Scheme 16).[129] However, the *S*-acyl derivatives of primary aliphatic carboxylic acids and especially those of benzoic acids were very reluctant to undergo this chemistry, a fact that was attributed to the reluctance of the intermediate radicals to undergo decarbonylation.

Subsequently, Zard and co-workers recognized that most of the above results could be readily interpreted in the context of a chain reaction and that the apparent lack of reactivity of benzoyl derivatives was due to their degenerate attack on the thiocarbonyl group of a further molecule of substrate.[130,131] This led them to propose that inclusion of a suitable alkene in the reaction mixture as a radical trap would lead to a useful carbon−carbon bond forming process. This indeed proved to be the case, and such examples are shown in section VIII.A.

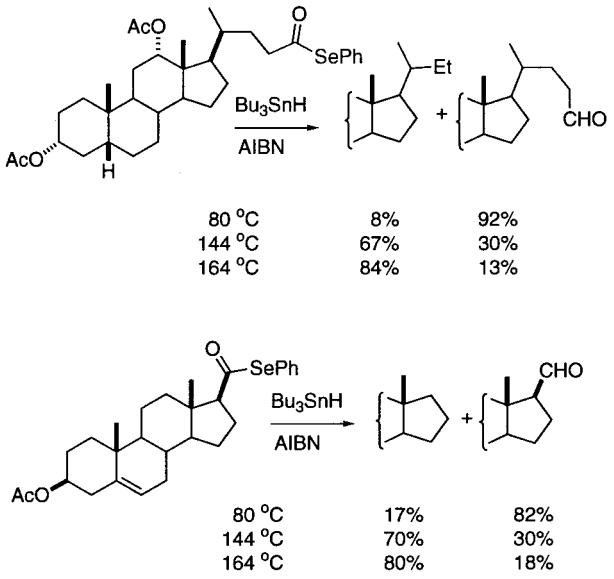
Finally, it is noted that Webster and Bond have recently reported that electrochemical reduction of thioesters can be used for the generation of acyl radicals.[132]

5. Acyl Radicals from Selenoesters (Acyl Selenides) (RCO–SeR′)

Unlike thioesters, selenoesters, with the weaker RCO−SeR′ bond, react readily with stannyl radicals to give acyl radicals. Moreover, selenoesters can be isolated and purified by silica gel chromatography and show none of the over-reductions that plague the reactions of acyl chlorides with stannanes. The seminal work was carried out by Graf and co-workers who investigated the reaction of selenoesters with tributyltin hydride.[133] It was demonstrated that selenoesters derived from tertiary carboxylic acids gave acyl radicals which underwent smooth decarbonylation in high yield. Selenoesters derived from primary acids, on the other hand, as might be expected from the rate constants for loss of CO from acyl radicals (section V.A), were reluctant to undergo decarbonylation, and those derived from secondary acids showed intermediate behavior (Scheme 17). Some synthetically useful decarbonylation reactions based on the selenoesters are summarized in section V.A.

Competition kinetic methods permitted the rate constants for the reaction of acyl phenyl selenides with both tris(trimethylsily)silyl and tributylstannyl

Scheme 17



radicals to be fixed at 2×10^8 M^{-1} s^{-1} at 80 °C.[75] More importantly for the planning of synthetic sequences, the Arrhenius parameters (section III.B, Scheme 1) for the quenching of typical acyl radicals by the silane and stannane were determined.[75] The slower rate of hydrogen-atom transfer from this silane means that in the absense of other competing reactions such as cyclization, more decarbonylation will be observed than with the tin hydrides under the same conditions of temperature and concentration. For example, phenylselenyl dodecanoate gave 35% of undecane on irradation at only 50 °C with this silane.[75]

The stability and smooth reactivity of selenoesters toward stannyl and tris(trimethylsilyl)silyl radicals has led to their widespread adoption as the precursors of choice in many synthetic schemes involving acyl radicals. Accordingly, numerous methods have been developed for their preparation. Selenoesters may be prepared by reaction of acyl chlorides with benzeneselenol in the presence of pyridine.[133] Likewise, acyl imidazolides are reported to react in high yield with benzeneselenol.[134] Mixed carboxylic−phosphoric anhydrides react with either the sodium[135] or thallium[136] salts of benzeneselenol to give selenoesters in good yield. Several more convenient methods avoid the use and handling of the vesicant benzeneselenol and instead make use of diphenyl diselenide which is reduced in situ. Sodium phenylseleno(triethoxy)borate generated in situ by the reduction of diphenyl diselenide with ethanolic sodium borohydride gives excellent yields of selenoesters on exposure to THF solutions of acyl chlorides.[125] The samarium(III) salt of benzeneselenol, generated by the in situ reduction of diphenyl diselenide with samarium iodide, also reacts conveniently with acyl chlorides.[137] Schwartz and Curran have reported the efficient formation of acyl methyl selenides by the reaction of methyl esters with dimethylaluminum methylselenide ($Me_2AlSeMe$) and their use as acyl radical precursors.[138] Two equivalents of stannane are required for complete consumption of the acyl selenide owing to competing cleavage of the Me−Se bond in the byproduct $Bu_3SnSeMe$.[138,139]

A second useful preparative method for the preparation of acyl selenides involves the reaction of benzeneselenenic acid derivatives (PhSeX) with tributylphosphine and the carboxylic acid. This chemistry has the considerable advantage of avoiding the formation of the acyl chloride as an intermediate, which both reduces the number of steps and avoids the formation of such an electrophilic moiety in sensitive substrates. The use of benzeneselenenyl chloride and even diphenyl diselenide in this context was alluded to in a footnote by Masamune in 1977, but no details were ever reported.[136] Grieco reported that the use of phenylselenocyanate or *N*-phenylselenophthalimide and tributylphosphine gave high yields of acyl selenides from carboxylic acids.[140] Crich and Batty found the use of the less expensive benzeneselenenyl chloride/tributylphosphine couple to be perfectly adequate provided that the acid is first converted to its triethylammonium salt.[141] More recently, it has been reported that tributylphosphine and diphenyl diselenide suffice to convert carboxylic acids to acyl selenides.[142]

A method which does not rely on the nucleophilic substitution of an activated carboxylate derivative by a nucleophilic selenium species involves the Tischenko-type reaction of aldehydes with diisobutylaluminum selenides. In practice, this method is only applicable to simple substrates owing to the obligatory reduction of 50% of the aldehyde to the alcohol.[143a] Aldehydes may also be converted to selenol esters with the combination of iodosobenzene diacetate and diphenyl diselenide.[143b]

Very recently, Hart has described efficient Diels–Alder cycloadditions of α,β-unsaturated selenoesters. This new reaction obviously provides a convenient entry into selenoesters of various substituted 4-cyclohexene carboxylic acids.[144]

6. Acyl Radicals from Telluroesters (Acyl Tellurides) (RCO–TeR′)

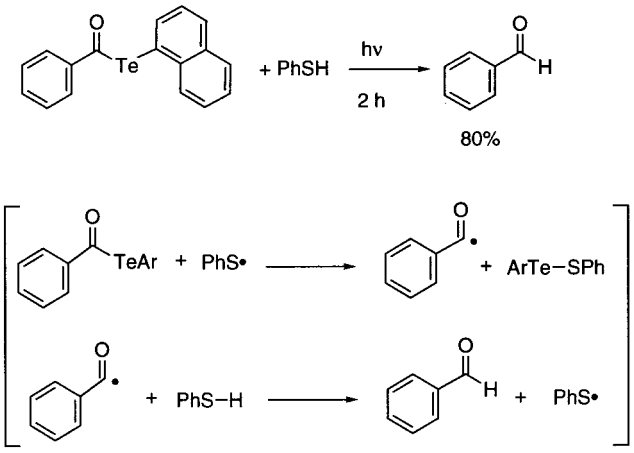
Telluroesters of aryl and vinyl carboxylic acids provide acyl radicals on white light photolysis, as demonstrated by Crich and co-workers. These may be trapped, for example, by thiols (Scheme 18).[145–147] This reaction is readily explained in terms of the chain sequence of Scheme 18. The reaction of acyl radicals with PhSH is well documented, and Ingold et al. found the absolute rate constants for isopropanoyl and benzoyl radicals to be 4.4×10^7 and 4.8×10^7 M^{-1} s^{-1}, respectively, at 24 °C.[55]

Analogously to selenoesters, telluroesters are conveniently formed by the in situ reduction of diaryl ditellurides with borohydride[147] or samarium iodide[137] followed by trapping with acyl chlorides or mixed anhydrides. Also in direct analogy to selenoesters, acyl tellurides may be accessed, at the expense of one-half of the substrate, by a Tischenko-like reaction between an aldehyde and diisobutylaluminum tellurides.[143] Schiesser has also described a further entry into telluroesters which involves the Pd(0)-catalyzed coupling of acyl halides with phenyltellurotris(trimethylsilyl)silane ($PhTeSiTMS_3$), which itself, unfortunately, has to be prepared in situ from cyclohexyl phenyltelluride and tris(trimethylsilyl)-silane.[148]

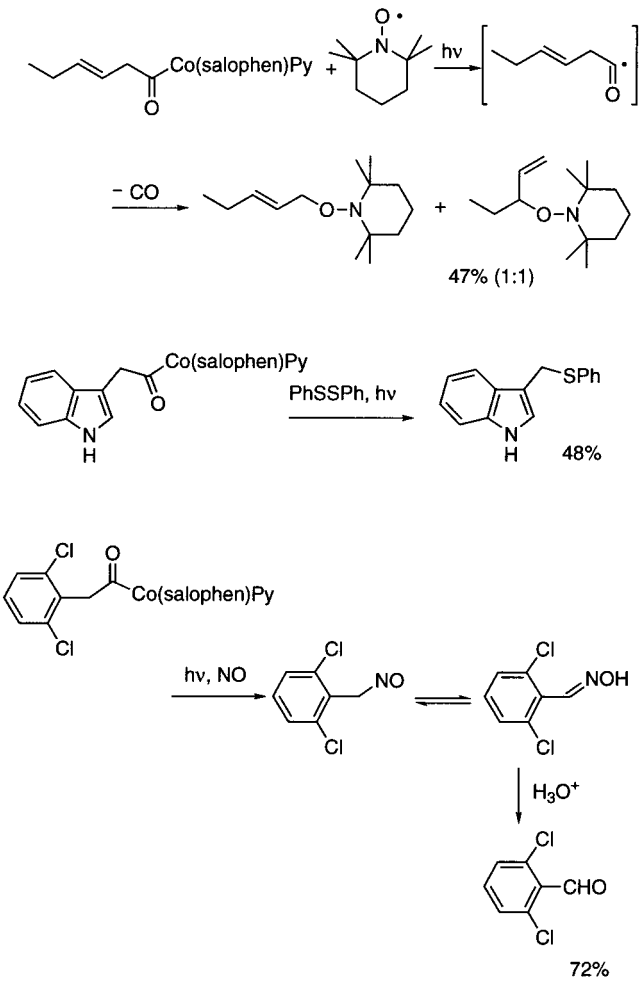
7. Acyl Radicals from Acylcobalt(III) Derivatives (RCO–CoL$_n$)

The well-known tendency of carbon–Co(III) bonds toward homolytic scission prompted Pattenden and co-workers to prepare a range of acylcobalt salophen complexes and to study their use as photolytic sources of acyl radicals. The acylcobalt salophens were readily obtained by the action of the highly nucleophilic Co(I) species, formed by in situ reduction

Scheme 18



Scheme 19

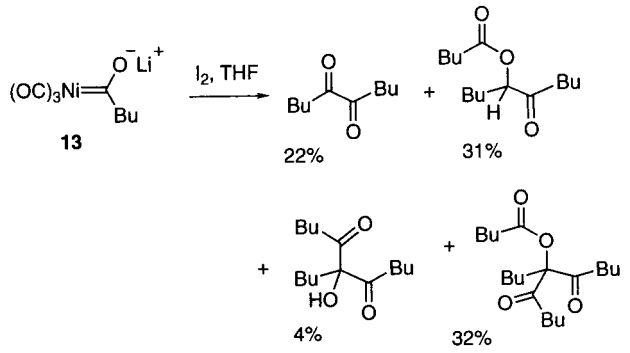


of the Co(III) halide, on acyl chlorides and proved, with the exception of benzoyl and *o*-, *m*-, and *p*-nitrobenzoyl derivatives, to be stable, highly colored crystalline solids. White light photolysis of allyl and arylacetyl cobalt salophens in the presence of diphenyl disulfide, and a number of other traps, provided the expected products of acyl radical formation, decarbonylation, and trapping in moderate to good yield (Scheme 19).[149] Migration of the acyl group from cobalt to the ligand resulting in the isolation of acyl salicyl aldehyde esters was reported to be a problem in certain aliphatic acylcobalt cases.[150]

8. Acyl Radicals from Metal Carbene Complexes

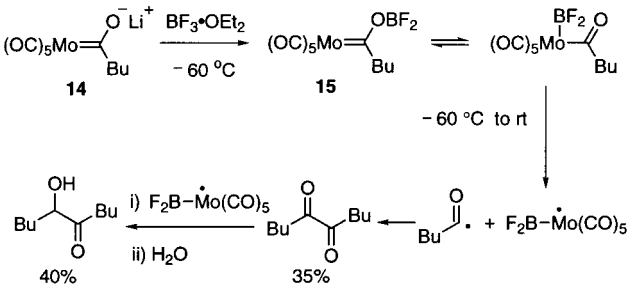
Certain types of transition-metal oxycarbene complexes appear to fragment to give acyl radicals. Thus, Simunic and Pinkas treated the nickelcarbene complex **13** with iodine and observed a spectrum of products consistent with the generation of acyl radicals and their self-reactions (Scheme 20).[151]

Scheme 20



Barluenga and co-workers reacted the oxymolybdenum carbene **14** with $BF_3{\cdot}OEt_2$ at low temperature to obtain an unstable adduct **15**, which on warming to room temperature followed by an aqueous work up, also provided products assumed to arise from the formation of acyl radicals (Scheme 21).[152]

Scheme 21

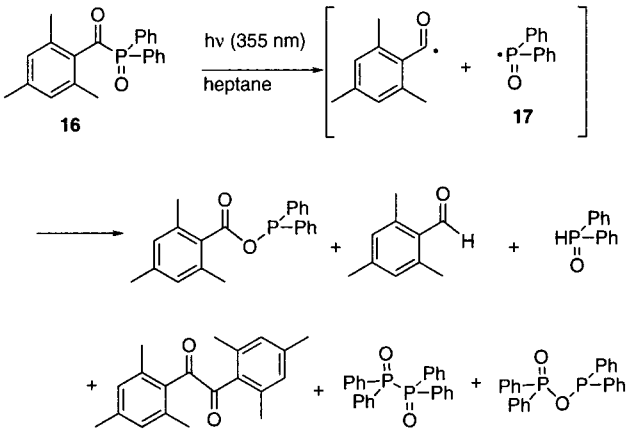


Unfortunately, in these sequences no attempt was made to employ standard tests for radicals, such as the use of cyclizable probes, and the evidence for acyl radical formation therefore rests wholly on the spectrum of products. However, we note that these and Narasaka's and other groups have used similar oxidative fragmentations of metal carbenes to generate acyl radicals in the presence of electron-deficient alkenes when standard adducts are formed, as discussed in section VIII.A.

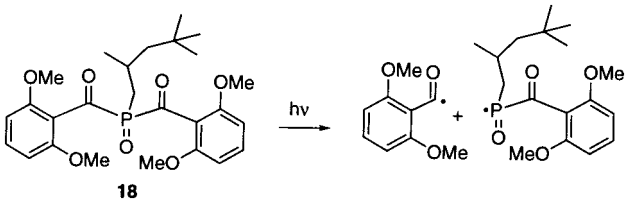
9. Acyl Radicals from Acylphosphine Oxides ($RCO{-}P(=O)Ar_2$)

Photolysis of benzoylphosphine oxides yields benzoyl radicals and phosphonyl radicals with high quantum efficiency ($\phi \approx 0.6$),[153] and (2,4,6-trimethylbenzoyl)diphenylphosphine oxide (**16**) has been developed as a commercial photoinitiator for the curing of polymer resins (Scheme 22).[154] The phosphonyl radical **17** is 1−2 orders of magnitude more reactive than the benzoyl radical toward unsaturated substrates, which places severe limits on this photolysis as a preparative source of acyl radicals. However, Turro et al. have taken advantage of this photocleavage to study the reactions of benzoyl radicals by time-resolved IR spectroscopy.[155] Rate constants for the reaction of the trimethylbenzoyl radical with bromotrichloromethane were determined and are comparable to those reported in section VI. It has also been demonstrated by Turro and co-workers that a bis(acyl)phosphine oxide (**18**) provides acyl radicals on photolysis (Scheme 23).[156]

Scheme 22



Scheme 23

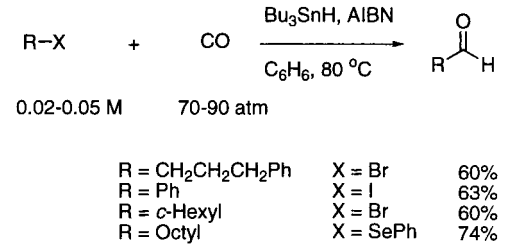


B. Generation of Acyl Radicals by Carbonylation

The carbonylation of alkyl, aryl, and vinyl radicals with CO to give acyl radicals has a relatively long and checkered history, which dates from 1939 when Faltings observed the formation of acetone on UV irradiation of ethane (giving methyl radicals) under CO pressure.[157] Most of the early work was characterized by low yields and inefficient reactions and, as the area has been recently reviewed by one of us,[2] will not be covered in detail here. The modern era of radical carbonylation began with the 1990 publication of Ryu, Sonoda, and co-workers in which it was demonstrated that alkyl halides could be carbonylated under moderate pressures of CO (70−90 atm) in benzene at 80 °C in the presence of tributyltin

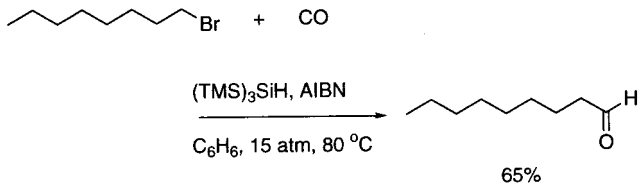
hydride, as a chain transfer agent, and AIBN, as an initiator.[158] The reaction is applicable to alkyl and aryl bromides, iodides, and selenides, as is evident from Scheme 24.

Scheme 24



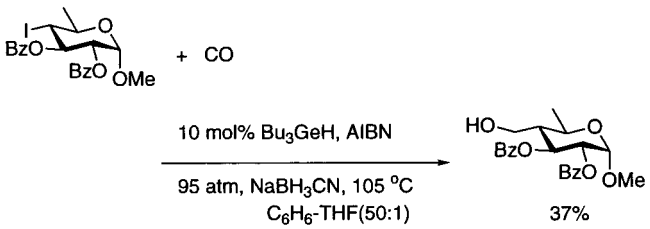
The success of the key carbonylation step is of course a function of the equilibrium constant (K) of this reversible reaction (section III) which, assuming steady-state conditions, is given by $K = k_{CO}[CO]/k_d$. It is evident from this equation that any acyl radical having an abnormally high rate of decarbonylation (k_d), i.e., leading to a resonance-stabilized radical ($R^\bullet$ = benzyl, alkoxyalkyl, aminoalkyl, etc.) will not perform satisfactorily in this chemistry, as is indeed found to be the case. Likewise, it is evident that any reaction which rapidly removes the acyl radical will drive the equilibrium in the forward direction, and any which consumes the alkyl radical will be detrimental to the carbonylation process. Evidently, a knowledge of the rate constants for both the forward and back reactions is invaluable and is now available (section III). Tris(trimethylsilyl)silane, $(TMS)_3SiH$, reacts with alkyl radicals more slowly than tributyltin hydride, which effectively means that the carbonylation reaction may be conducted at lower CO pressures with this reagent (Scheme 25).[159]

Scheme 25



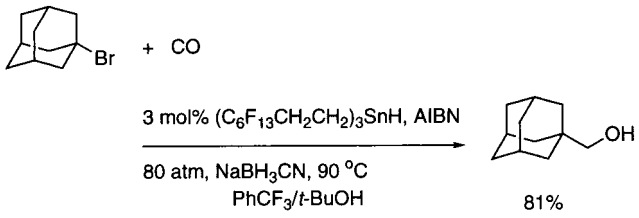
In a similar vein, the poorer hydrogen-atom donor tributylgermanium hydride may also be used to replace the tin hydride. In the example of Scheme 26, Kahne used only a catalytic quantity of the

Scheme 26



germane in the presence of sodium cyanoborohydride, as a stoichiometric reductant, which also brought about the in situ reduction of the aldehyde to the observed alcohol.[160] Interestingly, the stereoselectivity for trapping of the carbohydrate radical in this example was found to be 20:1 in favor of the isomer indicated. Ryu, Curran, and co-workers have achieved a similar result using a catalytic quantity of a fluorous tin hydride which permits purification by a simple three-phase (aqueous/organic/fluorous) extractive work up (Scheme 27). Used stoichiometrically,

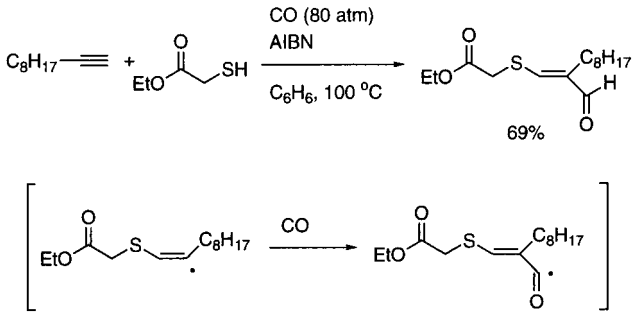
Scheme 27



without the cyanoborohydride, this reagent permits carbonylation and isolation of aldehydes in the normal way.[161]

Yoshida et al. reported that β-alkyl or arylthio-α,β-unsaturated aldehydes may be accessed in moderate to good yield by reaction of thiols with acetylenes in the presence of CO and AIBN as a radical initiator. In this chemistry the thiyl radical adds to the alkyne, giving a vinyl radical which is then carbonylated. Chain transfer is achieved by hydrogen-atom transfer from the thiol (Scheme 28).[162] There are two possible

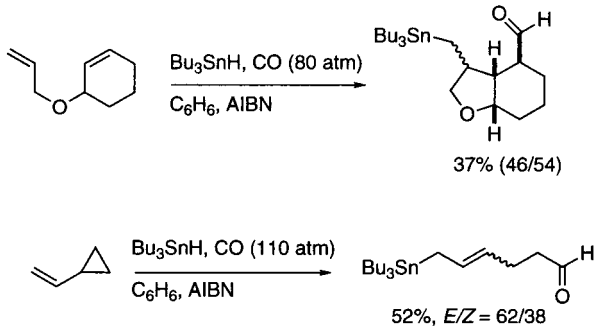
Scheme 28



explanations for the observed complete selectivity for formation of the E-product: (i) thiol-catalyzed isomerization of the initial product mixture[163] and (ii) stereoselective quenching of the α,β-unsaturated acyl radical. It is noteworthy that previous workers attempting the same reaction obtained much lower yields (<20%) while working at considerably higher pressures (~3000 atm).[164a] It appears likely that this was due to the use of the thiol as solvent, leading to a prohibitively high rate of trapping of the vinyl radical by the thiol. The related reaction involving thiyl radical addition to alkenes, followed by trapping with CO, was also reported by early workers to proceed in low yield when conducted at very high pressures.[164b] Unfortunately, this process also does not proceed well under the conditions of Scheme 28, apparently because thiol trapping of the initial adduct radical was too rapid.[162]

Of course, the tin hydride-mediated chemistry of Ryu and co-workers is readily applicable to carbon radicals formed by standard rearrangment reactions, as illustrated in Scheme 29, provided that the rearrangment is faster than the rate of CO trapping.[165,166]

Scheme 29

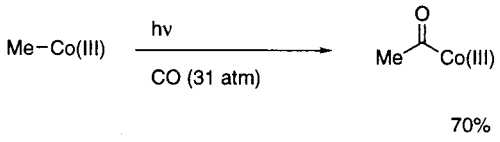


Radical carbonylation is not limited to chain sequences involving propagation by hydrogen-atom transfer or addition to carbon−carbon multiple bonds. It can be engineered such that the acyl radical is trapped by either reductive or oxidative electron-transfer processes. Such examples are treated in section IX.

Several groups have reported methods for the radical (and nonradical) carbonylation/carboxylation of alkanes in recent years, using a wide variety of electrophilic species to abstract a hydrogen atom from the alkane, and the area has been reviewed by Fujiwara, Takaki, and Taniguchi.[167] An example is provided by the work of Lin and Sen who were able to convert methane to acetic acid in good yield by heating to 105 °C under 68 atm of CO and using peroxydisulfate as a radical source and oxidant for the intermediate acyl radical (section IX.A.5).[168] Related carboxylation sequences have been described using $RhCl_3$[169] and Pd/Cu[170] in the presence of molecular oxygen as an overall oxidant. Crabtree has described a very interesting protocol for the photocarbonylation of cyclohexane, yielding cyclohexane carboxaldehyde, in which atomic mercury serves as the hydrogen-abstracting agent.[171] The identical transformation has been reported by Hill and Jaynes who made use of the photochemical stimulation of tetrabutylammonium polytungstate to achieve hydrogen abstraction.[172] Remarkably, this latter example proceeded under only 1 atm of CO pressure. Photochemical carbonylation of cyclohexane was also achieved by Goldman and Boese working at 82 atm with catalytic benzophenone or related ketones. Here, the excited ketone serves to abstract hydrogen from the alkane, giving the alkyl radical and protonated ketyl radical. The latter species donates hydrogen to the acyl radical after carbonylation and so regenerates the catalyst.[173] Unfortunately, while hydrocarbon functionalization reactions have potential industrial applications with simple hydrocarbon feedstocks, they are unlikely to be of significant use in synthesis because of the relatively low regioselectivity in the hydrogen-abstraction step.

Finally, the carbonylation of organometallic species is thought to proceed through free-radical mechanisms in some instances. A case in point, and one related to the acylcobalt salophens studied by the Pattenden group (section IV.A.7), is the carbonylation of methylcobalamine on exposure to light and 31 atm of CO pressure (Scheme 30). The likely mechanism involves homolytic scission of the Co−Me bond,

Scheme 30



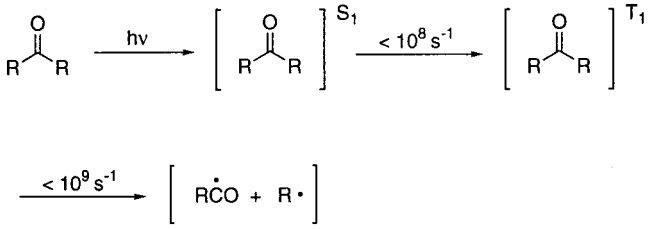
carbonylation of the methyl radical, and eventual recombination with the Co(II) radical.[174]

C. Generation of Acyl Radicals by Fragmentation of CO−C Bonds

1. Type 1 Cleavage of Ketones and α-Diketones

Perhaps, the best known method for the formation of acyl radicals by C−C bond cleavage is the Norrish type I photocleavage reaction.[175,176] Preparative applications of this venerable reaction to cycloalkanones have been reviewed,[177] and it is not our intention to repeat this coverage here. We simply note that it is one of the cleanest methods for the generation of acyl radicals for spectroscopic studies and has been widely used in this context. The photolysis of di-*tert*-butyl and dibenzyl ketones are classical type I cleavage reactions and follow the general Scheme 31.[175]

Scheme 31



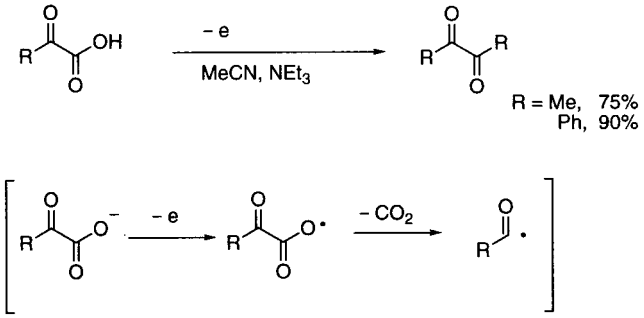
Generally, acyl radical precursors are ketones bearing a *tert*-butyl or benzyl moiety. Thus, the $CH_3C(O)^\bullet$ and $CH_3CH_2C(O)^\bullet$ radicals are generated by photolysis of $CH_3C(O)$Bu-*t* and $CH_3CH_2C(O)CH_2$-Ph, respectively. Although $PhC(O)^\bullet$ is readily generated by photolysis of PhC(O)Bu-*t* in the nπ^* transition band ($310 < \lambda < 380$ nm),[62] the analogous *p*-MeO-, *p*-Br-, and *p*-CN-substituted ArC(O)Bu-*t* are poor precursors of the corresponding $ArC(O)^\bullet$ radicals.[55]

The photochemistry of α-diketones has been thoroughly investigated and reviewed.[178] When δ-hydrogens are present, the Yang-type photocyclization is predominant and leads to the formation of α-hydroxycyclobutanones. With biacetyl and benzil, this chemistry is not possible and the major pathway in hydrogen-donating solvents is photoreduction to α-hydroxyketones. In non-hydrogen-donating solvents, biacetyl and benzil serve as good photochemical sources of acyl radicals. However, the chemistry is not entirely straightforward, and the photochemical event can simply serve as a chain initiation step. This is because the α-diketones themselves are good traps, at the carbonyl C, for alkyl and even acyl radicals. This addition process leads to an α-acylalkoxy radical (see section IV.C.3), which then fragments to a product and a new acyl radical. Examples of this type of process are discussed in sections VI.C and VII.B.

2. Decarboxylation of α-Keto Acids

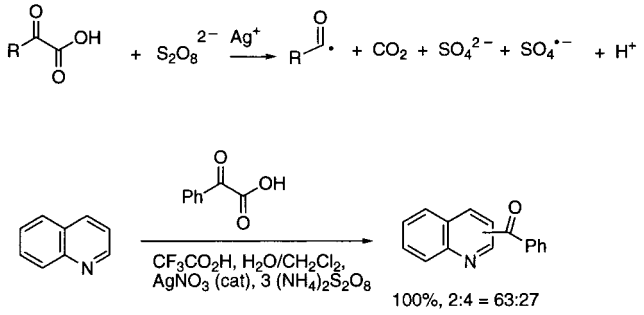
Loss of CO_2 from α-ketocarboxyl radicals provides acyl radicals. In the context of the Kolbé reaction, electrolysis of the corresponding acids can lead to the formation of α-diketones in good yield by coupling of the acyl radicals (Scheme 32).[179]

Scheme 32



Minisci and co-workers have developed the oxidative decarboxylation of α-ketoacids using the peroxydisulfate anion as the oxidant in conjunction with catalysis by Ag(I) as a source of acyl radicals for addition to protonated heteroatomic bases. This system has the advantage over hydrogen abstraction from aldehydes under Fenton type-conditions (Scheme 180 in section VIII.C), that the amount of diacylation of the base was reduced (Scheme 33).[180,181]

Scheme 33

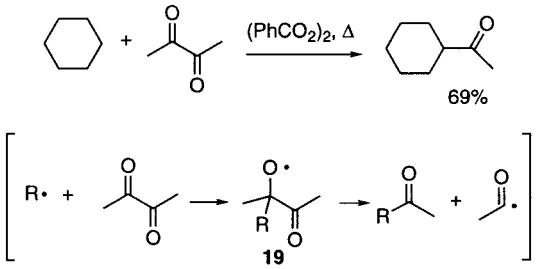


3. Cleavage of α-Acylalkoxy Radicals

A number of reactions have been described in which acyl radicals are generated by the cleavage of α-acylalkoxy radicals. For example, it is well established that, in the context of the chemistry of autoxidative cleavage of ketones, acyl radicals can be generated by decomposition of a variety of α-hydroperoxy ketones under a variety of conditions (photolysis, thermolysis, and Fenton's redox system)[182] via α-acylalkyloxy radicals. At the present time, these appear to be more curiosities than preparatively useful sources of acyl radicals. Nevertheless, we outline them here for the sake of completeness.

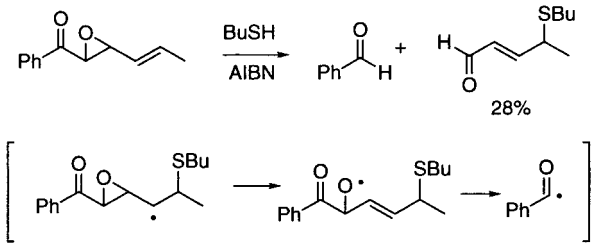
As Bentrude and Darnall have demonstrated, the benzoyl peroxide initiated reaction of cyclohexane with biacetyl provides cyclohexyl methyl ketone in 69% yield.[183] This reaction is thought to occur via addition of the cyclohexyl radical to a carbonyl C in the diketone, providing an alkoxyl radical **19** which fragments with expulsion of an acyl radical whose fate, unfortunately, was not accounted for (Scheme 34).

Scheme 34



More recently, Murphy and co-workers have generated α-acylalkoxy radicals by the cleavage of oxiranylcarbinyl radicals. These radicals in turn were obtained by the addition of thiyl radicals to alkenes. In the process illustrated, benzaldehyde, the product arising from quenching of the acyl radical in the chain transfer step, was unfortunately not quantified (Scheme 35).[184]

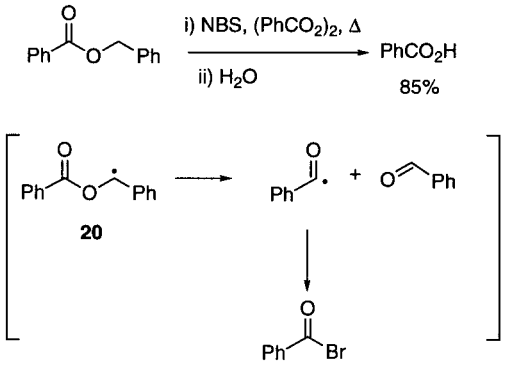
Scheme 35



4. Miscellaneous Fragmentations

Reaction of benzyl ethers with NBS, initiated by benzoyl peroxide in tetrachloromethane, followed by an aqueous workup, results in their cleavage in high yield. This reaction is thought to involve hydrogen abstraction from the benzylic position to give a carboxybenzyl radical **20**, which undergoes fragmentation to benzaldehyde and an acyl radical (Scheme 36). The acyl radical carries the chain, leading to the

Scheme 36



formation of the acyl bromide, which is hydrolyzed on workup.[185]

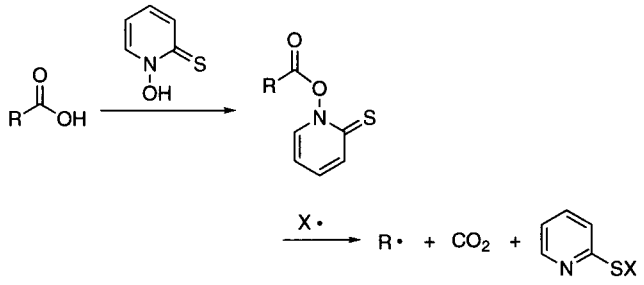
V. Synthetically Useful Decarbonylation and Coupling Reactions

A. Decarbonylation Reactions

Decarbonylation to give alkyl radicals and carbon monoxide is one of the most popular reactions of acyl

radicals, but synthetically useful applications have only begun to appear recently. The Barton reaction, which proceeds via the acyl derivatives of *N*-hydroxy-2-thiopyridone (Scheme 37), is probably the most

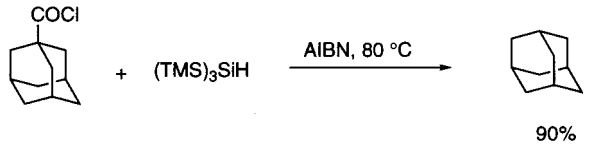
Scheme 37



popular reaction used in order to obtain an alkyl radical from the corresponding acid in a chain reaction.[186] However, the intermediate thiohydroxamates can be difficult to purify and cannot be stored because of their poor stability.

Alternative radical chain reactions in which alkyl radicals are generated from the corresponding acids are the reactions of acid chlorides or seleno esters with hydrides of group 14 as the reducing agents (sections IV.A.2 and IV.A.5). For example, tripropylsilane reacts with RC(O)Cl in the presence of di-*tert*-butyl peroxide at 140−170 °C to give the corresponding alkane RH with a 50−70% yield when R is a primary or secondary alkyl group. $(TMS)_3SiH$ reacts with acid chlorides at moderate temperatures to give alkyl radicals when the decarbonylation is sufficiently rapid. Thus, when R is a secondary or tertiary alkyl group, the decarbonylation is efficient at 80 °C.[189] An example is shown in Scheme 38. The

Scheme 38

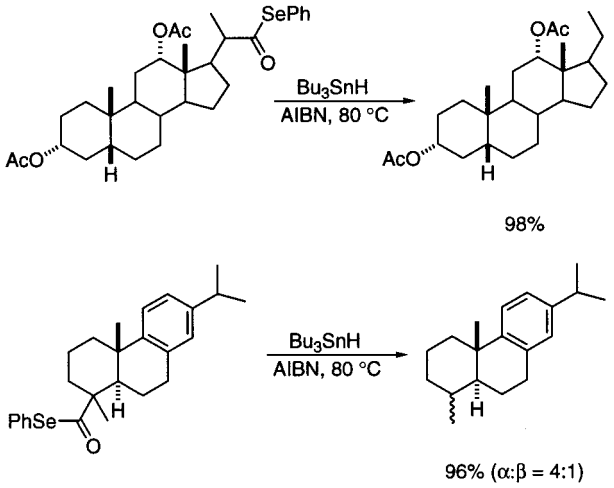


reaction of Bu_3SnH is not attractive from a preparative standpoint (section IV.A.2).[190]

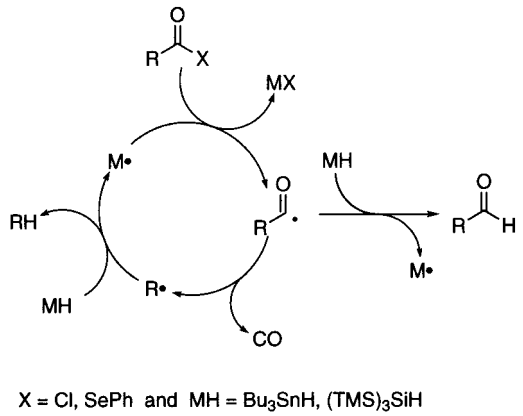
Seleno esters were first reported by Graf et al. to undergo reduction to the corresponding aldehydes and/or alkanes in the presence of Bu_3SnH (section IV.A.5).[133] Examples are reported in Schemes 17 and 39, in which the alkyl groups attached at the carbonyl moiety are primary, secondary, and tertiary. It was also demonstrated that using photoinitiation conditions, selenoesters derived from tertiary carboxylic acids gave acyl radicals which underwent smooth decarbonylation in high yield at room temperature.

Selenoesters have also been reported to undergo reduction to the corresponding aldehydes and/or alkanes in the presence of $(TMS)_3SiH$ under free-radical conditions.[75,191,192] The mechanism that operates in all the above-described reactions is outlined in Scheme 40. That is, silyl or stannyl radicals, initially generated by a small amount of initiator, abstract the phenylseleno group (or abstract a chlorine atom in the case of an acyl chloride with

Scheme 39



Scheme 40

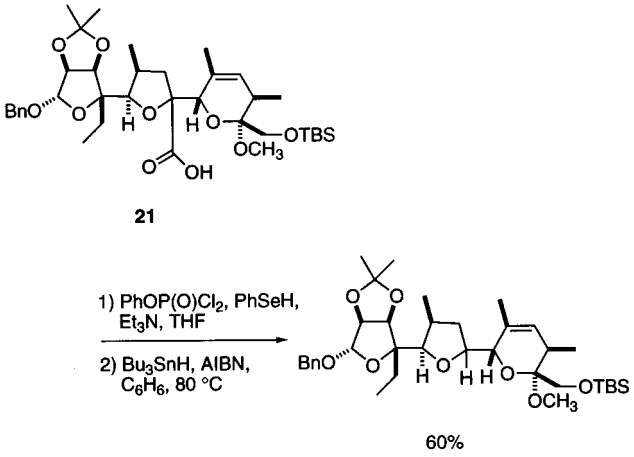


X = Cl, SePh and MH = Bu_3SnH, $(TMS)_3SiH$

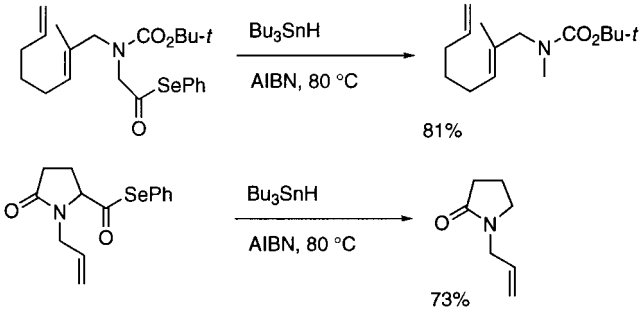
$(TMS)_3SiH$) to form an acyl radical intermediate which undergoes either an intermolecular hydrogen abstraction, giving the aldehyde, or an α-scission, to form an alkyl radical. Hydrogen abstraction from the hydrides by R• regenerates the silyl or stannyl radicals, thus completing the cycle of these chain reactions. Therefore, to obtain synthetically useful decarbonylation the rate of decarbonylation, must be faster than the rate of hydrogen abstraction. Activation parameters for the reaction of acyl radicals with Bu_3SnH and $(TMS)_3SiH$ (section III.B, Scheme 1) together with the decarbonylation rates reported in section III.B indicate that the decarbonylation of tertiary and secondary alkyl-substituted acyl radicals can be achieved under "normal" free-radical conditions (AIBN, 80 °C).[75] Obviously, acyl radicals with *β*-heteroatom substituents such as alkoxy or amino will decarbonylate much faster. Several examples which take advantage of this fact have been reported. For instance, Ireland and co-workers described the radical reductive decarboxylation of **21** via the phenylseleno ester derivative (Scheme 41; 60% combined yield of the two steps), which gave rise to a single isomer of the product.[193]

The generation of α-amino and α-amido alkyl radicals has recently been reported from the corresponding seleno esters. Boger and Mathvink previously reported that decarbonylation of an acyl radical to give an α-nitrogen-attached alkyl radical is faster than cyclization (Scheme 42).[135] Crich and co-workers

Scheme 41

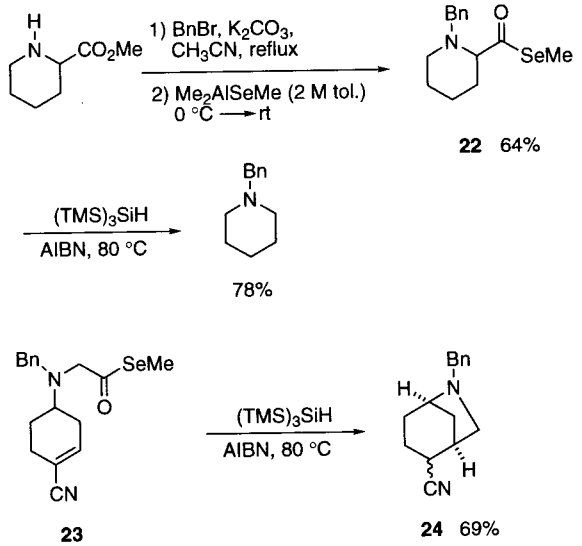


Scheme 42



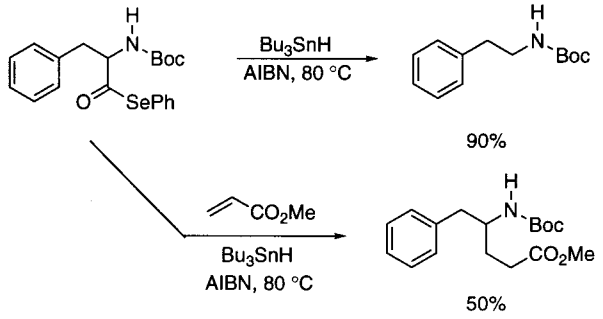
also found that the decarbonylation course was favored in an attempted cyclization of an acyl selenide derived from *N*-allyl pyroglutamate (a second example in Scheme 42).[194] Bonjock and co-workers recently reported that the methylseleno ester **22** prepared from the methyl ester when treated by $(TMS)_3SiH$ gave the reduction product in 78% yield (Scheme 43).[195] In appropriate circumstances, the

Scheme 43



aminoalkyl radical may take part in a subsequent cyclization reaction as, for example, in the formation of the normorphan **24** from **23** (Scheme 43).[196] Scheme 44 represents the reaction of a seleno ester with Bu_3SnH in the presence and in the absence of

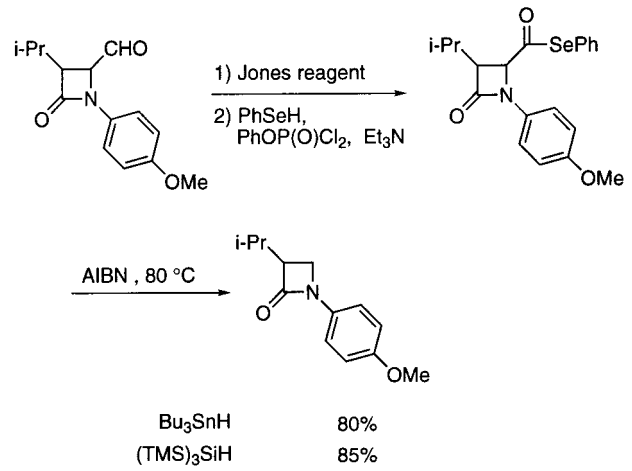
Scheme 44



a radical trap.[196] The reduction gave the corresponding decarboxylated protected amide in 90% yield, whereas in the presence of methyl acrylate, the alkyl radical intermediate is trapped by the olefin prior to the hydrogen abstraction to give the adduct in 50% yield.

The synthesis of C4-substituted β-lactams has been conveniently achieved from easily available 4-formyl-β-lactams.[197] An example is shown in Scheme 45 in which the initial aldehyde is transformed into a

Scheme 45

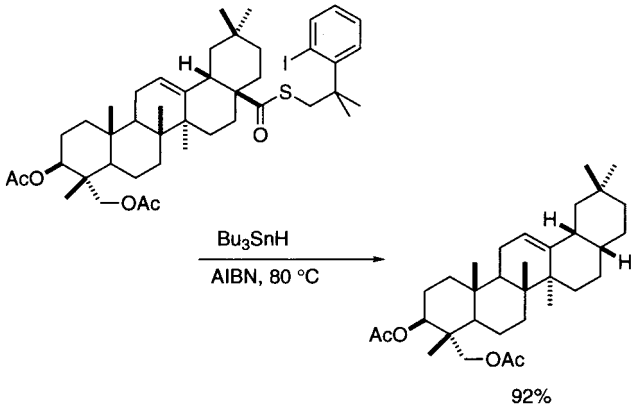


phenylseleno ester and the subsequent reaction either with Bu_3SnH or $(TMS)_3SiH$ afforded the decarbonylation product with an 80−85% yield.

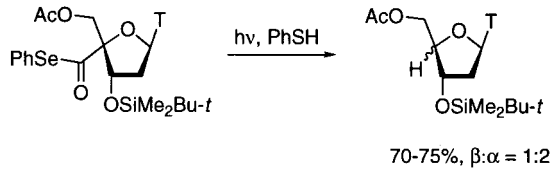
As noted previously (section IV.A.4), thioesters do not readily take part in the cycle of Scheme 40. To overcome this problem, Crich et al. introduced a homolytic internal substitution at sulfur by aryl radicals.[198,199] Two examples are reported in Scheme 46 which illustrate the potential of this methodology to perform synthetically useful decarbonylation reactions. In the second of these examples, the starting material is a 2:1 mixture of thioester of acid and α-ketoacid (i.e., $n = 1$ and 2, respectively). Furthermore, the alkyl radical bearing two alkoxy substituents after decarbonylation abstracts the hydrogen selectively from the axial position.

Useful decarbonylations have also been reported for the selective generation of C-4′ radicals in nucleosides and nucleotides. In particular, the C-4′ radicals were generated either by continuous photolysis of phenylseleno esters in the presence of thiophenol, which was reported by Giese and co-workers,[200] or by Crich's thioester approach on treatment with Bu_3-

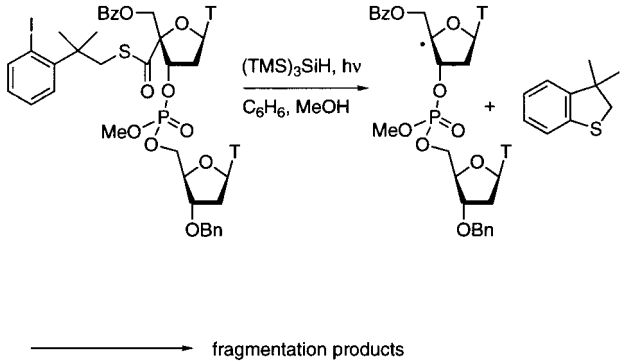
Scheme 46



Scheme 47



Scheme 48



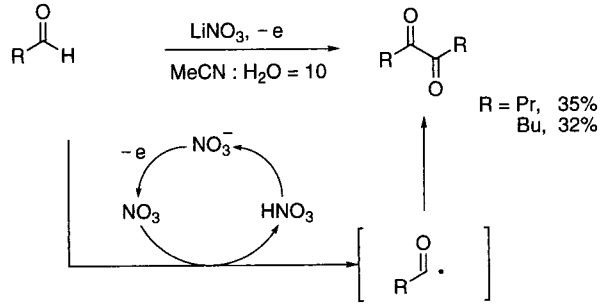
SnH or $(TMS)_3SiH$.[201] These examples are illustrated in Schemes 47 and 48, respectively.

B. Coupling Reactions

Acyl radicals, like many transient free radicals, in the absence of appropriate traps combine in solution with rate constants of the order of magnitude expected for diffusion-controlled processes. For example, the self-termination rate constant of benzoyl radicals to give benzil has been determined by EPR and optical spectroscopy and is well described by von Smoluchowski's equation.[62] In free-radical chain reaction systems, such dimerization to give 1,2-diketones is not usually observed because of the low concentrations of acyl radicals, although it is possible that it serves as a chain breaking event.

As already shown in Scheme 32 (section IV), Kolbe electro-oxidation of α-ketoacids, such as of pyruvic acid and phenylglyoxylic acids, in acetonitrile gave high yields of the homocoupling products, biacetyl and benzil, respectively.[179] Iqbal and co-workers reported that cobalt(II)-catalyzed reaction of aromatic aldehydes with molecular oxygen in the presence of butanal gave moderate to good yields of 1,2-diones, which are most likely obtained via dimerization of aromatic acyl radicals.[202a] Vitamin B_1 catalyzed dimerization of furaldehyde was reported by Kascheres and co-workers, where pH control (pH = 9) and a long reaction time (30 days) are necessary.[202b] Scheme 49

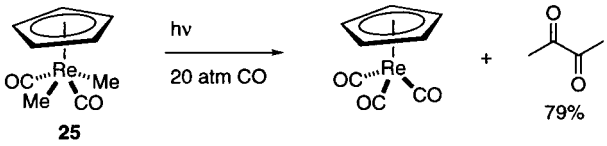
Scheme 49



also shows a related example of dimerization of acyl radicals, which were generated from aldehydes via hydrogen-atom abstraction by electrochemically generated NO_3 radical. [203]

The photolysis of a dimethylcyclopentadienylrhenium complex **25** in CD_2Cl_2 under 20 atm of CO pressure was reported by Bergman and Goldberg to give good yields of biacetyl (Scheme 50).[204] When the

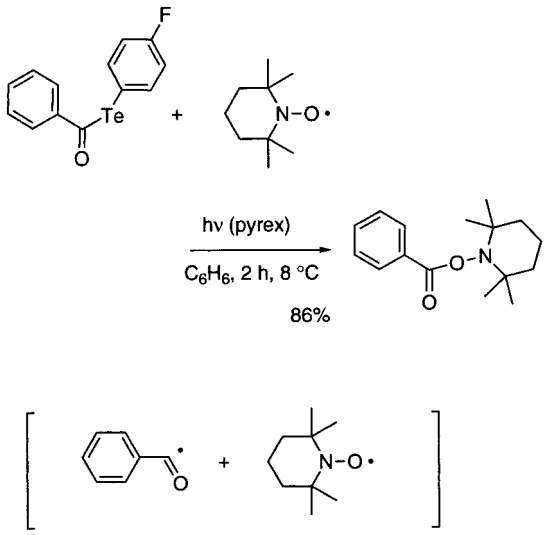
Scheme 50



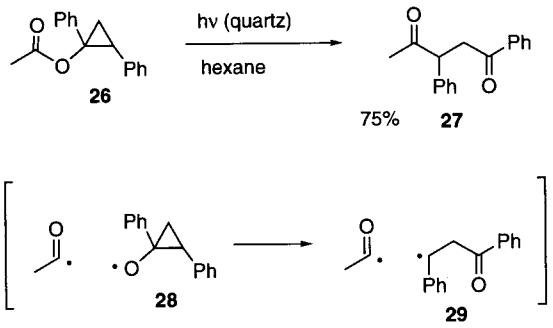
photolysis was conducted under ^{13}C-labeled CO, 98% of the biacetyl was labeled at both carbonyl carbons, which was considered to be strongly suggestive of a mechanism involving homolytic scission of the Re−Me bond, followed by carbonylation and combination of two acetyl radicals. When the same chemistry was conducted in tetrachloromethane solution, the major product, formed in 152% yield indicating that both Re−Me bonds may be cleaved, was acetyl chloride, which is consistent with the abstraction of chlorine from the solvent by an acetyl radical.

Absolute rate constants for the reaction of acyl radicals with nitroxyl radicals have been measured by time-resolved spectroscopies. For example, using time-resolved methods, Lusztyk, Ingold, and coworkers determined the rate constant for the trapping of the benzoyl radical by TEMPO to be 1.0×10^9 M^{-1} s^{-1}.[55] This type of radical/radical coupling

Scheme 51



Scheme 52



reaction was successfully employed in trapping of acyl radicals generated by irradiation of acyl tellurides (Scheme 51).[147]

Irradiation of 1-acetoxy-1,2-diphenylcyclopropane (trans:cis = 3:1) **26** in hexane, using a 125 W medium-pressure mercury lamp, for 2 h led to the formation of the 1,4-diketone **27** in 75% yield (Scheme 52). It is suggested that the carbonyl−oxygen cleavage is the preferred pathway from the excited singlet state and that prior to this in-cage recombination rearrangement of cyclopropoxy radical **28** to β-acyl radical **29** would take place.[205]

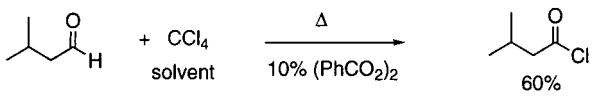
VI. Homolytic Substitution

A. Homolytic Substitution at Halogen

1. At Chlorine

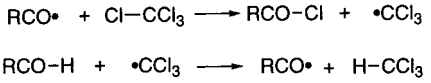
Homolytic substitution reactions were among the first reactions of acyl radicals to be reported. Thus, as long ago as 1947, Winstein and Seubold reported the formation of acyl chlorides on refluxing of aldehydes in tetrachloromethane with initiation by benzoyl peroxide (Scheme 53).[206] A simple chain process

Scheme 53



is involved in which the acyl radical abstracts chlorine from the solvent, the homolytic substitution step, and the ensuing trichloromethyl radical carries the chain by hydrogen-atom abstraction from further aldehyde (Scheme 54).

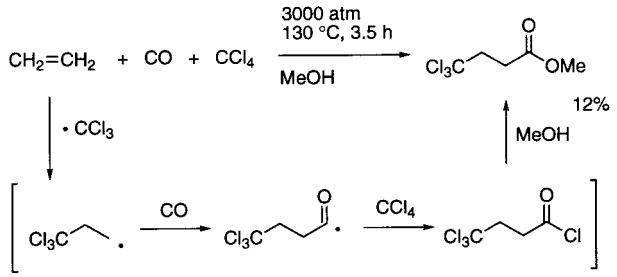
Scheme 54



Subsequently, Ginsburg studied the chlorination of aromatic aldehydes with *tert*-butyl hypochlorite. In acetic acid or *tert*-butyl alcohol as solvent, chlorination of the aromatic nucleus was a problem, especially with electron-rich substances. However, in tetrachloromethane, this polar process could be suppressed in favor of the radical chlorination of the aldehyde, giving the acid chloride. It seems more than likely that tetrachloromethane plays an active role, akin to that described in Scheme 54, in this process, above and beyond that of mere nonpolar solvent.[207]

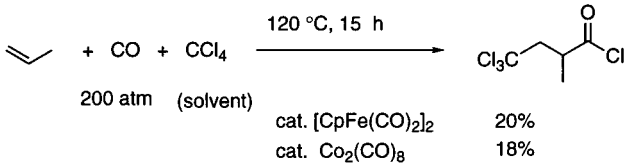
The free-radical carbonylation of alkenes in the presence of tetrachloromethane was described by Foster and collaborators (Scheme 55). Here, a chain

Scheme 55



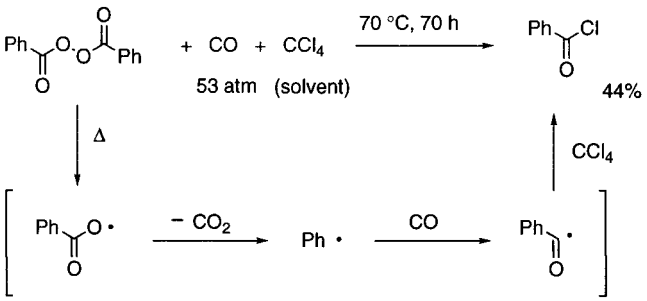
sequence is initiated by the addition of the trichloromethyl radical to the alkene. The adduct radical undergoes carbonylation to an acyl radical, which subsequently carries the chain by homolytic substitution at chlorine of CCl_4. Methanol was used as the solvent in this high-pressure reaction, meaning that the ultimate product was a methyl ester. The yield of monomeric adduct was low, but it should be remembered that the main aim of this industrial group was to optimize conditions for telomer formation.[208] Later a closely related process was reported by Suzuki and Tsuji using catalytic metal carbonyls as initiators. Tetrachloromethane was used as the solvent in this case, enabling the isolation of acid chlorides (Scheme 56).[209]

Scheme 56



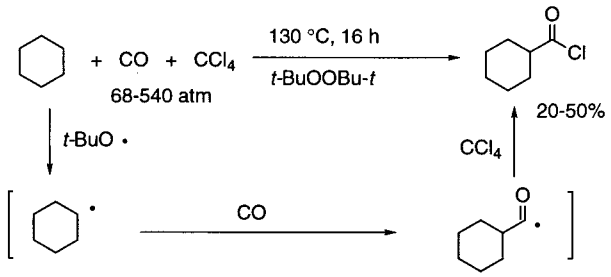
Walling and Savas generated phenyl radicals by thermally induced decomposition of benzoyl peroxide in tetrachloromethane at various CO pressures. The phenyl radical was found to undergo carbonylation to the benzoyl radical, which, in line with the above work, abstracted chlorine from the solvent giving benzoyl chloride (Scheme 57).[210]

Scheme 57



The radical chlorocarbonylation of cyclohexane has been reported by Thaler who initiated his sequence either with di-*tert*-butyl peroxide (Scheme 58) or by γ-irradiation using a ^{60}Co source.[211]

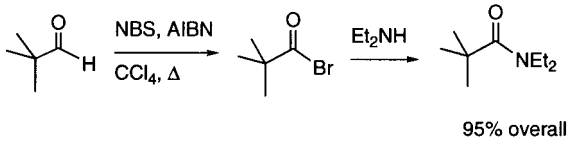
Scheme 58



2. At Bromine

Marko has described the radical bromination of aldehydes with NBS. The reaction, which proceeds with AIBN initiation in tetrachloromethane at reflux, provides good yields of acyl bromides from simple aliphatic and aromatic aldehydes. Most frequently, these were not isolated but simply allowed to react further with amines giving amides (Scheme 59). The nature of the hydrogen-abstracting species,

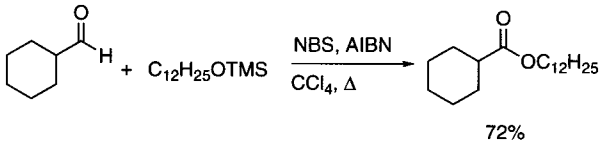
Scheme 59



Br• or the succinimidyl radical, was not determined.[99a]

A related process in which aldehydes were heated with NBS and AIBN in tetrachloromethane in the presence of trimethylsilyl ethers led directly to esters, through the presumed intermediacy of acyl bromides (Scheme 60). Curiously, this latter reaction proceeded

Scheme 60



well with aliphatic aldehydes, but failed with aromatic ones unless catalyzed by trimethylsilyl triflate. It was suggested, with some supporting evidence, that in the case of aromatic aldehydes, hydrogen abstraction was occurring from an acetal formed in situ rather than directly from the aldehyde.[99]

3. At Iodine

Ryu and co-workers have developed a carbonylative iodine transfer chain reaction in which alkyl iodides are transformed into acyl iodides. The key step in this sequence, apart from carbonylation of the alkyl radical, is a homolytic substitution reaction in which an acyl radical abstracts iodine from the substrate (Scheme 61).[212] This iodine transfer step was thought

Table 10. Absolute Rate Constants for the Reaction of Acyl Radicals with Polyhalomethanes at 24 °C

RC(O)•	CX_4	solvent	k, M^{-1} s^{-1}	ref
$CH_3C(O)$•	CCl_4	*n*-hexane	9.6×10^4	55
$CH_3CH_2C(O)$•	CCl_3Br	*n*-hexane	7.0×10^8	55
$(CH_3)_2CHC(O)$•	CCl_4	*n*-hexane	3.1×10^5	55
	CCl_3Br	*n*-hexane	5.9×10^8	55
$(CH_3)_3CC(O)$•	CCl_4	*n*-hexane	8.8×10^4	55
$C_6H_5C(O)$•	CCl_4	*n*-hexane	6.0×10^4	55
	CCl_3Br	*n*-hexane	2.2×10^8	55
p-$MeOC_6H_4C(O)$•	CCl_4	(*t*-BuO)$_2$	1.4×10^5	55
p-$BrC_6H_4C(O)$•	CCl_4	(*t*-BuO)$_2$	4.2×10^4	55
mesityl-C(O)•	CCl_3Br	*n*-heptane	1.7×10^8	155

Scheme 61

to be an equilibrium, in addition to the reversible carbonylation, as any attempt to isolate the acyl iodides failed, even under 78 atm of CO. Consequently, reactions were carried out in the presence of alcohols[212] or amines[213] such that the acyl iodides were trapped out, leading to esters and amides, respectively, driving the equilibrium in the forward direction (Scheme 62).

4. Rate Constants for Homolytic Substitution at Halogen

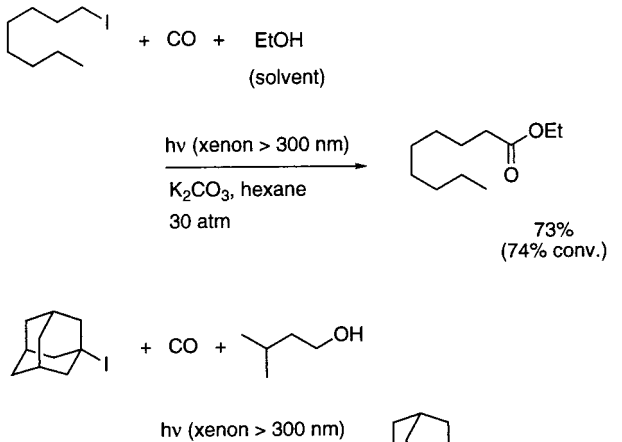
It is only very recently that kinetic data has become available for the abstraction of halogen atoms from perhalomethanes by acyl radicals. The rate constants given in Table 10 show, not surprisingly, that bromine abstraction is more rapid than that of chlorine and that saturated acyl radicals are marginally more reactive than unsaturated ones in this process.[54,55]

B. Homolytic Substitution at Chalcogen

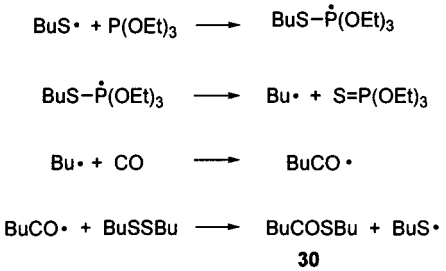
1. At Sulfur

The reaction of acyl radicals with disulfides was described by Walling and co-workers in the course of an investigation into the reaction of alkoxy and thiyl radicals with phosphites. In this chemistry, a mixture of dibutyl disulfide and triethyl phosphite was heated in the presence of di-*tert*-butyl peroxide under a range of CO pressures. It was shown by GC analysis of the reaction mixture that the products were *S*-butyl thiopentanoate **30** and dibutyl disulfide (Scheme 63). The reaction is envisaged as proceeding by the four propagation steps indicated which include the homolytic displacement of a thiyl radical from a disulfide by the acyl radical.[214a] Typically, dibutyl sulfide is formed as a byproduct in this reaction owing to the competing trapping of the butyl radical by the disulfide. At high CO pressures (325 atm), when carbonylation is rapid, this side reaction can be effectively suppressed. Takagi and co-workers examined the reaction of aldehyde cyclic disulfides and found excellent yields for the opening of 1,2-dithiolanes (Scheme 64) and of 1,2-dithianes.[214b]

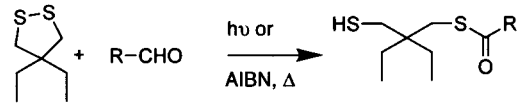
Scheme 62



Scheme 63



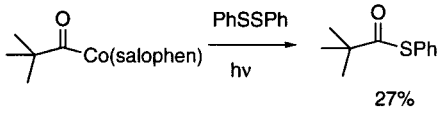
Scheme 64



Acyclic disulfides were also employed in an analogous sequence, leading to the formation of thioesters and thiols. A number of aldehydes were examined in the two processes, and it was found that all aliphatic ones, regardless of branching, gave good yields. Unfortunately, aromatic aldehydes were less cooperative and gave a number of byproducts including benzils. Evidently, as noted by the authors, these reactions proceed via a simple chain sequence in which the acyl radical adds to the disulfide, providing the thioester and a thiyl radical primed to propagate the sequence by hydrogen abstraction from further aldehyde.

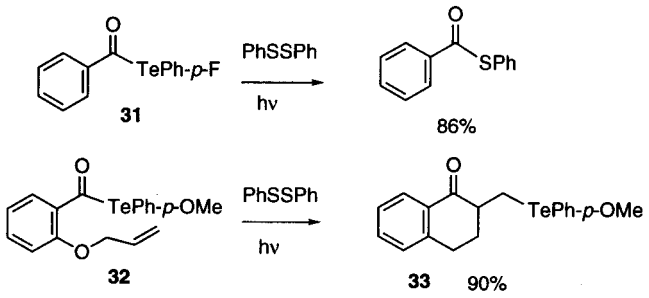
Much later, Pattenden reported that the generic reaction of aliphatic acylcobalt salophen complexes with diphenyl disulfide gave 70−80% yields of thioesters by a reaction involving acyl radical attack at the disulfide.[215] Unfortunately, in the only specific example advanced (Scheme 65), the yield was a mere

Scheme 65



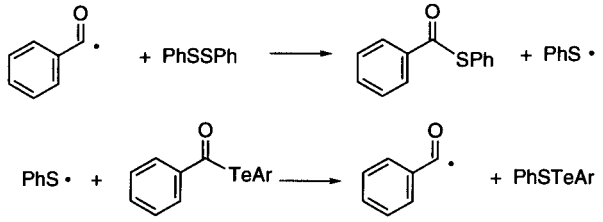
27%.[149] When the identical reaction was conducted with various phenylacetyl cobaltsalophen derivatives, decarbonylation of the acyl radical to give the benzyl radical was unable to compete with its trapping by the disulfide (cf. Scheme 19).[149] Crich and co-workers photolyzed the simple acyl aryl telluride **31** in the presence of diphenyl disulfide and observed an 86% yield of the thioester (Scheme 66). A two propagation

Scheme 66



step chain sequence (Scheme 67) was thought to be occurring in this example.[147] However, this sequence

Scheme 67

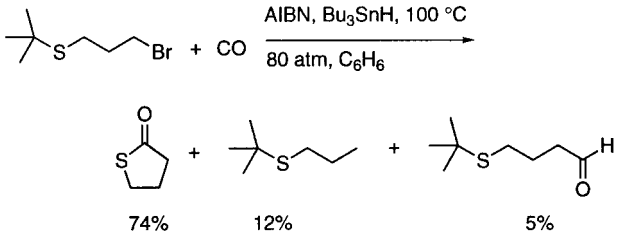


could not compete with a straightforward 6-exo-trig acyl radical cyclization, as is clear from the transformation of **32** to **33** (Scheme 66).

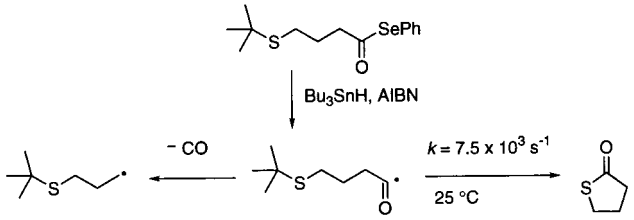
Ryu, Sonoda, and co-workers studied the cyclization of acyl radicals onto *tert*-butyl sulfides with expulsion of the *tert*-butyl radical and formation of γ-thiolactones. In the first instance, using acyl selenide/tin hydride chemistry and competition kinetic methods, the rate constant for the cyclization was determined to be 7.5×10^3 s^{-1} at 25 °C (Scheme 68).[216]

Subsequently, the acyl radical was generated by carbonylation of an alkyl radical as shown in Scheme 69. This process was shown to be applicable to a range of substituted 3-(*tert*-butylthio)propyl bromides

Scheme 69

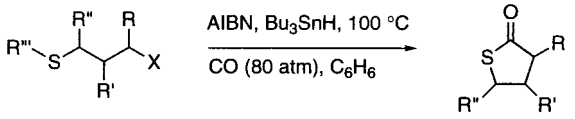


Scheme 68



and iodides giving moderate to excellent yields of the corresponding thiolactones (Scheme 70).[216]

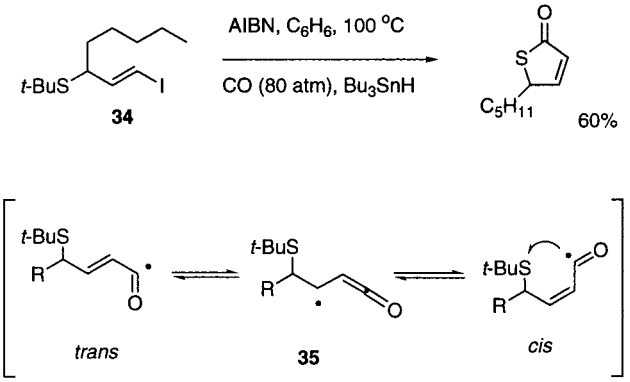
Scheme 70



R	R'	R"	R"'	X	% yield
H	H	H	*t*-Bu	Br	74
H	H	H	Bn	Br	51
H	H	Me	*t*-Bu	I	75
H	Bu	H	*t*-Bu	I	86
Me	H	H	*t*-Bu	I	64
Me	H	H	Bn	I	51

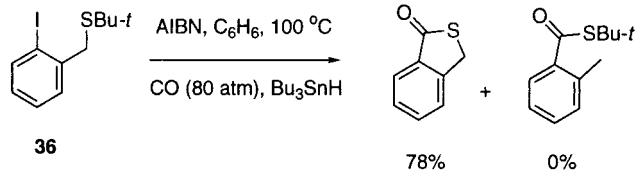
Two examples deserve special comment. First, as seen from Scheme 71, carbonylation of a trans vinyl

Scheme 71



iodide **34** was followed by a successful cyclization with displacement of the *tert*-butyl radical. The implication is that the barrier to rotation about the double bond in the intermediate α,β-unsaturated acyl radical **35** is sufficiently low, allowing rapid equilibration under the reaction conditions.[216] Second, an acyl radical derived from carbonylation of an aryl iodide **36** cyclized with expulsion of the *tert*-butyl radical rather than the benzyl radical (Scheme 72). The authors conclude that the transition state for homolytic displacement of carbon-centered radicals

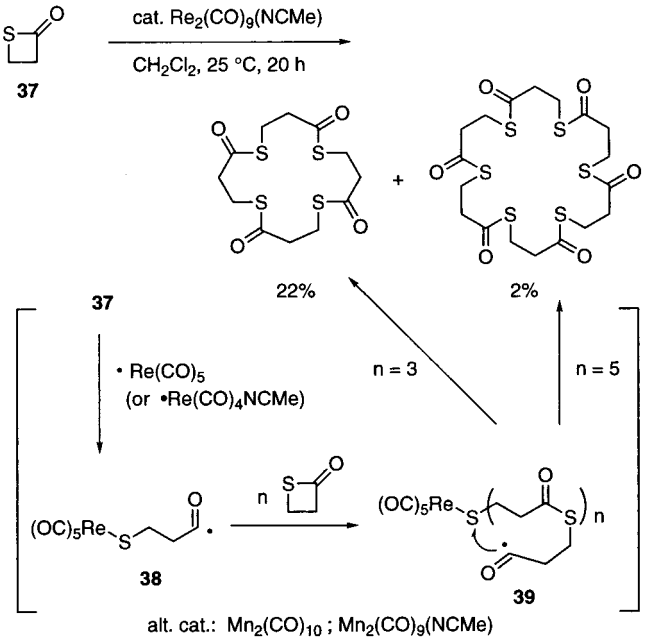
Scheme 72



from sulfides by an acyl radical involves backside rather than frontside attack.

A particularly interesting example, involving three types of homolytic substitutions at sulfur, was provided by Adams and co-workers.[217] In this sequence, which is initiated by exposure to white light, an organometallic initiator radical attacks at sulfur of the β-thiolactone **37** with expulsion of the acyl radical **38**. This initial acyl radical then attacks a second molecule of the β-thiolactone with expulsion of a further acyl radical **39**. This sequence of acyl radical-initiated β-thiolactone opening is repeated until the chain is sufficiently long to bite its own tail, that is, undergo cyclization by a third homolytic substitution at sulfur with expulsion of the initial organometallic radical (Scheme 73).

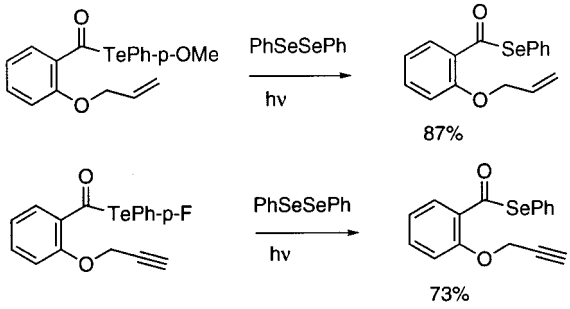
Scheme 73



2. At Selenium

Pattenden and co-workers reported a generic reaction whereby acyl radicals generated by photolysis of acylcobal salophen derivatives gave acyl selenides in high yield, but unfortunately, they did not give any specific examples. However, it was noted that decarbonylation of phenylacetyl radicals, to give benzyl radicals, competed effectively with the homolytic substitution.[149,215] The first concrete examples of the reaction of acyl radicals with diselenides were presented by Crich and co-workers using acyl tellurides as precursors (Scheme 74).[147] It will be noted that, at the concentrations employed (~0.1 M), the homolytic substitution at selenium was able to compete

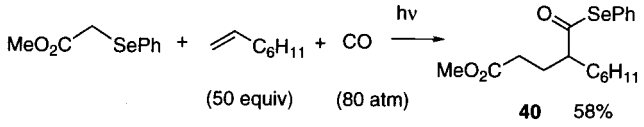
Scheme 74



effectively with otherwise efficient cyclization processes. This is to be contrasted with the second example of Scheme 66 which demonstrates that trapping by diphenyl disulfide is unable to compete with one of the same cyclizations.

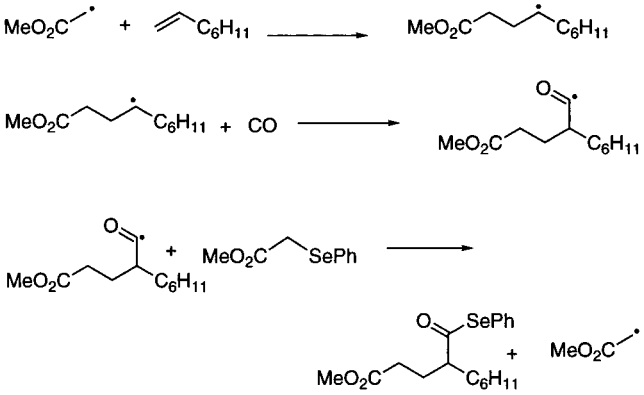
Ryu, Sonoda, and co-workers have developed the useful phenylselenyl group transfer sequence illustrated in Scheme 75. A three propagation step

Scheme 75



chain sequence (Scheme 76) is involved in which a β-carbonyl-substituted, ambiphilic alkyl radical adds

Scheme 76



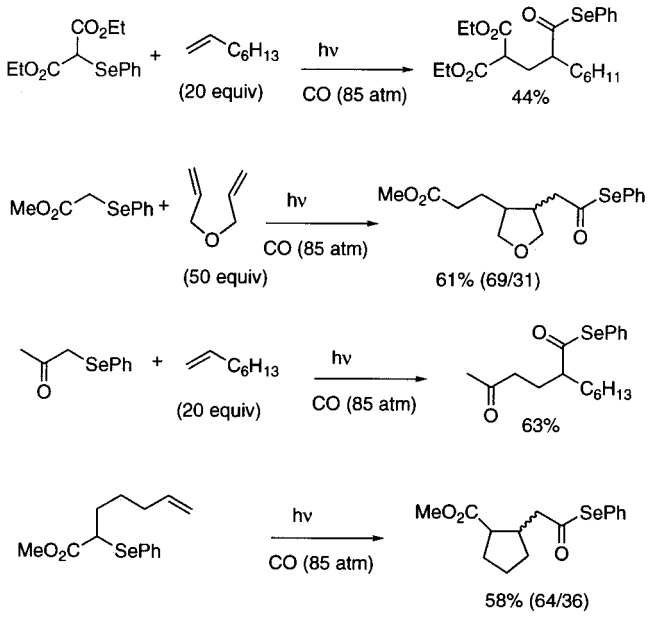
to a nonpolarized alkene giving a new alkyl radical. This then undergoes radical carbonylation, generating an acyl radical which carries the chain by a homolytic substitution process.[218] The obvious utility of this process, aside from the formation of two new C−C bonds, is the termination of the sequence by formation of a selenoester which may be subsequently used in further radical or nonradical reactions. For example, reduction of the product **40** from Scheme 75 with tributyltin hydride and catalytic tetrakis(triphenylphosphino)palladium(0) provided the corresponding aldehyde in 95% yield.

Further examples of this class of reaction, some including rearrangements of the intermediate radicals, are given in Scheme 77.[218]

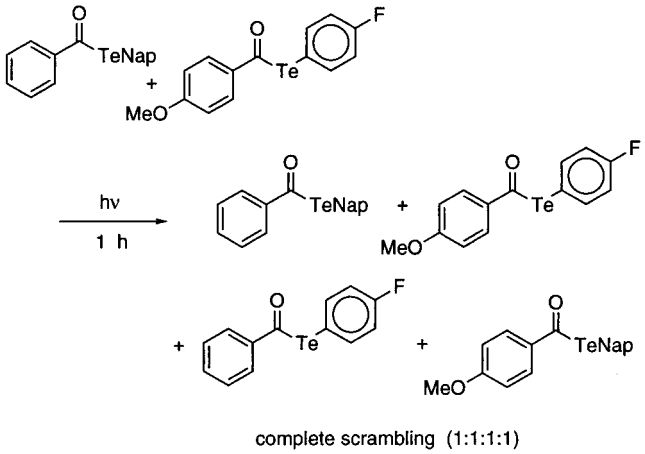
3. At Tellurium

Very few examples exist of homolytic substitution involving attack by an acyl radical at tellurium with

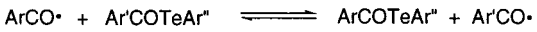
Scheme 77



Scheme 78



Scheme 79

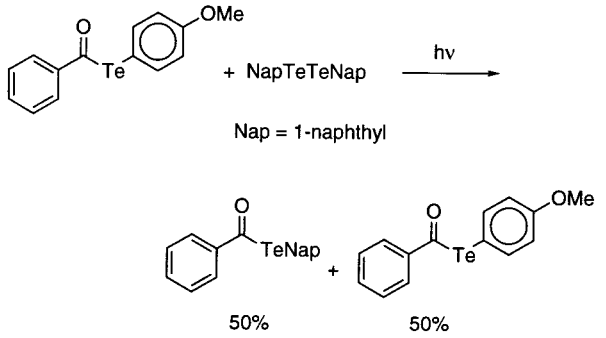


expulsion of a further carbon radical, all of which make use of acyl tellurides themselves as the acyl radical precursor. Thus, it was demonstrated by the Crich group that on white light photolysis, a mixture of two distinct acyl tellurides undergoes complete scrambling within minutes at room temperature (Scheme 78). The crossover, which is thought to involve the degenerate process of Scheme 79 whereby one acyl radical expels a second in a homolytic substitution at tellurium, is a likely undetected background process to all radical chemistry of acyl tellurides.[147] It was also demonstrated that, not surprisingly, acyl radicals displace aryltelluryl radicals efficiently from diaryl ditellurides (Scheme 80).[147]

C. Homolytic Substitution at Carbon

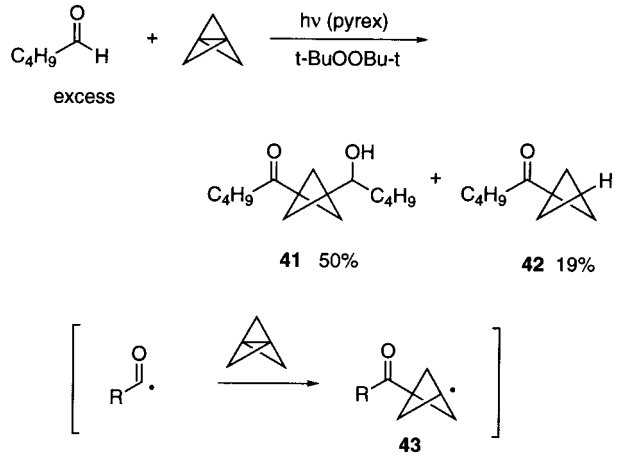
Homolytic substitution at carbon is a very rare process. The peroxide-initiated reaction of acetaldehyde with [1.1.1]propellane may be considered as such a reaction. This process was studied by Wiberg

Scheme 80



and Waddell who found that the peroxide-initiated radical reaction of [1.1.1]propellane with aldehydes took place to give two types of addition products across the central σ-bond.[219] With a large excess of acetaldehyde and using a peroxide initiator, a 2:1 adduct predominated over the 1:1 adduct. With butyraldehyde, more 1:1 adduct (**42**) was formed, although the reaction still favored the 2:1 adduct (**41**). Both adducts may be viewed as being formed in chain processes initiated by the attack of an acyl radical at a bridgehead carbon in the propellane, which is effectively a homolytic substitution at carbon. Subsequently, chain transfer occurs when the 3-acetylbicyclo[1.1.1]pentyl radical **43** either abstracts hydrogen from the aldehyde, leading to the 1:1 adduct, or adds to an aldehyde carbonyl, leading to the 2:1 adduct (Scheme 81). The change in ratio in going

Scheme 81



from acetaldehyde to butyraldehyde suggests that the addition to the carbonyl carbon is subject to steric hindrance.

Michl and co-workers studied the reaction of [1.1.1]-propellane with biacetyl and benzil.[220] Photolysis of biacetyl with [1.1.1]propellane leads to addition of the acetyl radical across the central C−C bond, exactly analogously to the process outlined in Scheme 81. This is followed by addition of the adduct radical to a carbonyl C of biacetyl (see section IV.C.3) and subsequent fragmentation giving 1,3-diacetylbicyclo-[1.1.1]pentane as the overall product.[220a] A similar reaction is observed on photolysis with benzil; however, the concentrations were adjusted such that the initial adduct (**43**, in Scheme 81) underwent reaction with one or more further molecules of the propellane before final chain transfer by attack at the carbonyl C of benzil. In this manner a series of doubly end-functionalized rigid polymers, dubbed the staffnanes, were prepared.[220b]

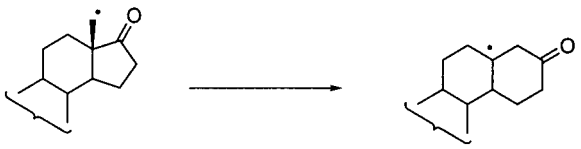
VII. Cyclization Reactions of Acyl Radicals

A. Cyclization onto C–C Multiple Bonds

1. Mechanism and Regiochemistry: The Exo/Endo Problem

The controlled cyclization of acyl radicals onto carbon−carbon double bonds constitutes a very useful synthesis of cycloalkanones, albeit one that is complicated by the possible formation of regioisomeric (exo/endo)-mixtures. The origin of these isomers has long been a subject of debate, and an appreciation is of some importance in selecting the correct conditions for such a cyclization. For instance, for any given example, the exo/endo ratio of products may simply reflect the intrinsic kinetic partitioning between direct ring closure in the exo- and endo modes. If so, the ratio will not be adjusted by changing the concentration of the trapping reagent but might still be manipulated by adjusting the reaction temperature. On the other hand, if the ratio is a function of an equilibration process, then it can be readily biased by changing the concentration of the trapping reagent. The precise mechanism of thermodynamic equilibration of β-acylalkyl radicals has been the subject of considerable discussion in the literature. As early as 1961, a group of workers at Schering noted the rearrangement of a 17-ketosteroid, following hydrogen-atom abstraction from the C13 methyl group, to give a D-homo-18-norsteroid (Scheme 82).[221]

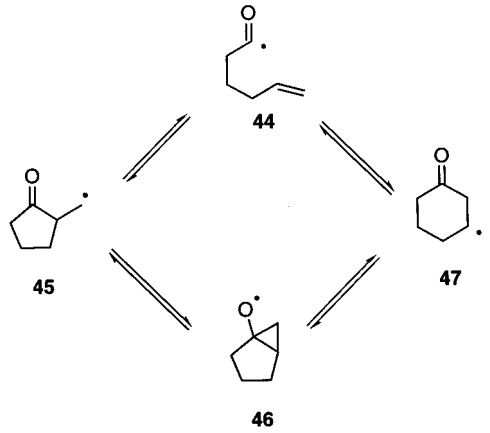
Scheme 82



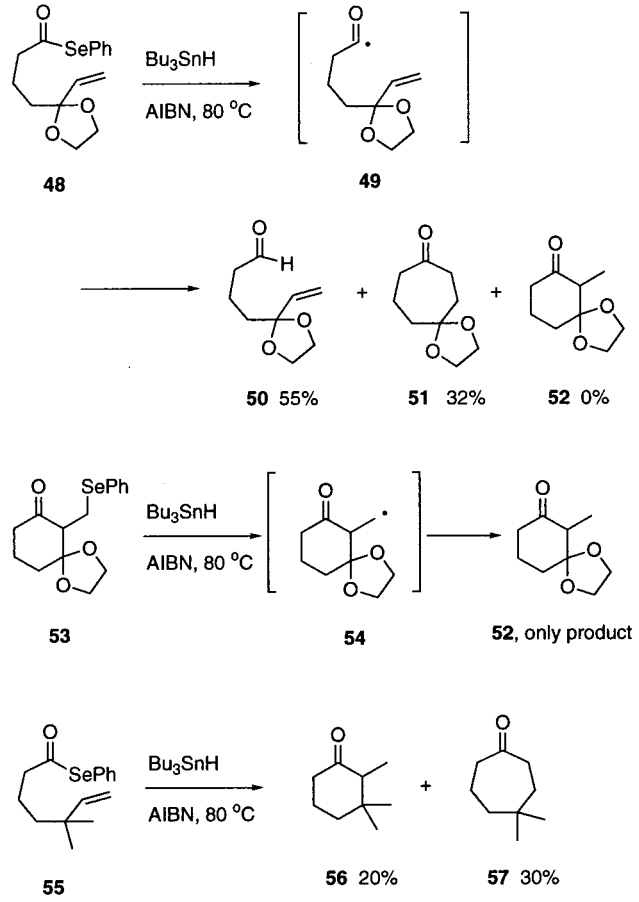
In collaboration with Barton, they suggested that the expansion might occur via β-scission to give an acyl radical followed by recombination to give the larger ring. Following the exploitation of this type of rearrangement some 25 years later by the Beckwith and Dowd groups,[222−224] the discussion has expanded to encompass the question of rearrangement via a cyclopropyloxyl radical either as a true intermediate or a transition state (Scheme 83). Subsequently, all of the major players in the field have addressed aspects of this problem. In their study of the tin hydride mediated cyclizations of 6-heptenoyl selenides, Crich and co-workers noted the formation of significant proportions of cyloheptanones in addition to the anticipated 2-methylcyclohexanones.

In an extreme example, acyl selenide **48** was found to give aldehyde **50** and cycloheptanone **51** in 55% and 32% yields, respectively, while no cyclohexanone **52** was identified (Scheme 84).[125] Subsequently, the alkyl selenide **53** was prepared and treated with tin hydride under comparable conditions when the me-

Scheme 83



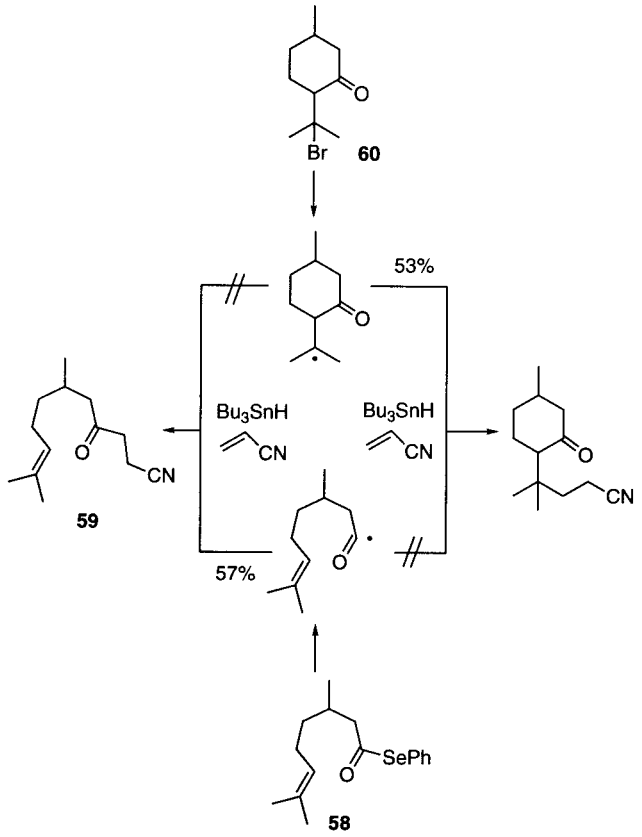
Scheme 84



thylcyclohexanone **52** was formed to the exclusion of the cycloheptanone and the aldehyde (Scheme 84).[226] The authors concluded (i) that the acyl radical **49** derived from acyl selenide **48** cyclized directly in the endo mode and (ii) that fragmentation of cyclohexylmethyl radical **54** to acyl radical **49** is not a viable process, i.e., acyl radical cyclization is not reversible. Cyclization of the acyl selenide **55** (Scheme 84) gave cyclohexanone **56** and cycloheptanone **57** in 20% and 30% isolated yields, respectively, from which it was concluded that the endo-directing effect of the allylic acetal in radical **49** is not merely steric but derives in part from the conformational bias of allylic ethers.

Boger and Mathvink also arrived at the conclusion that acyl radical cyclizations are irreversible on the

Scheme 85



basis of the experiment outlined in Scheme 85. Here, it was demonstrated that the acyl radical derived from selenide **58** was efficiently trapped by acrylonitrile, to the exclusion of cyclization, whereas none of the ring-opened product **59** was formed on treatment of bromide **60** with tin hydride and acrylonitrile under the same conditions.[135]

In a further experiment, Chatgilialoglu and coworkers studied the cyclization of acyl selenide **61** with tin hydride in benzene at 80 °C. At the concentrations employed, the products (ratios) were aldehyde **62** (36%), alkene **63** (11%), cyclopentanones **64** (47%), and cyclohexanones **65** (6%) (Scheme 86). At the same time, the stereoisomerically pure thiocarbonate **66** was heated to 80 °C in benzene with a lower concentration of the poorer hydrogen-atom donor tris(trimethylsilyl)silane. The only products formed were the stereoisomerically pure *trans*-cyclopentanone **64** and the cyclohexanones **65** in the ratio 6:1. The stereochemically pure nature of the cyclopentanone and the absence of aldehyde and alkene in this latter experiment exclude any possibility of the rearrangement occurring via an acyl radical.[227] Thus, three different groups have independently arrived at the same conclusion, namely, that acyl radical cyclizations are not reversible on any kinetically significant time scale and that endo mode products can arise both by Beckwith/Dowd-type rearrangement of exo cyclized radicals or directly from the acyl radical depending on the substitution patterns employed. On the basis of these results earlier,[190] and even later,[55] interpretations of the formation of cyclohexanone in the cyclization of 5-hexenoyl chloride and 5-hexenal in terms the

Scheme 86

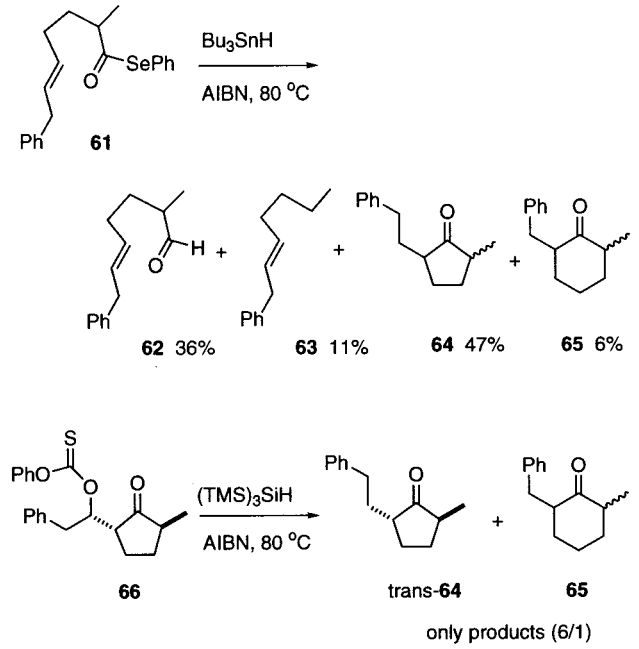
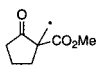
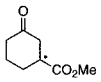


Table 11. Kinetic Parameters for Rearrangement of *β*-Ketoalkyl Radicals

substrate	product	log A (log A/s^{-1})	Ea (kcal mol^{-1})	k_{25} (s^{-1})	ref
		10.6 ± 0.6	8.0 ± 0.9	5.2×10^4	225
		10.5 ± 0.5	9.4 ± 0.6	4.2×10^3	225, 227

reversibility of the acyl radical cyclizations may be reasonably discounted.

Accurate kinetic data for the ring expansion of cyclopentanonylmethyl radicals have recently been determined and are collected in Table 11.[225] Rate constants for related ring expansions have also recently been determined by the Curran group.[228] Kinetic parameters for the cyclizations of a number of acyl radicals have also been determined, and these are grouped in Table 12. Ingold and co-workers determined the rate constant for disappearance of the parent 5-hexenoyl radical (Table 12, entry 1) by the laser flash photolysis method but did not characterize the product mixture which might consist of a combination of 5-exo and 6-endo cyclized radicals.[55] Nevertheless, it is reasonable to assume in this example that by far the kinetically most significant process will be the 5-exo cyclization. Chatgilialoglu and co-workers, using a competition kinetic method, were able to tease out the full set of kinetic parameters for the 5-exo and 6-endo cyclization processes for all stereoisomers as indicated in Table 12, entries 2−5. As anticipated, the 5-exo process was found to be significantly more facile than the 6-endo one, despite the thermodynamic preference for the latter, reflecting the early transition state for this type of radical cyclization.[227]

Theoretical calculations on acyl radical cyclizations and the subsequent ring expansion process have been

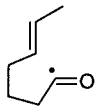
Table 12. Kinetic Parameters for Acyl Radical Cyclizations

substrate	product	log A (log A/s^{-1})	Ea (kcal mol^{-1})	k_{25} (s^{-1})	ref
	a	nd	nd	$2.2 \pm 0.2 \times 10^5$	55
		9.6	6.0	1.6×10^5	227
		9.6	6.1	1.3×10^5	227
		9.0	6.4	2.0×10^4	227
		8.7	6.8	5.2×10^3	227

[a] Products undetermined, see text.

conducted by two groups. Chatgilialoglu and co-workers used high-level ab initio methods to study the chemistry of the simple 5-hexenoyl radical (**44**). As illustrated in Figure 3, the transition state **67** for cyclization in the 5-exo mode was found to be some 1.7 kcal mol^{-1} than that of **68** for the 6-endo mode. Both transition states were found to be chairlike. Interestingly, in the 5-exo mode the approach vector was found to subtend an almost perfect tetrahedral angle with the alkene, whereas in the 6-endo mode a more perpendicular approach was indicated (Figure 3)

The same group used semiempirical methods to assess the cyclization and subsequent rearrangement of the homologous radical **69** and found the transition state for the 5-exo cyclization to be 0.65 kcal mol^{-1}, lower than that for the 6-endo process, in excellent agreement with experiment. This study also tenta-



69

tively concluded that the direct rearrangement of the 5-exo-closed radical to the 6-endo radical was more facile than any mechanism involving opening to the acyl radical or going via a cyclopropyloxyl radical intermediate.

Ryu and co-workers have also examined the chemistry of acyl radical **44** by ab initio methods, with particular emphasis on the mechanism of rearrangement of the 5-exo-closed radical **45** to the 6-endo one **47**.[229] The transition state **70** for the closure of **45** to **46** was localized, as was that (**71**) for the subsequent cleavage to **47**. Interestingly, the cyclopropyloxyl radical **46** was found to be in a very shallow potential well and, at some levels of theory, not even a

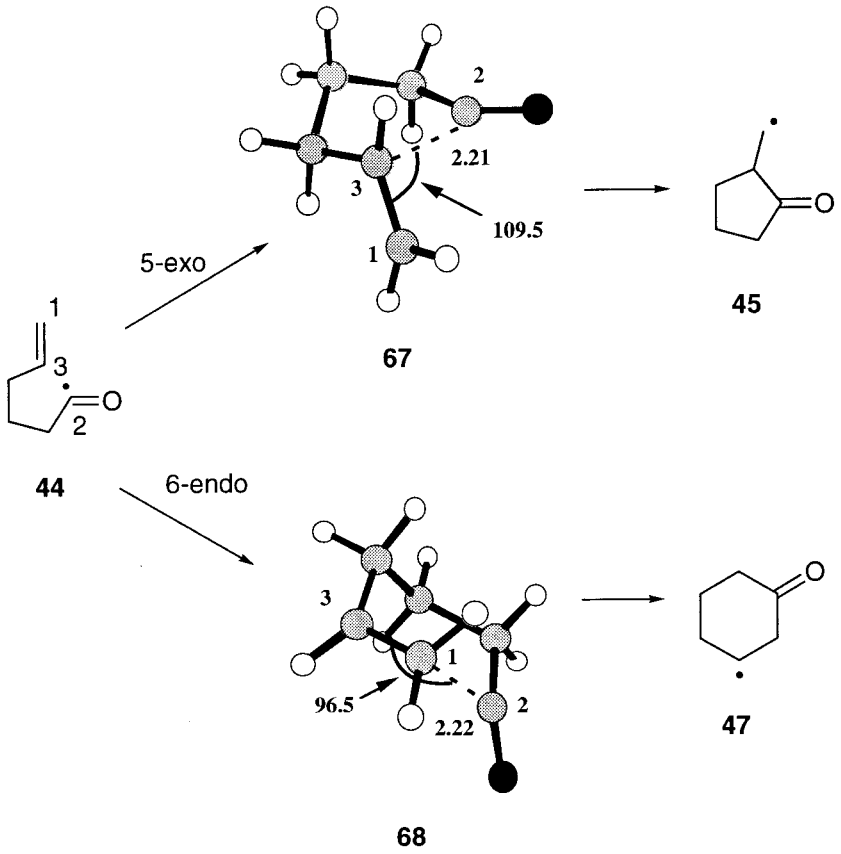


Figure 3.

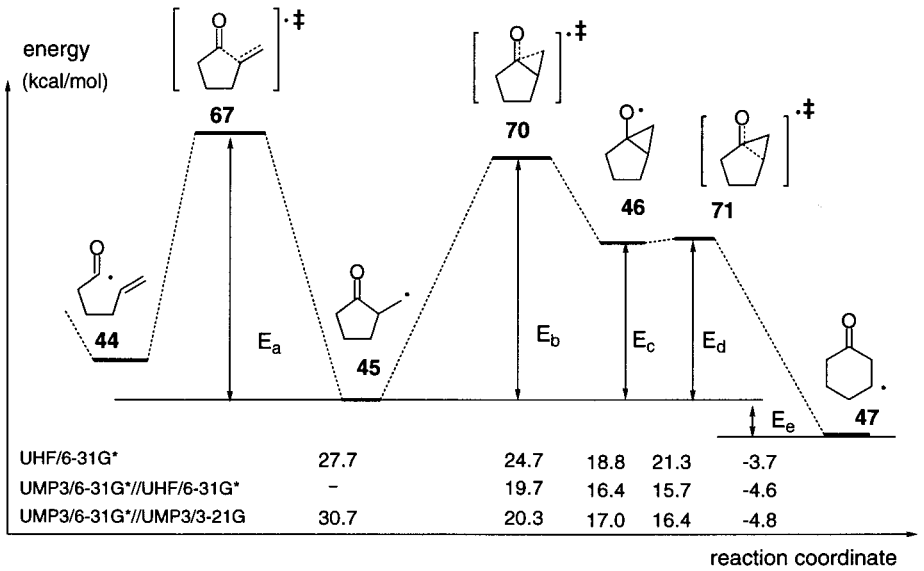


Figure 4.

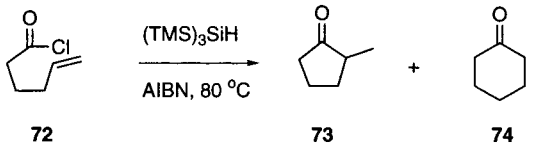
minimum (Figure 4). The conclusion, which is in accord with the above study of Chatgilialoglu and coworkers, is that the ring expansion process does not necessarily proceed via a discrete cyclopropyloxyl radical intermediate and that there is a low-energy direct path.[230] It is also readily seen from Figure 4 that the unambiguous generation of any fused cyclopropyloxyl radical akin to **46** will result in preferential cleavage of the endocyclic bond for kinetic, as well as thermodynamic, reasons. Indeed, this is known to be the case in practice,[231−237] unless cleavage of the exocyclic bond is favored by radical stabilizing substituents.[237] Finally, it is again evident from this study that any mechanism for rearrangement of the kinetic closed product to the thermodynamic one involving cleavage to an acyl radical may be discounted.

2. Cyclizations of 5-Hexenoyl Radicals

The cyclization of the parent 5-hexenoyl radical was first described in 1972 by Cekovic who reported the isolation of cyclohexanone (**74**) in 36% yield and the absence of methylcyclopentanone[238] on treatment of 5-hexenoyl chloride (**72**) with tributyltin hydride

under unspecified conditions. Subsequently, the same cyclization was investigated by Walsh with contradictory results, namely, the predominant formation of 2-methylcyclopentanone (**73**).[239] Both groups noted the formation of esters as important byproducts and of the simple reduction product (see section IV. A.2). In light of the above discussion, it is clear that the differing spectra of 5-exo to 6-endo products in these reactions arise from the use of different concentrations of stannane, with that of Walsh being sufficient to quench the kinetic 5-exo-closed radical whereas Cekovic must have operated under more dilute conditions, leading to the observed thermodynamic product. Chatgilialoglu investigated the same cyclization but replaced tributyltin hydride by $(TMS)_3SiH$. A much cleaner reaction mixture and a 4:1 ratio of methylcyclopentanone and cyclohexanone was obtained owing to the various nonradical reactions of acyl chlorides and stannanes having been eliminated.[189] Nevertheless, some aldehyde was obtained, and hydrosilylation of the alkene reduced the overall yield. The definitive experiment was performed by Ingold and co-workers (Scheme 87) who

Scheme 87

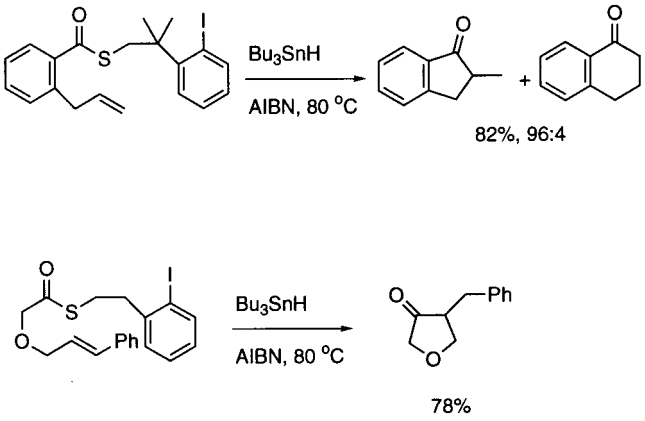


$[(TMS)_3SiH]$ (M)	ratio (5-exo:6-endo)
0.04	1.5:1
0.10	2.4:1
0.30	5.9:1
0.60	9.7:1

reacted 5-hexenoyl chloride (**72**) with $(TMS)_3SiH$ and AIBN under a range of concentrations. The increased ratio of methylcyclopentanone (**73**) to cyclohexanone (**74**) at higher concentrations of silane clearly establishes the nature of the kinetic and thermodynamic products.[55]

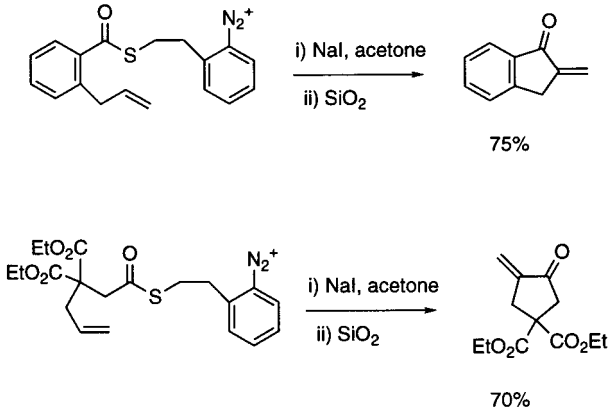
Crich and Yao described several cyclizations of substituted 5-hexenoyl radicals using their novel thioester precursors. The examples in Scheme 88[198]

Scheme 88



were conducted using 3.2×10^{-2} M Bu_3SnH in benzene at reflux with AIBN initiation, whereas

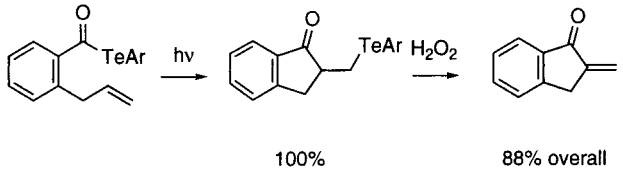
Scheme 89



those in Scheme 89 were run in acetone solution with iodide as the initial electron donor.[128] Under the tin hydride conditions, the reaction is necessarily reductive. Using the diazonium salt precursors, the initial product is an iodomethyl ketone which rapidly loses HI to give the product of an overall oxidative cyclization: this is the synthetic equivalent of cyclization onto an alkyne under tin hydride conditions.

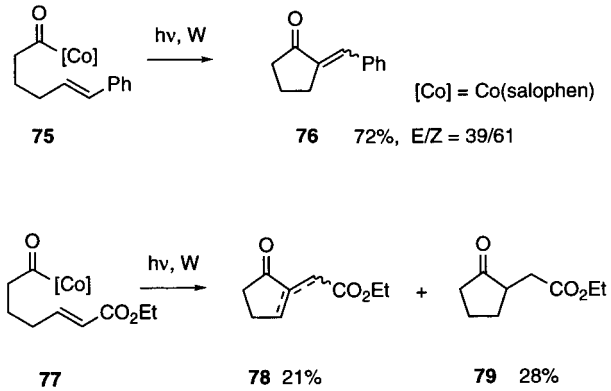
An exactly analogous overall oxidative cyclization, leading to exomethylene cyclopentanones, may be effected on simple white light photolysis of an acyl aryl telluride followed by brief treatment with hydrogen peroxide (Scheme 90).[147]

Scheme 90



Yet another method of achieving the same type of oxidative cyclization involves the use of acylcobalt salophens as demonstrated by the work of Pattenden (Scheme 91). Here, however, the effect of alkene

Scheme 91

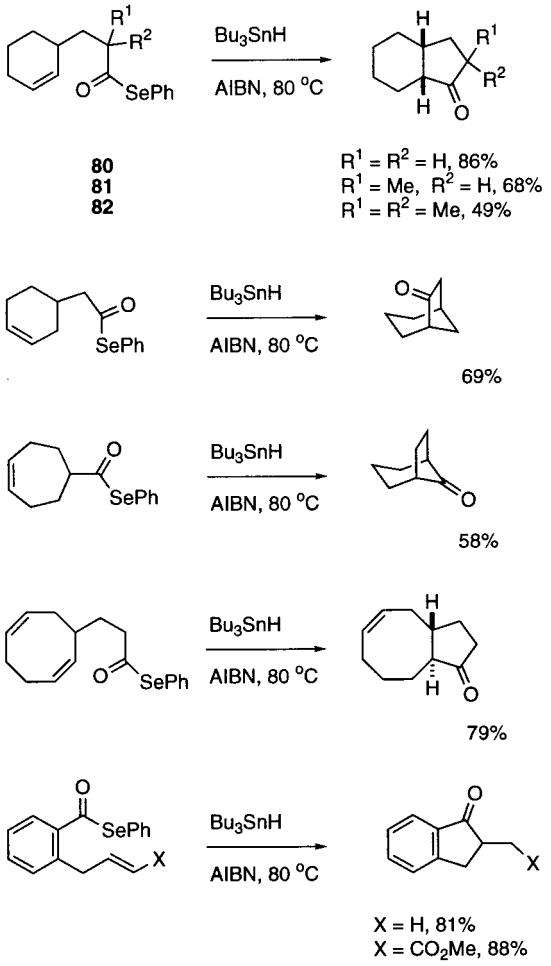


substituents on the decomposition of the intermediate alkylcobalt salophen must be recognized. Thus, in the case of **75**, the initial cyclized product is a benzylcobalt salophen which undergoes a formal β-elimination to give the final product **76**, whereas with the related substance **77**, the intermediate is a 1-carboethoxy-

cobalt salophen in which the elimination to **78** is less favored. The competing process of protonolysis of the final C−Co bond to give **79** therefore comes into play.[215]

By far the most common source of acyl radicals for use in 5-exo/6-endo-type cyclizations has been the acyl selenides used in conjunction with stannanes. Many examples of this type were described by Boger and Mathvink. Those presented in Scheme 92 all

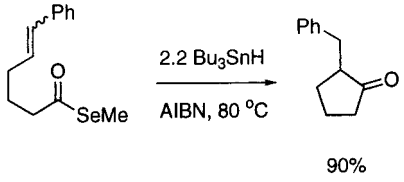
Scheme 92



involve cyclization in the 5-exo mode and proceed to give fused and bridged systems.[5,135] Noteworthy is the fall off in yield in the series **80**−**82** with increasing methylation α to the acyl selenide. Thus, the normal cyclization rate acceleration brought about by the presence of a *gem*-dimethyl group is not sufficient to compensate for the increased rate of decarbonylation to give a tertiary radical.

Scheme 93 shows a rare example of the use of an

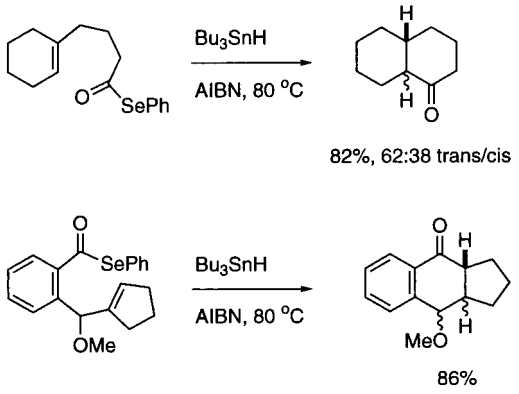
Scheme 93



acyl methyl selenide in a tin hydride mediated cyclization reported by Schwartz and Curran. An excellent yield was obtained in this 5-exo cyclization, but 2 equiv of stannane was used to fully consume the substrate owing to competing reaction of $MeSeSnBu_3$ with the stannane (see section IV.A.5).[138]

Scheme 94 shows two further examples taken from

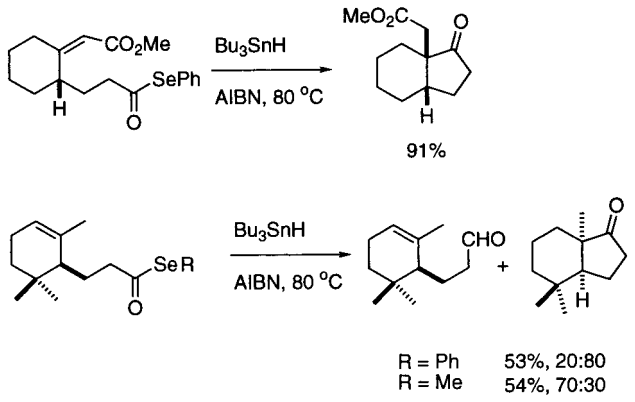
Scheme 94



the work of Boger and Mathvink in which cyclization occurs in the formal 6-endo mode.[135] The likelihood is that these cyclizations, which set the stage for a series of elegant tandem processes (section X), take place in the direct 6-endo mode, rather than by the 5-exo followed by a rapid Beckwith/Dowd expansion, owing to the 5-exo mode being retarded by the additional alkene substitution.

By way of contrast, we draw attention to the two examples of Scheme 95 taken from the work of

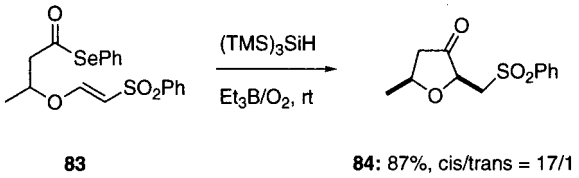
Scheme 95



Whiting,[240] Fernandez-Mateos,[241] and their respective co-workers. These two cyclizations proceed in the 5-exo mode despite substitution at the internal position of the alkene. In the one case this must be due to the polarization of the alkene and in the other further retardation of the 6-endo mode by a higher energy conformation required at the transition state for the formation of a bicyclic skeleton.

P. A. Evans has reported on the highly diastereoselective 5-exo-trig cyclization of the acyl selenide **83** giving the cis-disubstiuted tetrahydrofuran **84** in 87% yield on exposure to $(TMS)_3SiH$ and the Et_3B/O_2 combination as the initiator at room temperature (Scheme 96).[242] The selectivity is explained in the standard manner through the intervention of a Beckwith, chairlike transition state. Related ex-

Scheme 96

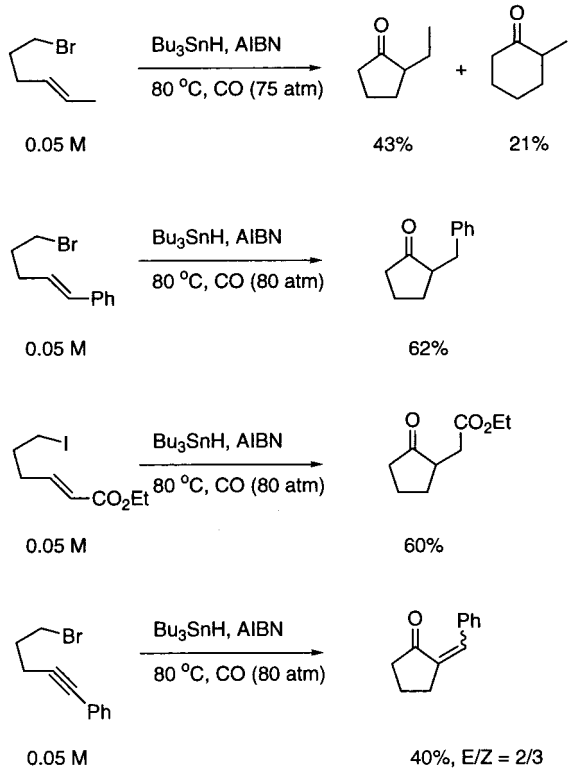


83 **84:** 87%, cis/trans = 17/1

amples in which the SO_2Ph group was replaced by CO_2Me behaved similarly.[243,244]

Ryu, Sonoda, and co-workers have developed their radical carbonylation chemistry into an elegant [4+1] annelation sequence for the synthesis of cyclopentanones from 4-pentenyl halides.[245,246] In this chemistry a stannane, silane, or germane is used to generate a 4-pentenyl radical in the presence of 80 atm of CO pressure. Carbonylation occurs to give a 5-hexenoyl radical, which then undergoes cyclization. Examples of this type of process are given in Scheme 97. The last example in this scheme shows a rare

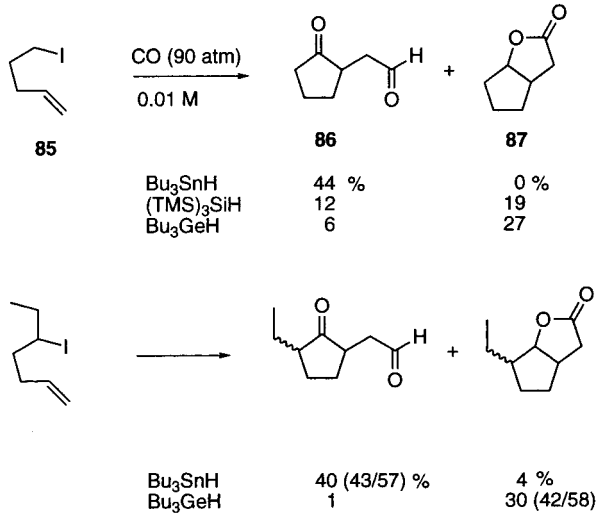
Scheme 97



example of a 5-exo-dig cyclization of an acyl radical onto an alkyne.

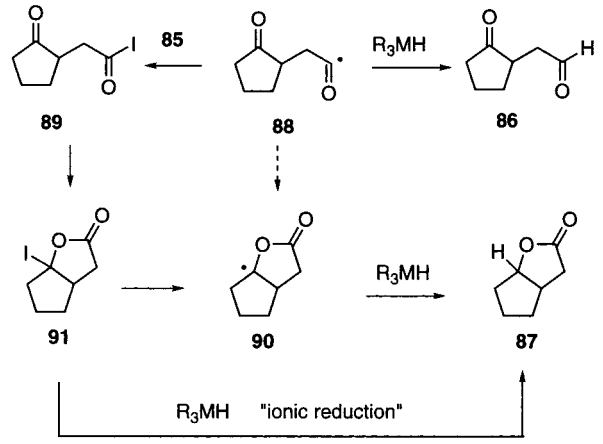
When the same reaction is conducted under a higher pressure of CO and at a lower concentration of Bu_3SnH, the 5-exo cyclized radical is trapped by a further molecule of CO which leads, after chain transfer, to an aldehyde, as exemplified by the transformation of **85** to **86** in Scheme 98. Although this is formally a tandem CC bond-forming sequence, it is considered here because it is effected by only a minor change in reaction conditions from those employed in Scheme 97.[247] When attempts were made to further increase the yield of **86** by substituting Bu_3GeH for Bu_3SnH, with its poorer hydrogen-donating capabilities, lactone **87** was unexpectedly

Scheme 98



observed as the major product (Scheme 98). The authors advance two possible mechanisms to rationalize the formation of this product. In one the initial cyclized, carbonylated radical **88** undergoes a 5-endo cyclization onto the ketone giving rise to radical **90**, which is then trapped by the hydride to give the observed product **87**. In the other, **88** takes place in an iodine-atom transfer chain with the substrate **85** to give the highly electrophilic acyl iodide **89**. This then undergoes cyclization to give the iodide **91**, which is finally reduced by the stannane by radical or ionic mechanism (Scheme 99). The failure of

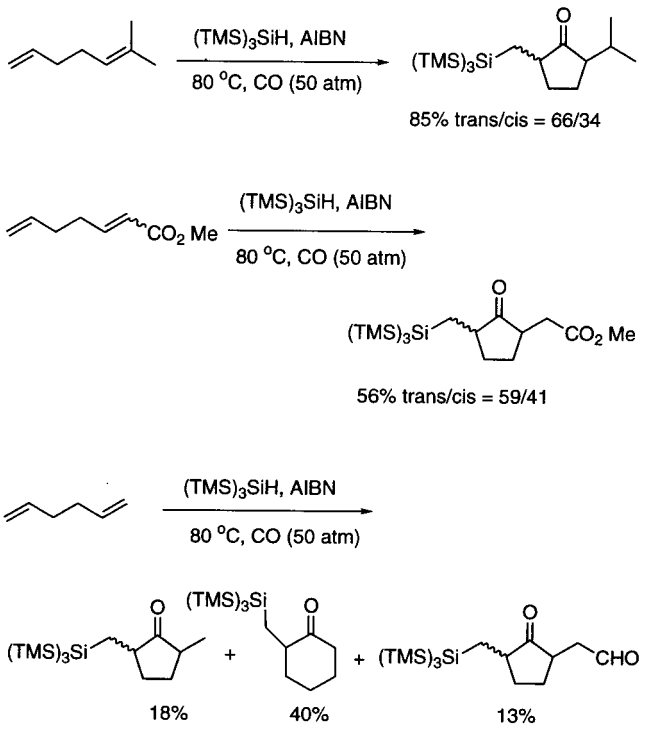
Scheme 99



5-endo cyclization with the corresponding bromides favors the latter atom transfer mechanism. As might be expected, $(TMS)_3SiH$ has intermediate behavior between that of the stannane and germane (Scheme 98).

A further variant on the radical carbonylation/acyl radical cyclization theme involves the silyl carbonylation of hexa-1,5-dienes (Scheme 100).[248] Here, the sequence is initiated by addition of a tris(trimethylsilyl)silyl radical to the least substituted terminus of the diene. Carbonylation and acyl radical cyclization then ensues in the normal way. When the cyclization takes place onto an internal alkene, only the 5-exo mode is observed and further carbonylation was not a problem. However, with simple hexa-1,5-

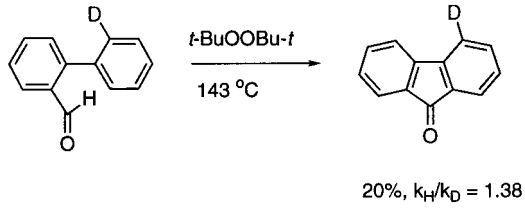
Scheme 100



diene, the formation of 6-endo products and overcarbonylation complicated matters.

In addition to the above body of work, there are several early examples of acyl radicals, derived by hydrogen-atom abstraction from aldehydes, cyclizing onto arenes, albeit not efficiently. Thus, in one of the first studies in this area, Denney and Klemchuk heated 2-phenylbenzaldehyde in the presence of di-*tert*-butyl peroxide and observed the formation of fluorenone in 20% yield (Scheme 101). Through the

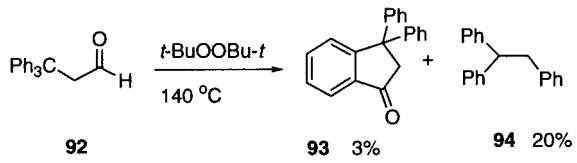
Scheme 101



use of labeled material, an isotope effect of k_H/k_D = 1.38 was obtained for the ring closure.[249]

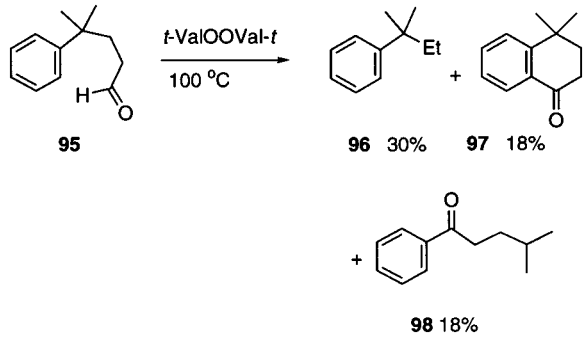
Curtin and Kauer studied the pyrolysis of β,β,β-triphenylpropionaldehyde (**92**) in the presence of di-*tert*-butyl peroxide and observed a meager yield of a diphenylindanone **93**, together with 1,1,2-triphenylethane (**94**) resulting from decarbonylation and a subsequent neophyl rearrangement (Scheme 102).[250]

Scheme 102



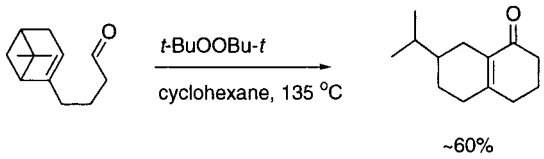
Urry and co-workers described an interesting reaction in which a 4-phenylbutyraldehyde (**95**) was heated to 100 °C in the presence of a peroxide initiator. The products were the expected decarbonylated species (**96**), that of a formal 6-endo-ring closure (**97**) and, most interestingly, a rearranged species (**98**) resulting from *ipso*-substitution on the aromatic ring (Scheme 103).[251]

Scheme 103



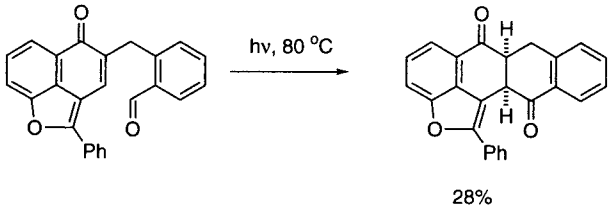
A further example of an aldehyde-derived acyl radical cyclization is given in Scheme 104. This

Scheme 104



formal 6-endo cyclization is followed by a cyclobutylcarbinyl ring opening: a well-known reaction in the pinene series. Here the substitution pattern is such that the cyclization probably takes place directly in the 6-endo mode, although the conditions are such that rapid equilibration of any kinetic 5-exo cyclized products would certainly take place.[252,253] In this context, we note that Julia studied the cyclization of 5-hexenal under closely analogous conditions and obtained only cyclohexane, thus clearly illustrating the equilibrating nature of the conditions.[254,255] Yet another 6-endo cyclization of an aldehyde-derived acyl radical is taken from Barton's approach to the tetracyclines (Scheme 105).[256]

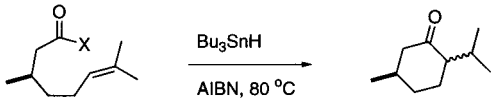
Scheme 105



3. Cyclizations of 6-Heptenoyl Radicals

Early work on the cyclization of 6-heptenoyl radicals was conducted by Cekovic who studied the reaction of citronelloyl chloride (**99**) with tributyltin hydride (Scheme 106) and obtained a 43% yield of an unspecified mixture of menthone and isomenthone (**101**).[238] Bachi and Denenmark studied the identical reaction several years later and obtained an 85% yield of cyclized products with a 60/40 menthone/isomenthone ratio.[257] Evidently these authors were

Scheme 106



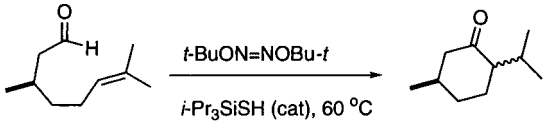
99: X = Cl
100: X = SePh

101 43% [85%, 60/40 (trans/cis), 59%]
101 84%, 56/44 [98%, 60/40]

able to suppress the competing polar reactions which normally plague the chemistry of acyl chlorides and stannanes (section IV.A.2). Boger and Mathvink obtained a 59% yield for the same transformation. Using the acyl selenide (**100**), however, Boger and Mathvink obtained an 84% yield of cyclized products as a 56:44 unspecified mixture of diastereomers,[135] whereas Bachi and Denenmark reported a 98% yield of **101**, as 1.6/1 menthone/isomenthone mixture, from **100** with tributyltin hydride.[257] Schwartz and Curran, using the acyl methyl selenide corresponding to **100**, obtained 85% of **101** as a 2/1 mixture in favor of menthone.[138] Excluding Bachi and Denenmark's cyclization of **99**, with its abnormally high yield, it is clear that acyl selenides are superior to acyl chlorides in this type of tin hydride mediated chemistry.

The cyclization of the same radical, but derived by hydrogen-atom abstraction from citronellal, has been investigated by several groups. Montheard reported that a 2/1 mixture of menthone and isomenthone was obtained when citronellal was refluxed with diacetyl peroxide in hexane,[253] whereas Kampmeier and coworkers obtained only 19% of a similar 2/1 mixture on heating citronellal to 100 °C in benzene with dibenzoyl peroxide.[258] Recognizing that the problem step in this chemistry is poor chain propagation by hydrogen abstraction from the aldehyde, Dang and Roberts heated citronellal to 60 °C in dioxane with *tert*-butylhyponitrite as the initiator and catalytic quantities of a thiol as the catalyst (Scheme 107).[259]

Scheme 107

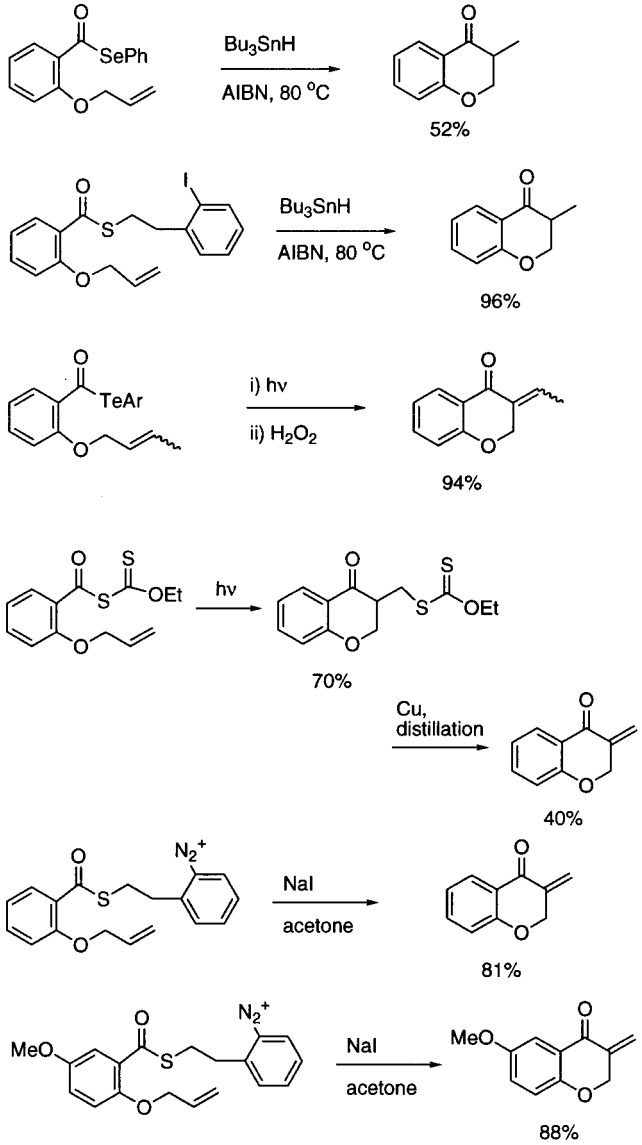


101 75%, 58/42 (trans/cis)

In this demonstration of Roberts' general concept of polarity reversal catalysis, the more electrophilic thiyl radical serves to pluck off the aldehydic hydrogen atom. The thiyl radical is regenerated by reaction of the thiol with the cyclized radical. Yields of up to 75% were reported using triisopropylsilyl thiol, and the menthone/isomenthone ratio was found to be 58/42, in fair agreement with the work of Boger and Mathvink.

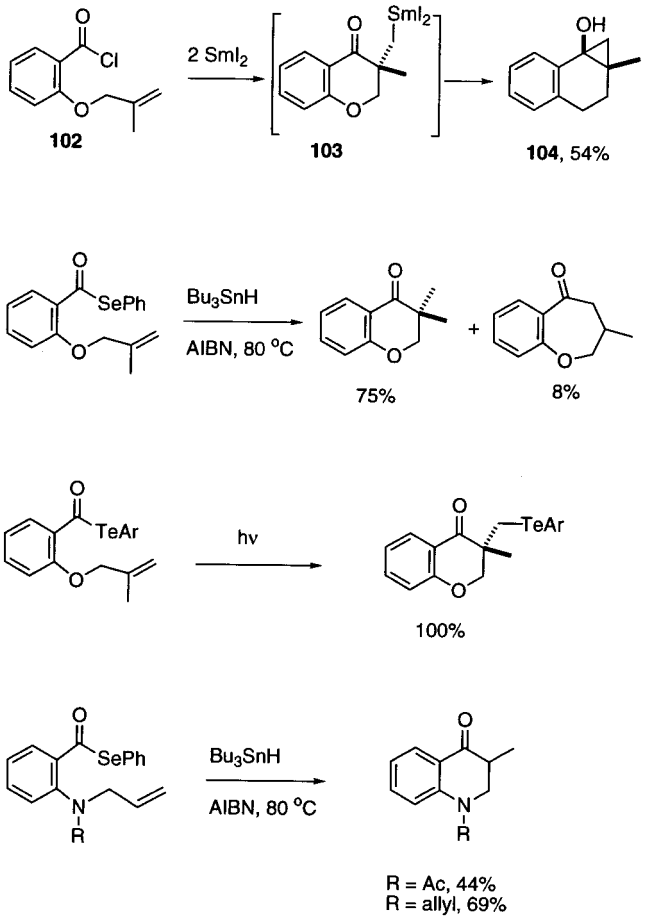
Several groups have examined the cyclizations of acyl radicals derived from allyl ethers of salicylic acid, as well as of related derivatives of anthranilic acid. Various methods of acyl radical generation have been used including the photolysis of acyl tellurides[147] and *S*-acyl xanthates,[131] the reaction of acyl selenides with tributyltin hydride,[135,260] the generation of acyl

Scheme 108



radicals from thioesters under reductive and nonreductive conditions,[128,199] and the reaction of acyl chlorides with samarium(II) iodide.[261] The examples presented in Schemes 108 and 109 serve to illustrate this type of cyclization and to highlight the differing fates of the cyclized radical according to the type of precursor used. Of particular interest is the cyclization of **102** with samarium(II) iodide giving ultimately the cyclopropanol **104** (Scheme 109). It seems most likely that the initial ring-closed radical is trapped by Sm(III) to give an organometallic species **103**, which then closes in a two-electron fashion onto the ketone giving the final product.[261] It is also noteworthy that the acyl radical derived from **102** closes in the exo mode despite the substitution at the internal position of the alkene. In contrast, Bachi and Denenmark reported that mixtures of exo and endo mode product were obtained when the same acyl radical cyclization was conducted using acyl selenide/tin hydride chemistry. Moreover, they suggested that the 6-endo product was obtained directly, rather than by the Beckwith/Dowd rearrangement, as the product ratio was independent of stannane concentration.[257] With the corresponding acyl telluride, Crich and co-

Scheme 109

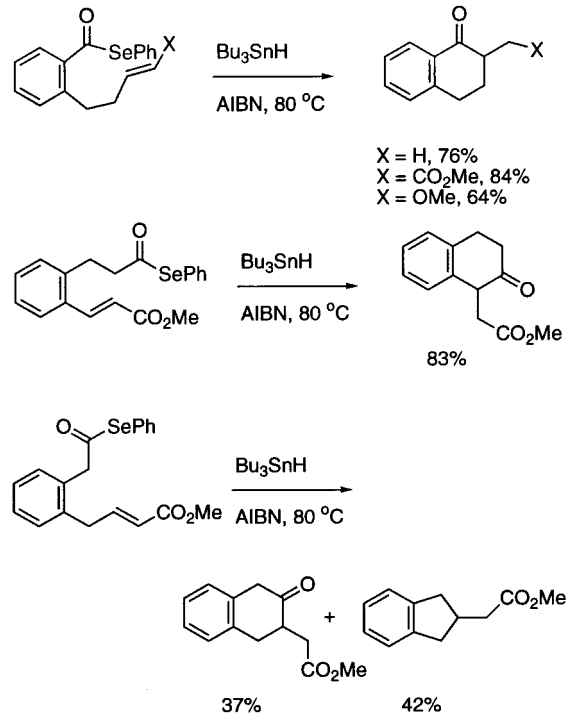


workers saw only the exo mode product, in line with the work of Kagan.[147] It is also noteworthy in these and all other 6-exo-type cyclizations that 1,5-hydrogen-atom abstraction, by the acyl radical, to give an aldehyde and an allylic radical is not a problem. This feature is especially noteworthy in the examples of Schemes 108 and 109 where the allyl C−H is further weakened by the α-oxygen atom.

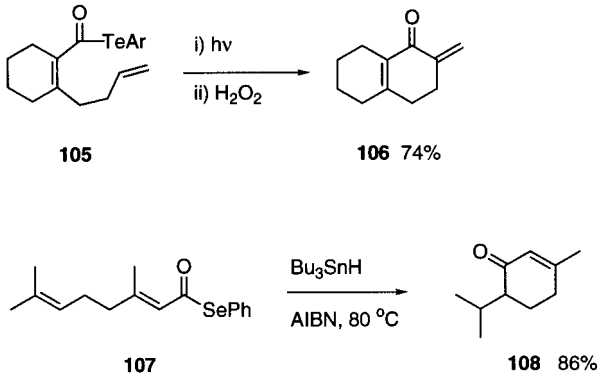
Related, fully carbocyclic examples are presented in Scheme 110.[135] The first three of these serve to highlight the nucleophilic character of the acyl radical, with higher yields being obtained with the more electron-deficient olefins. The last example in this scheme demonstrates that decarbonylation to give a benzyl radical is a competing process with a 6-exo-trig cyclization.

Simple α,β-unsaturated acyl radicals also take part readily in 6-exo-trig cyclizations, as shown by the examples in Scheme 111. Remarkably, the transformation of **105** to **106** goes in good yield, even after the oxidative elimination of the first formed α-telluromethyl ketone, with the product showing no tendency to undergo aromatization.[147] The efficient cyclization of the geranoic acid derived selenide **107** to piperitone **108** illustrates the lack of importance of the initial alkene stereochemistry on these α,β-unsaturated acyl radical cyclizations. In effect the acyl radical must be delocalized to some extent, as shown in Scheme 112 (but see section II.B), which reduces the barrier to rotation about the C=C double bond and permits cyclization even starting from a

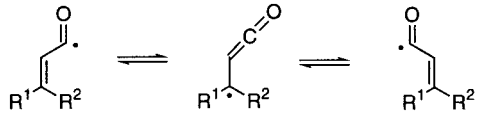
Scheme 110



Scheme 111



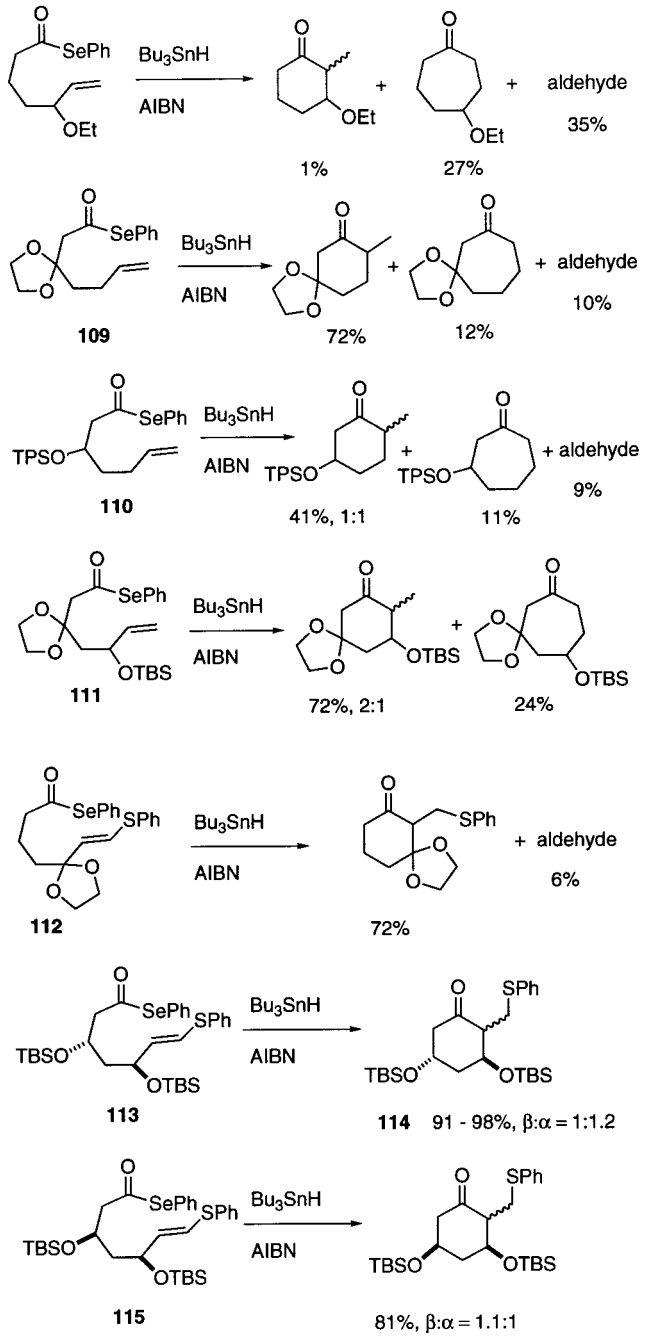
Scheme 112



trans-alkene (also see Scheme 71).[262]

The influence of ethers and ketals on the cyclization of 6-heptenoyl radicals was studied by Crich and co-workers in the course of their synthesis of the 1α,-25-dihydroxyvitamin D_3 A ring.[125,260,263] As is readily apparent from the body of work assembled in Scheme 113 and that already shown in Scheme 84, a single acetal or ketal in the allylic position apparently retards cyclization and directs any cyclization that does occur to the 7-endo mode. As discussed above (section VII.A.1), it was felt that this was a consequence of the conformation of the allylic ether moiety. Moving the ketal to the 3-position (**109**) has the effect of significantly increasing the cyclization yield; moreover, the favored product is now the six-membered ring. A similar, but smaller, effect is seen when a silyl ether (**110**) is placed at the 3-position. These latter

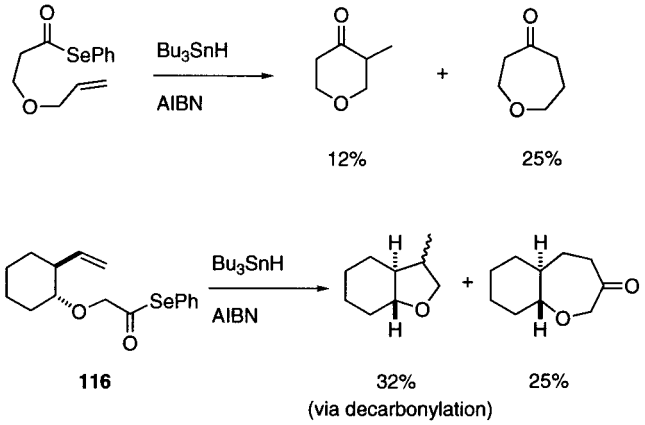
Scheme 113



effects obviously arise from the restriction of conformation imposed by the substituents and are related to the well-known "gem-dimethyl" effect. A combination of a 3-ketal and an allylic ether (**111**) results in almost quantitative cyclization, but again the endo-directing effect of the allylic ether is noticeable. This directing effect may be overcome by substituting the terminal position of the olefin as in **112**. Finally, the combination of two ethers at the 3- and 5-positions and a terminally substituted alkene (**113** and **115**) permits excellent yields of the 6-exo-substituted products. Unfortunately, there was little or no stereoselectivity in either of these two cyclizations, but this had no consequence on subsequent synthetic work which involved oxidation of **114** to the corresponding sulfoxide, followed by syn-elimination to give an α-methylene cyclohexanone.

The consequences of placing the allylic ether moiety in the 6-heptenoyl chain were also briefly investigated (Scheme 114). Again, a substantial proportion

Scheme 114



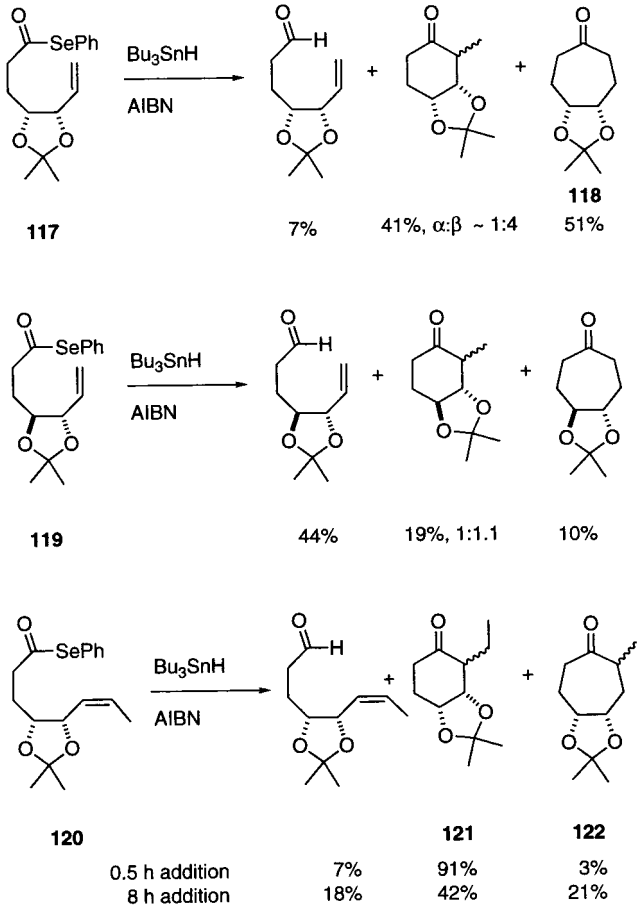
of the endo cyclized product was observed.[260] Moreover, the contrast between this example with its endocyclic allylic ether giving mainly the endo product and the closely related examples of Schemes 108 and 109 should be noted. Evidently, the exo-directing effect of the benzene ring overcomes any effect of the allylic ether. In a further saturated substrate **116** containing endocyclic oxygen, endo mode cyclization was again preferred.[260] Here, too, it is noteworthy that decarbonylation to the alkoxymethyl radical competes effectively with the cyclization (Scheme 114).

Scheme 115 presents examples conducted with a view to ascertaining the effect of an allylic oxygen constrained within a five-membered ring.[226] In the *erythro* series (**117**), the cyclization is efficient and the exo/endo ratio was found to be 4/5. With the corresponding *threo* substrate **119**, the overall yield of cyclized product was much lower. This difference in passing from the *erythro* to the *threo* series giving cis- and trans-fused products, respectively, presumably simply reflects the fact that in the *erythro* series the two chains are somewhat preorganized for cyclization whereas the *threo* substrate has a tendency to splay them apart. When the *erythro* precursor is further substituted at the alkene terminus as in **120**, the exo/endo-ratio increases enormously and an excellent yield of cyclohexanone **121** is obtained. The implication is that the *meso*-cycloheptanone **118** obtained from **117** in 51% yield was formed predominantly by direct endo cyclization. However, it is also to be noted that increasing the time for tin hydride addition to **120** results in an increased proportion of cycloheptanone **122**. Self-evidently, in this instance cyclization is taking place kinetically in the 6-exo mode and is followed, when conditions permit, by a Beckwith/Dowd-type rearrangement.

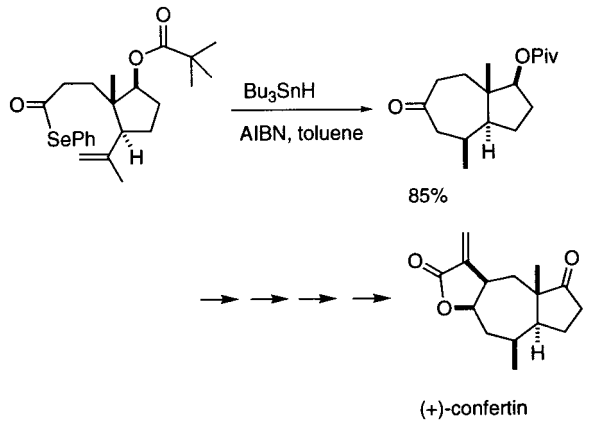
Further examples of 7-endo cyclizations of acyl selenide-derived acyl radicals have recently been described by Shishido and co-workers in the context of an entry into the pseudo-guaianolide *Confertin* (Scheme 116).[264]

In recent years P. A. Evans has described a number of very highly diastereoselective acyl radical cycliza-

Scheme 115

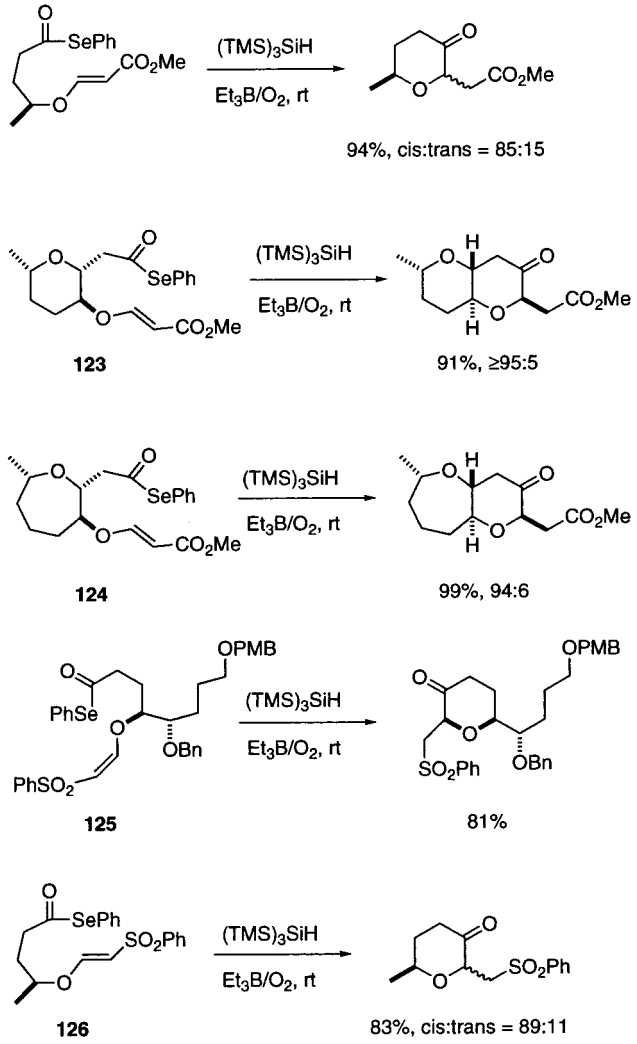


Scheme 116



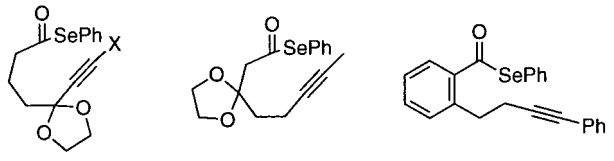
tions (Scheme 117).[242,265,266] The substrates are all derived from vinyl ethers, and in each case the cis-disubstituted product is formed preferentially. This selectivity is rationalized in the usual way by advocating a Beckwith-type chairlike transition state with all substituents equatorial. Attention is drawn to the improved selectivity obtained with the fused ring systems **123** and **124**, which is thought to arise from the increased rigidity imposed on the transition state by the preexisting ring. The increased selectivity with the cis alkene **125** as compared, for example, to **126** is thought to arise from increased 1,3-diaxial interactions in the chairlike transition state for formation of the minor isomer, an observation, and rationale, which had previously been advanced by Hanessian

Scheme 117



for the 6-exo cyclization of a simple alkyl radical.[267] It is also noteworthy that each of these cyclizations proceeds exclusively in the exo mode, which is perhaps not surprising in view of the nucleophilic character of the acyl radical and the polarity of the acceptor alkene.

There are fewer examples of 6-exo-dig/7-endo-dig cyclizations of acyl radicals than of their trigonal counterparts. Early attempts by Crich and Fortt to bring about the cyclization of **127**−**129** were not encouraging, and the only products obtained were aldehydes arising from quenching of the acyl radicals by the stannane and, in the case of **127**, the aldehyde with additional hydrostannylation of the alkyne.[125]

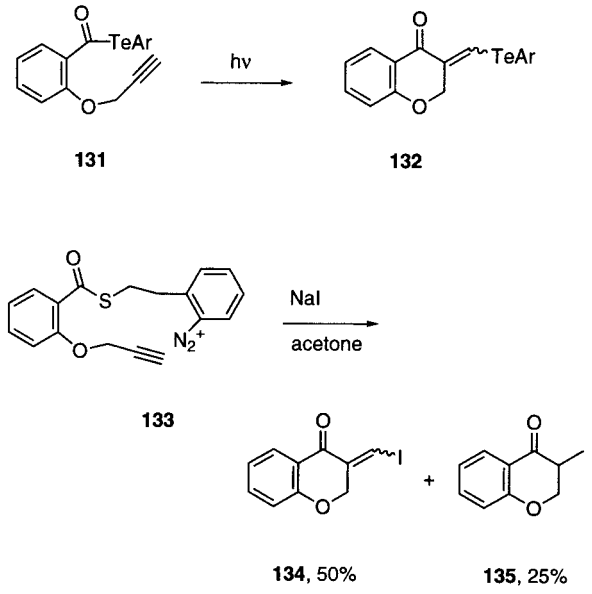


127: X = H
128: X = tms
129
130

Similarly, unpromising results were also recorded by Boger and Mathvink who observed only aldehyde formation on the reaction of alkyne **130** with tributyltin hydride.[135]

Initially, Crich and Fortt were inclined to the opinion that 6-exo-dig cyclizations of acyl radicals did not proceed owing to a steric interactions in the transition state;[268] however, subsequent work by Bachi and Bosch, in which it was shown that two closely related alkoxy carbonyl radicals, generated from selenoformates with tin hydride, cyclized efficiently in the 6-exo-dig mode, suggested that the reactions were merely slower than might have been expected.[269] Thus primed, Crich and co-workers photolyzed the acyl telluride **131** and obtained a quantitative yield of the cyclized vinyl telluride **132** (Scheme 118). This reaction succeeds because of the

Scheme 118



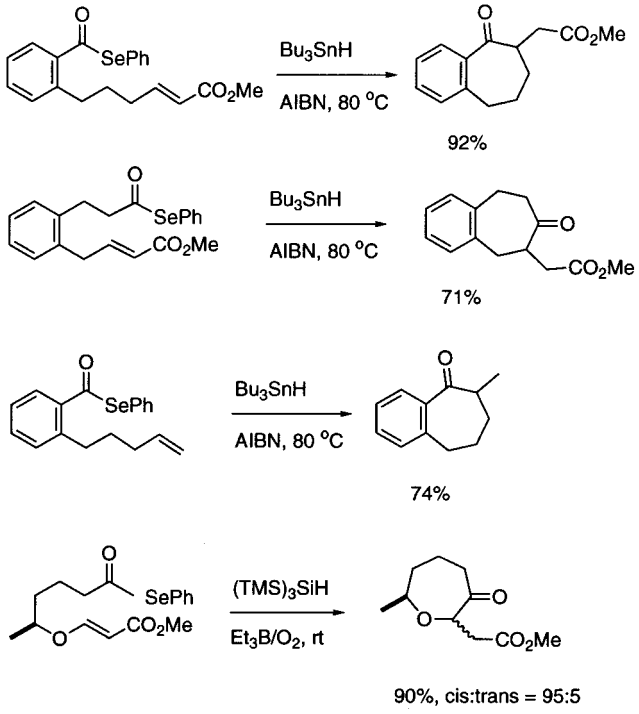
lack of alternative modes of trapping of the intermediate acyl radical in this acyl telluride chemistry, which permits the slower cyclization to take place. The identical acyl radical cyclization could also be achieved from thioester **133** on exposure to sodium iodide in acetone. The final product in this reaction is a vinyl iodide **134**, but some of the reduced product **135** was also formed (Scheme 118).[128] Presumably, Zard's *S*-acyl xanthate precursors, which are similarly designed to the acyl telluride **131**, would also allow such cyclizations, but we know of no such examples.

4. Cyclizations of 7-Octenoyl Radicals

As might be expected there are relatively few examples of 7-octenoyl radical cyclizations. Such radicals evidently may cyclize in either the 7-exo mode, giving 2-substituted cycloheptanones, or in the endo mode, giving cyclooctanones. Examples of 7-octenoyl radical cyclizations conducted with acyl selenides and tin hydride are given in Scheme 119.[135,265] The reader will note that all four examples proceeded exclusively in the 7-exo mode.

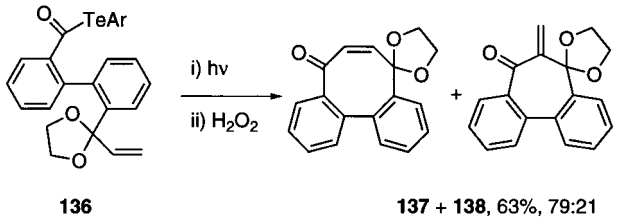
Crich and co-workers, recalling their study of the influence of allylic ethers and ketals on the mode of cyclization of the lower homologues (Schemes 84 and 113), prepared the conformationally constrained acyl telluride **136** bearing an allylic ketal. In line with

Scheme 119



their expectations, photolysis and subsequent oxidative elimination of the telluride moiety provided a 3.7:1 mixture of the endo- and exo cyclized products **137** and **138**, respectively (Scheme 120).[147]

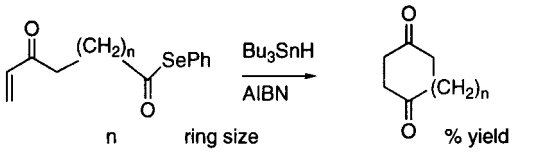
Scheme 120



5. Medium-Sized and Large Rings

The formation of medium and large rings by acyl radical cyclizations was first described by Boger and Mathvink using tin hydride/acyl selenide methodology.[270] As is seen from Scheme 121, it was possible

Scheme 121

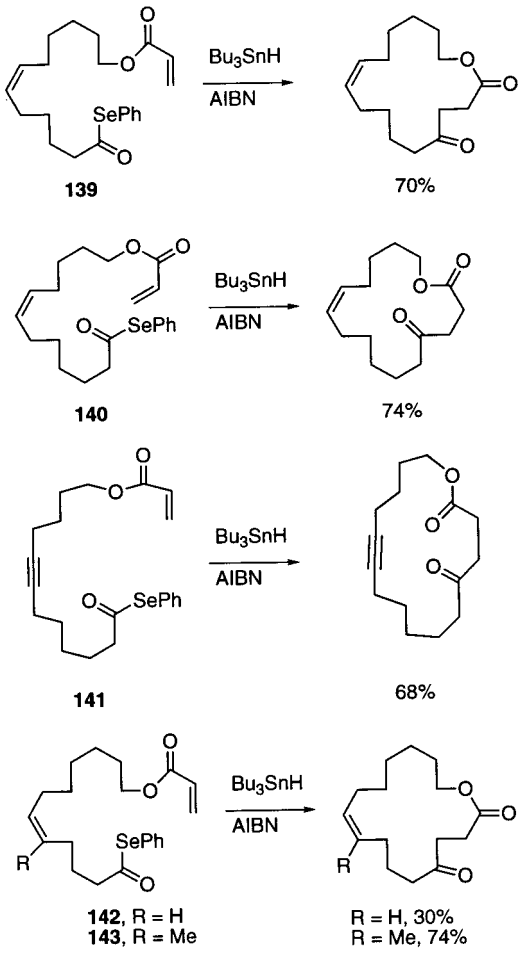


n	ring size	% yield
15	20	57
11	16	68
9	14	55
7	12	46
6	11	47

to cyclize acyl radicals onto activated alkenes in the endo mode, leading to the formation of 11-membered, and larger, cyclic ketones. Lower yields were obtained for the 11- and 12-membered cyclic ketones than for the larger rings, which, no doubt, reflects on the strain present in the lower members of the series.

The same authors also successfully investigated acyl radical cyclization onto acrylate esters with the consequent formation of 16-membered macrolides (Scheme 122).[270] The most noteworthy feature of all

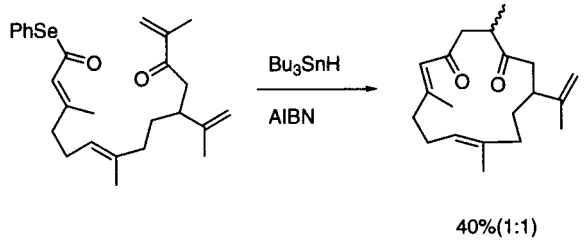
Scheme 122



five examples in Scheme 122 is the ability of the macrocyclization to compete with alternative modes of cyclization onto the unsaturated chains. Thus, with **139** it is clear that the 16-endo cyclization onto the activated double bond is more rapid than the alternative 6-exo-trig cyclization. In the case of **140** and **141**, 7-exo-trig and 7-exo-dig cyclizations, respectively, are out-competed by the macrocyclization. With **142**, the competing reaction is a 5-exo-trig reaction and from the low yield isolated it would appear to be a serious parasite. Substitution at the 5-position as in **143** retards the 5-exo process as noted above and restores the high yielding macrocyclization process.

A further macrocyclization of an acyl radical is taken from the work of Pattenden on the synthesis of furanocembranoids (Scheme 123).[271] Again, the acceptor alkene is activated by a carbonyl group. The competing reaction in this 14-membered ring forming reaction is a potential 6-exo-trig cyclization, and although no mention was made of this process, it seems likely to have been problematic given the low yield reported. It is also interesting to note that this particular cyclization involves an α,β-unsaturated acyl radical, with its propensity for alkene isomer-

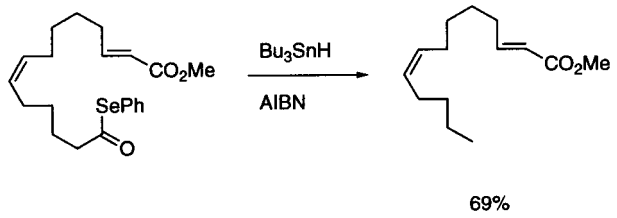
Scheme 123



ization (Schemes 71, 111, and 112), which was apparently not reflected in the product.

Scheme 124 illustrates a failed 12-membered mac-

Scheme 124



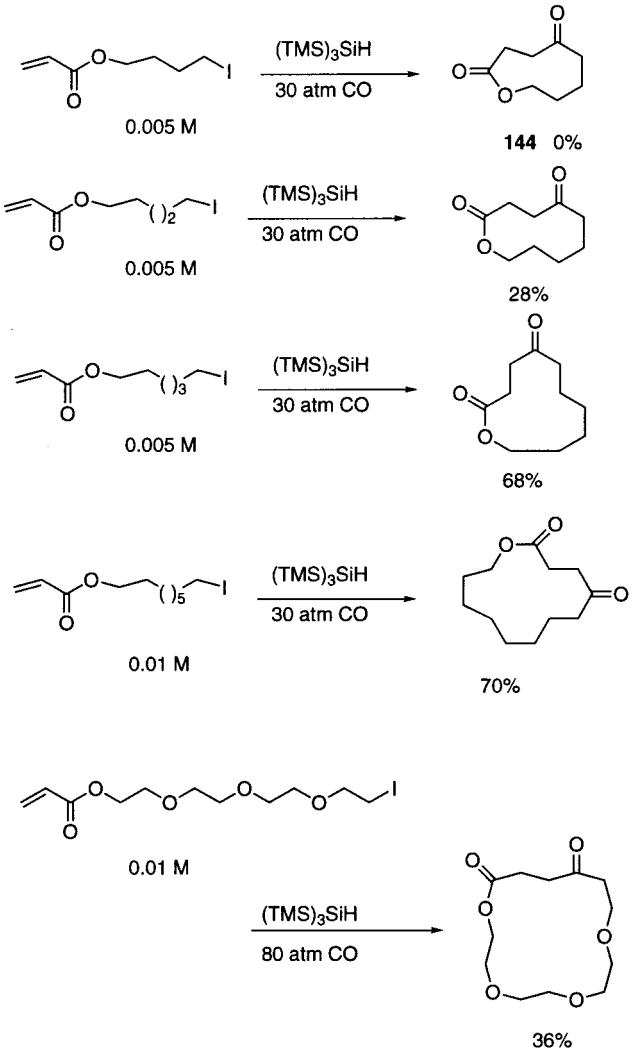
rocyclization taken from the work of Boger and Mathvink.[270] This failure draws attention to the need for the acceptor alkene to be terminal for successful macrocyclization to occur, even if activated. Curiously, in this example decarbonylation to give a primary alkyl radical also appears to win out over the alternative 6-exo-trigonal cyclization.

Ryu, Sonoda, and co-workers have investigated the macrocyclization of acyl radicals, generated by carbonylation of alkyl radicals (Scheme 125).[272] The attempted formation of a nine-membered macrolide (**144**), perhaps not too surprisingly, failed, but ring sizes from 10 upward could be successfully synthesized in this manner. Competing macrocyclizations of the initial alkyl radical do not appear to have been problematic in this work. In this light, it is interesting that the authors were able to work at only 30 atm of CO pressure, substantially below the 80−90 atm they usually recommend for their other carbonylative acyl radical reactions. The examples in Scheme 125 employ $(TMS)_3SiH$ as the reductant and chain carrier, but it was also noted that tributyltin hydride could be successfully employed for this purpose given suitable adjustment of the concentration.[272,273]

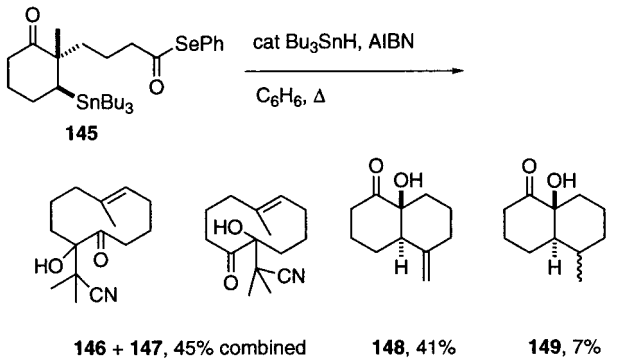
B. Cyclization onto Carbonyl Groups

The vast majority of preparative work with acyl radicals involves cyclizations and additions to carbon−carbon multiple bonds. Nevertheless, there also exist examples of addition to carbonyl groups. Thus, Baldwin and co-workers reported that the reaction of acyl selenide **145** with catalytic tributyltin hydride in benzene at reflux gave the four products **146**−**149** in a combined yield of 93% (Scheme 126).[274] All four products were thought to arise from cyclization of the initial acyl radical **150** onto the C of the ketone carbonyl group, giving an alkoxy radical **151**. This then undergoes a radical-type Grob fragmentation with cleavage of the transannular bond and expulsion of the chain carrying stannyl radical (Scheme 127).

Scheme 125



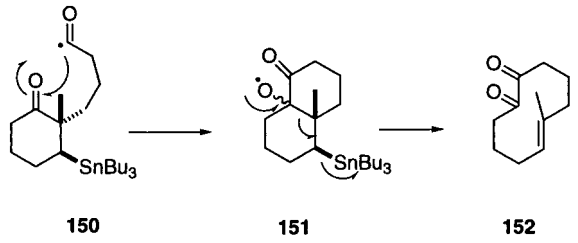
Scheme 126



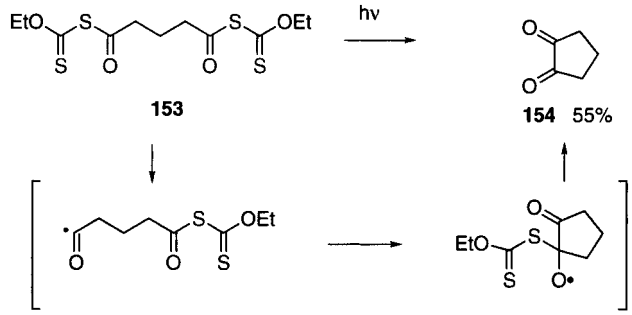
The cyclodecadione **152** is therefore the primary product of this radical process. Evidently, **146** and **147** arise from addition of initiator-derived cyanoisopropyl radical to one or the other of the carbonyl groups of **152**. Given that **146** and **147** were isolated in a combined yield of 45%, the implication must be that overall propagation was poor and that significant quantities of initiator were required to drive the reaction to completion. Products **148** and **149** evidently arise from nonradical transannular reactions of **152**.

Another apparent example of cyclization of an acyl radical onto a carbonyl group, although not recognized as such at the time, is provided by Barton's photolysis of the bisacyl xanthate **153** giving cyclopenta-1,2-dione **154** (Scheme 128).[275] This reaction

Scheme 127



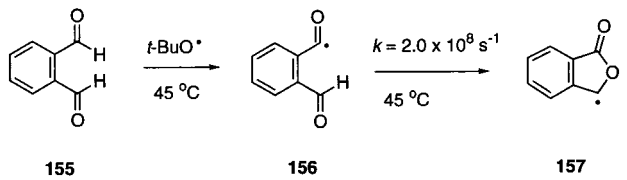
Scheme 128



is best interpreted in terms of cyclization of an initial acyl radical onto the carbonyl C of the second acyl xanthate, providing an alkoxyl radical. Product formation ensues following elimination of the sulfur-centered radical. The alternative explanation of the intramolecular coupling of two acyl radicals seems unlikely in view of the low probability of generating two acyl radicals in the same molecule within the lifetime of an acyl radical.

Following early work by J. Kagan, in which a radical intermediate was detected in the photocyclization of *o*-phthaldehyde to phthalide,[276] Mendenhall and co-workers generated the acyl radical **156** by hydrogen-atom abstraction from *o*-phthalaldehyde **155** with the *tert*-butyloxyl radical, itself generated from *tert*-butylhyponitrite at 45 °C. All products in this reaction derived from cyclization of the acyl radical **156** to the phthalide-derived benzyl radical **157**, which was observed to undergo dimerization or trapping by nitroxides according to the reaction conditions (Scheme 129).[277] The rate of this

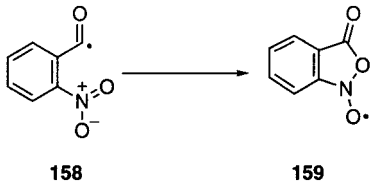
Scheme 129



formal 5-endo-trig process was determined to be 2.0×10^8 s^{-1} at 45 °C. [277] A similar cyclization, that of acyl radical **158** onto a nitro group with formation of a cyclic nitroxide **159**, was reported by Janzen and Oehler (Scheme 130).[278]

Eguchi and co-workers sought to ingeniously exploit this type of formal 5-endo cyclization of acyl radicals. They prepared a range of 4-hydroxy-

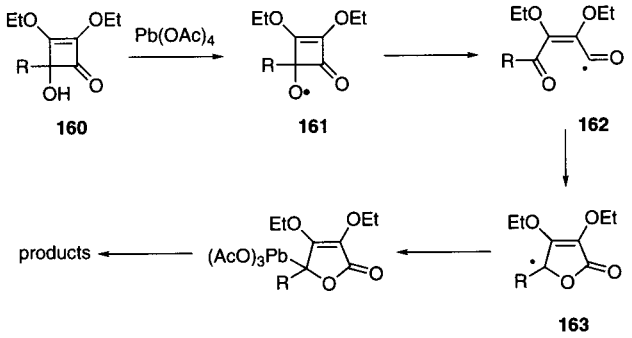
Scheme 130



158 159

cyclobutenones **160** from squaric acid and exposed them to lead tetraacetate in the expectation that the initial alkoxy radical **161** would fragment and generate an acyl radical **162** primed for a 5-endo cyclization onto a carbonyl (Scheme 131).[279] In the event, two

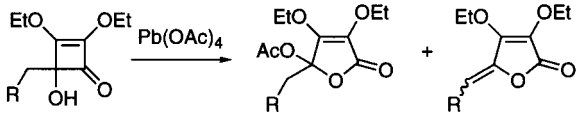
Scheme 131



160 161 162 163

series of ring-expanded products were obtained, both of which could be readily explained by the action of lead tetraacetate on the radical **163** formed on ring closure (Scheme 132). Closely related products were

Scheme 132



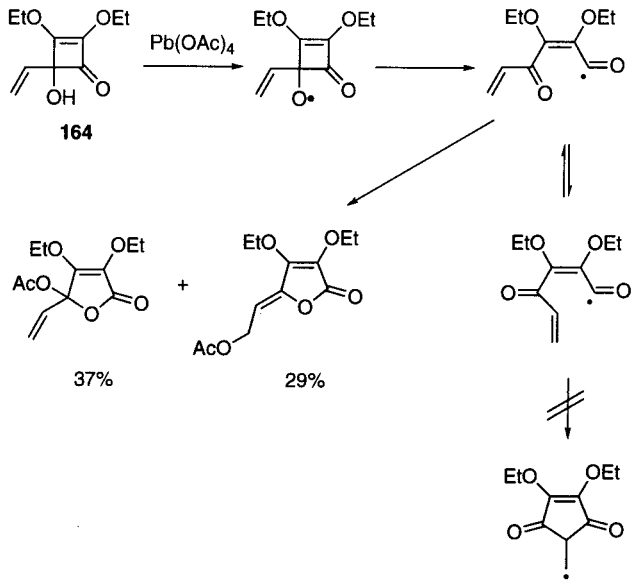
R = H	51%	5%
R = Pr	60%	23%
R = COPh	28%	52%

obtained when lead tetraacetate was replaced by ceric ammonium nitrate and by the mercuric oxide/iodine couple, which lends support to the radical mechanism proposed.

Internal competition experiments using **164** showed that the 5-endo cyclization was more rapid than a possible 5-exo-trig cyclization onto an alkene (Scheme 133),[279] in agreement with the rate constant determined by Mendenhall and co-workers (Scheme 129).

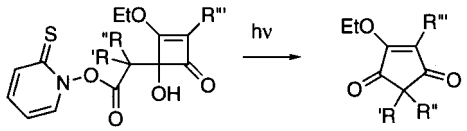
Finally, although not a cyclization onto a carbonyl, we note the related process in Scheme 134, also described by Eguchi and co-workers.[279] This most intriguing reaction is thought to involve fragmentation of the initial radical **166** to give the acyl radical **167**, which then cyclizes onto the enol in a 5-endo fashion giving **168**. Chain transfer with the thiohydroxamate **165** then provides **169**, which is the precursor to the final product (Scheme 135). This process is rendered all the more curious by the fact that the highest yield is reported when the intermediate enol is substituted at the terminal position by two methyl groups (Scheme 134), i.e., when R′ and

Scheme 133



164 37% 29%

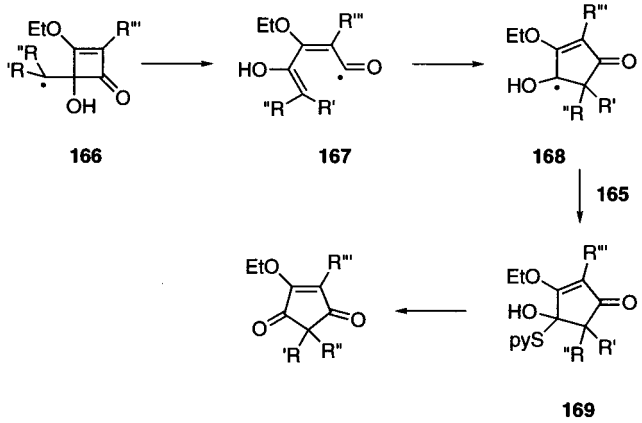
Scheme 134



165

R' = R" = H, R'" = OEt, 50%
R' = R" = H, R'" = Bu, 50%
R' = R" = H, R'" = Ph, 32%
R' = Me, R" = H, R'" = OEt, 51%
R' = R" = Me, R'" = OEt, 84%

Scheme 135



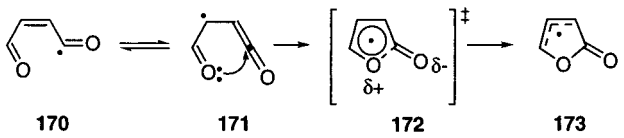
166 167 168 165 169

R″ are Me. Added to this is the well-known slow rate of fragmentation of cyclobutylcarbinyl radicals ($\sim 10^3$ s^{-1}),[3a] all of which suggested that an alternative mechanism involving the conversion of **166** to **168** via a Beckwith/Dowd-type ring expansion could be operating. However, ab initio calculations indicated that closure of **166** to the bicyclo[2.1.0]pentenoxyl intermediate or transition state required for such a process was prohibitively high in energy.[279]

Ab initio calculations of acyl radical **170**, considered to be a model for **162**, revealed it to be extensively delocalized and better represented as the α-ketenyl structure **171**.[280] This radical was found to cyclize through a polar transition state **172** arrived at by

attack of a lone pair on the carbonyl oxygen at the electrophilic ketenyl carbon, the activation energy being 9.6 kcal mol^{-1} (Scheme 136). Analysis of the

Scheme 136

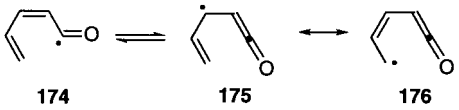


170 **171** **172** **173**

SOMO throughout the course of the ring closure showed it to change very little, meaning that the single electron is not greatly involved in the cyclization. Overall, the cyclization to radical **173** is exothermic by 20.9 kcal mol^{-1} owing to the delocalized nature of the product radical. This exothermicity contributes to the facility of this cyclization.[280] Closely related conclusions were reached for radical **156** studied by Mendenhall and co-workers. Thus, the facile cyclizations of **156** and **170** are best considered not as radical cyclizations but as polar cyclizations of radicals.

Comparable calculations were conducted for the pentadienoyl radical **174**, a model for **167** (Scheme 137). Like **170**, it was found to be better represented

Scheme 137



174 **175** **176**

by an α-ketenyl radical structure **175**/**176**. However, as **175** lacks the lone pairs for the novel cyclization mechanism open to **170**/**171**, the transition state for its cyclization is best represented as the attack of an acyl radical on a diene. Alternatively, it seems reasonable that the cyclization might be viewed as a 5-exo cyclization of **176** onto the carbonyl group. The activation energy for cyclization of **174** was calculated to be 21.7 kcal mol^{-1}, but the cyclization was found to be facilitated by the exothermicity (26.7 kcal mol^{-1}), which is a function of the formation of a delocalized allylic radical in the product.[280]

C. Cyclization onto Carbon–Nitrogen Multiple Bonds

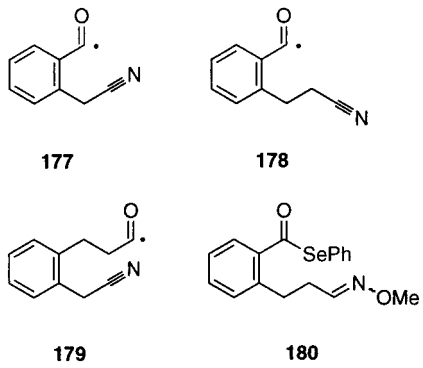
1. Nitriles

Boger and Mathvink attempted cyclization of the acyl radicals **177**−**179** using acyl selenide/tin hydride chemistry. In each case, it was reported that the cyclizations failed with the major isolated products being the corresponding aldehydes.[135]

2. Oximes, Hydrazones, and Imines

An attempted 6-exo cyclization of the acyl radical derived from selenide **180** was reported to be unsuccessful by Boger and Mathvink under standard tin hydride/AIBN conditions.[135]

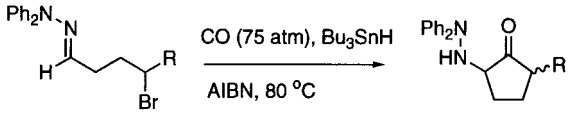
Brinza and Fallis studied the carbonylative cyclization of bromobutanes onto *N*,*N*-diphenyl hydrazones and found them to be synthetically useful entries into 2-hydrazinocyclopentanones (Scheme



177 **178** **179** **180**

138). Conditions were developed for the selective reduction of the products to either cis or trans 2-hydrazinocyclopentanols.[281]

Scheme 138

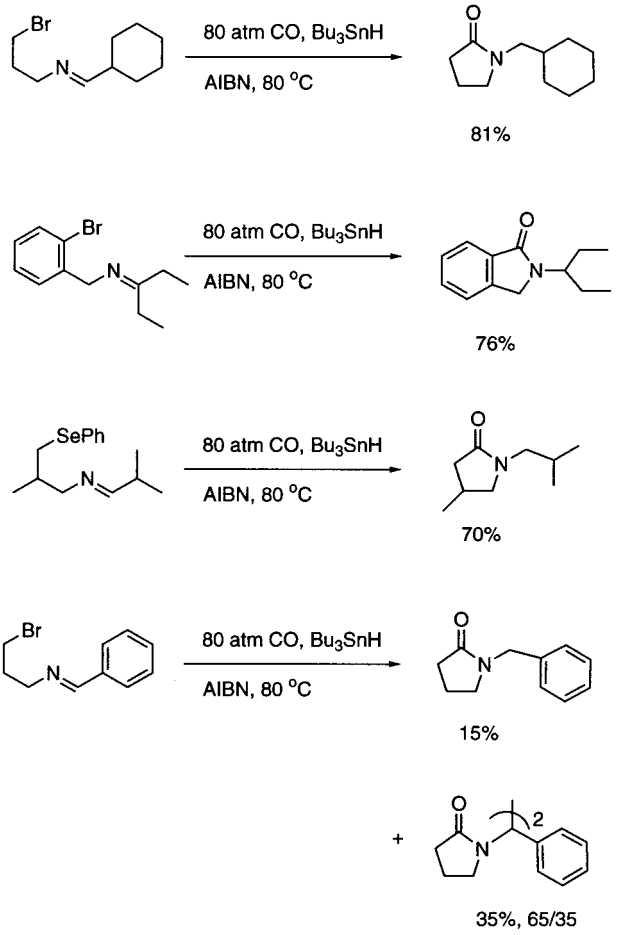


R = H, 69%
R = Me, 75%, cis/trans = 50/50
R = *i*-Pr, 71%, cis/trans = 48/52
R = C_6H_{11}, 67%, cis/trans = 45/55

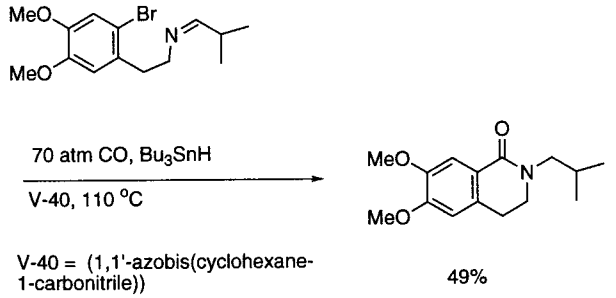
Finally, Ryu, Komatsu, and co-workers introduced a "nitrogenphilic cyclization" of acyl radicals which leads to the formation of γ-lactams. As usual, the Ryu group exploited the radical carbonylation of alkyl and aryl halides as their preferred entry into acyl radicals.[282] As seen from the examples in Scheme 139, this [4+1] annulation protocol may be induced from alkyl bromides or selenides and tolerates the use of both aldimines and ketimines. Unfortunately, cyclization onto a benzaldehyde imine, perhaps the synthetically most desirable case, was complicated by the stabilized nature of the cyclized radical, which led to poor chain propagation and the isolation of dimerization products. A single example of an *N*-philic 6-exo acyl radical cyclization was also presented (Scheme 140).[282]

In view of the nucleophilic character usually exhibited by acyl radicals in their additions to C−C multiple bonds, these cyclizations are unusual with the addition taking place at the more electron-rich nitrogen atom. The 5-exo selectivity is in contrast to the corresponding vinyl radical cyclization onto aldimine N=C proceeding in 6-endo mode.[283] Calculations showed the observed 5-exo mode ring-closed radicals to be thermodynamically more stable than the corresponding 6-endo closed radicals by some 17 kcal mol^{-1}, which prompted the authors to consider an alternative mechanism in which a kinetic cyclization occurred in the 6-endo mode, followed by a ring contraction related to the Beckwith/Dowd rearrangement to the formal 5-exo product. However, reactions at higher concentrations of tin hydride revealed the 5-exo mode of cyclization to be kinetically as well as thermodynamically favored.[282] A further mechanistic possibility raised by the authors involves nucleophilic attack by the lone pair of the imine nitrogen on the

Scheme 139

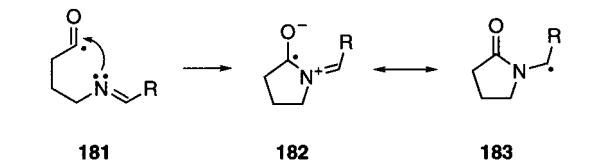


Scheme 140



acyl radical **181** to give what is formally a resonance structure (**182**) of the ring-closed radical **183** viewed from the standpoint of an acyl radical cyclization (Scheme 141). Seen in this way, this type of *N*-philic

Scheme 141



acyl radical cyclization would be, like that of **170**/**171** above, not a radical cyclization but a cyclization of a radical.

VIII. Intermolecular Addition

A. Intermolecular Addition to C–C Double Bonds

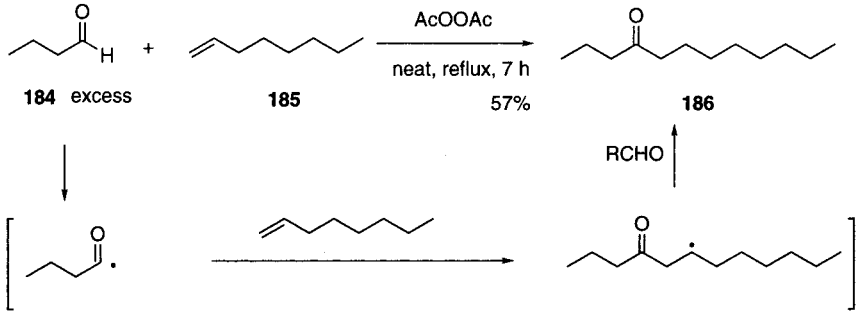
Intermolecular addition of acyl radicals to C−C double bonds provides a useful method for the synthesis of unsymmetrical ketones. Since acyl radicals add more efficiently to alkenes having electron-withdrawing groups than to ordinary and electron-rich alkenes, they are regarded as nucleophilic radicals. Styrene can also serve as a good acyl radical acceptor. In general, the reactivity of nonterminal alkenes toward the attack of acyl radicals is not high mainly for steric reasons. Earlier reviews by Walling,[284] Nikishin,[4a] and Minisci[4b] include excellent coverage of intermolecular addition reactions of acyl radicals published prior to the recent blooming of radicals in synthesis. A recent account by Lusztyk, Ingold, and co-workers provides some important kinetic aspects required for synthetic planning of intermolecular reaction of acyl radicals.[55]

In 1949, Kharasch and co-workers reported that unsymmetrical ketones are prepared by the reaction of aldehydes with alkenes under free-radical reaction conditions.[285] The reaction is initiated by UV irradiation or thermal decomposition of diacetyl peroxide and proceeds via a radical chain process which involves (i) the addition of an acyl radical to an alkene and (ii) abstraction of formyl hydrogen from aldehyde by the resulting radical leading to an unsymmetrical ketone and an acyl radical. Scheme 142 illustrates the peroxide-induced reaction of butanal (**184**) with 1-octene (**185**), which gives 4-undecanone (**186**). A nearly 3-fold excess of butanal and a high concentration are necessary to ensure the radical chain cascade, since abstraction of hydrogen from the aldehyde by a nucleophilic alkyl radical is a relatively inefficient step as discussed in section IV.A.1.

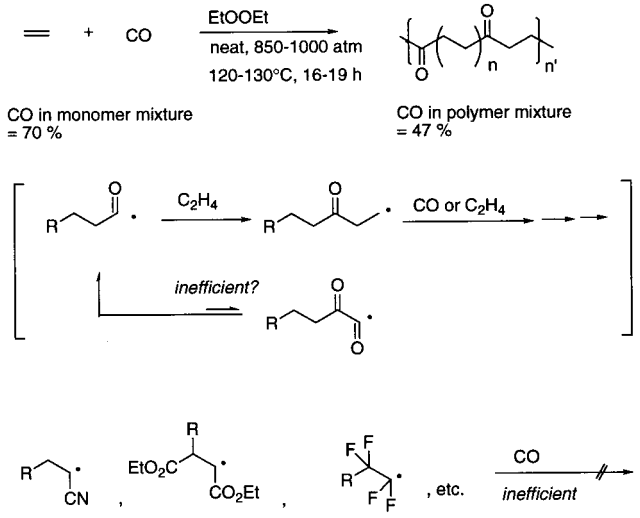
In the case that the product radical resulting from addition of acyl radical to alkene does not find an appropriate C−H bond (like formyl hydrogen) to abstract, radical polymerization can take place. Copolymerization of carbon monoxide and ethylene, which was mainly pursued by Coffman and coworkers in the 1950s, provides such an example (Scheme 143).[286] The CO content in the product polymer is dependent on the CO content of the starting gas mixture but there is an upper limit. Thus, even in the case that CO is used in the large excess, the CO content in the polyketone never exceeds 50% (Scheme 143). This may suggest that addition of acyl radicals to carbon monoxide is highly inefficient. Copolymerization of carbon monoxide and electron-deficient alkenes, such as acrylonitrile, diethyl maleate, and tetrafluoroethylene, is not successful, since the polymers contained only a small portion of CO.[287] The reaction of the stabilized radicals, formed from addition to these alkenes, with CO is highly inefficient, presumably due in each case to the backward decarbonylation being very fast.

Shortly after the report of Kharasch, Patrick found that benzoyl peroxide-initiated addition of acetaldehyde (**187**) to diethyl maleate (**188**) proceeds smoothly to give 2-acetyl succinate (**189**) (Scheme 144).[288a] Subsequently, Huang reported a similar addition of

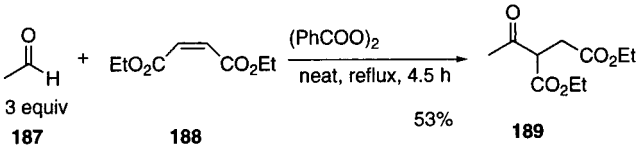
Scheme 142

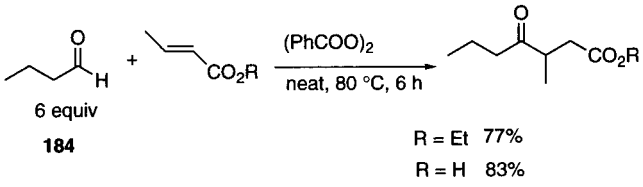


Scheme 143



Scheme 144

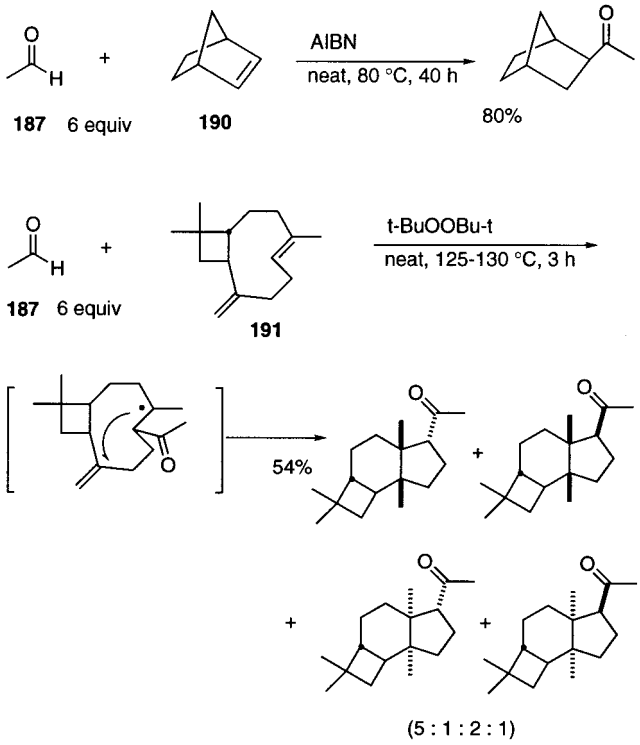




butyraldehyde (**184**) (6-fold excess) to electron-deficient alkenes, such as ethyl crotonate and crotonic acid, which gave good yields of the corresponding 1,4-dicarbonyl compounds (Scheme 144).[288b]

The following two examples show that the acetyl radical, generated from acetaldehyde (**187**) by hydrogen abstraction, adds to strained C−C double bonds. Stockman reported that treatment of norbornene (**190**) with acetaldehyde (**187**) and a catalytic amount of AIBN at 80 °C results in the formation of *exo*-2-norbornyl methyl ketone in 80% yield (Scheme 145).[289] The second example shown in Scheme 145, which was reported by van der Linde and van der Weerdt, is the addition of acetaldehyde (**187**) to the trans C−C double bond of caryophyllene (**191**). After the addition of the acetyl radical, the resulting alkyl

Scheme 145

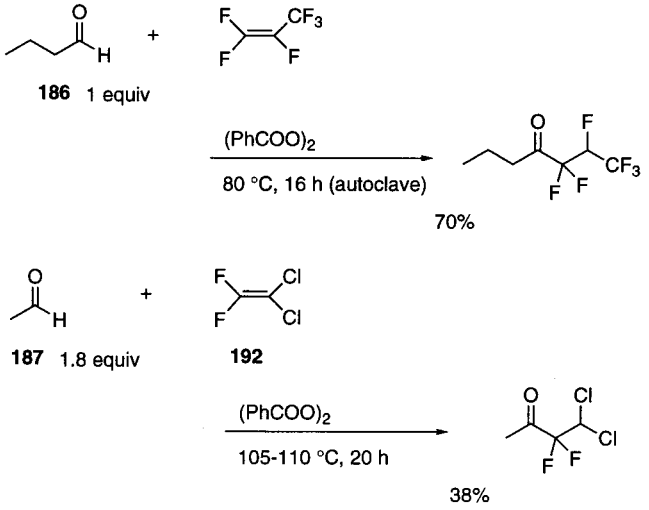


radical is ready to undergo the subsequent 5-exo mode of cyclization to give tricyclic products.[290] In a related example, radical addition of acetaldehyde to 1,5-cyclooctadiene is known to give *exo*-2-acetylbicyclo-[3.3.0]octane.[291]

LaZerte and Koshar found that terminally unsaturated perfluoroalkenes are good acceptors in acyl radical addition reactions.[292a] The first example of Scheme 146 illustrates the benzoyl peroxide-initiated addition of butyraldehyde (**187**) to perfluoropropene. Muramatsu and Inukai reported peroxide-initiated radical addition of aldehydes to 1,1-dichloro-2,2-difluoroethylene (**192**) (Scheme 146). The addition takes place regioselectively, forming 1,1-difluoro-2,2-dichloroethyl alkyl ketones.[292b]

As discussed in section IV.A.1., thiols can catalyze the decarbonylation of aldehydes to alkanes. Similarly, a catalytic amount of thiol can effect the radical addition of aldehydes to alkenes. Electrophilic thiyl radicals bypass the somewhat inefficient H-abstraction step from aldehydes by alkyl radicals, making the total chain propagation smoother. Indeed, a recent report from Roberts's laboratory treated the scope of the thiol-catalyzed addition of aldehydes to

Scheme 146

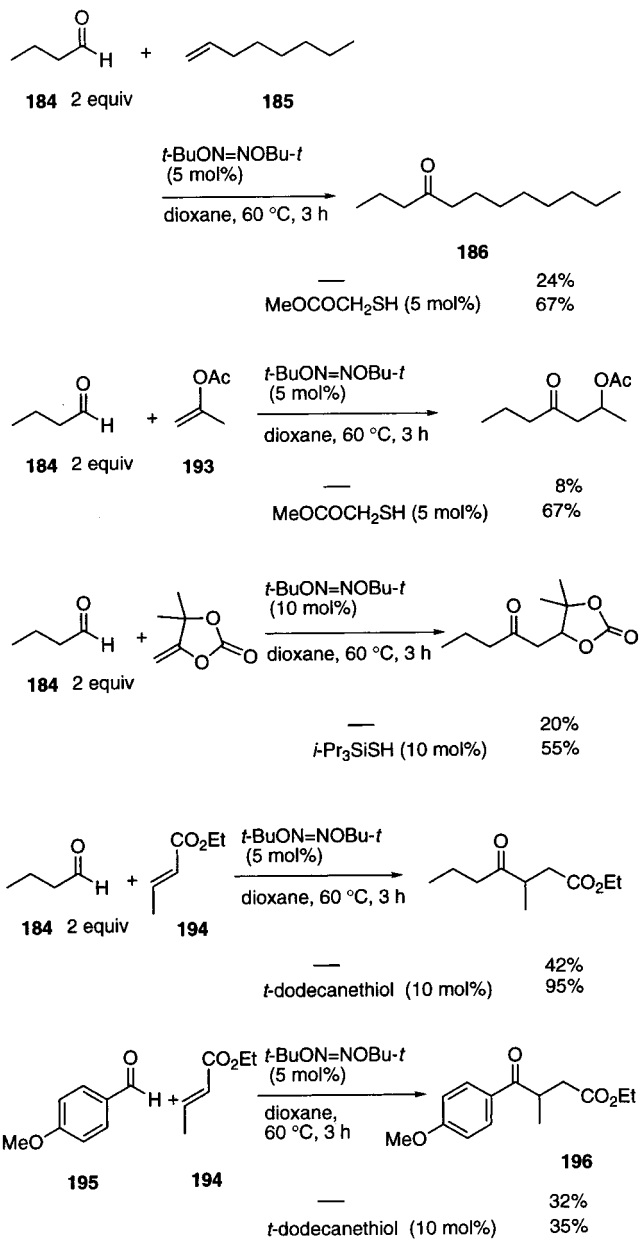


alkenes.[259] The reaction takes place under mild reaction conditions (60 °C) using dioxane as the solvent and di-*tert*-butyl hyponitrite as the initiator. Scheme 147 shows that addition of butanal **184** to a variety of alkenes can be effected by the two-portion addition of 5−10 mol % of thiols. In the case of electron-rich alkenes, the use of a thiol catalyst appears particularly effective. For example, the product radical arising from the addition of the acyl radical to isopropenyl acetate (**193**) is expected to be nucleophilic due to the adjacent oxygen substituent and therefore would not abstract hydrogen from the aldehyde smoothly. But the use of a thiol as a *polarity reversal catalyst* can circumvent the inefficient chain propagation step, since the electrophilic thiyl radical abstracts the hydrogen instead. In an opposite sense, in the addition of aldehydes to electron-deficient alkenes, as in the case of ethyl crotonate (**194**), the effect of thiol catalyst is not always dramatic, since the product radical is electrophilic enough to abstract hydrogen from the aldehyde itself. The last example in Scheme 147 shows the result of the addition of *p*-anisaldehyde (**195**) to ethyl crotonate, where almost no improvement in the yield of the adduct **196** was observed on incorporation of a thiol. Perhaps abstraction of hydrogen from aromatic aldehydes by the electrophilic product radical would be so fast that thiol could not play a meaningful role.

Scheme 148 lists the results of the addition of butanal (**184**) to alkenes having *N*-, *Si*-, and *S*-substituents.[259] The thiol-catalyzed reaction works well for these terminal alkenes, but unfortunately, cyclic vinylsilane **197** gave only traces of addition product.

As noted in section IV, homolysis of acylmetals can generate acyl radical/metal radical pairs. This particular type of acyl radical generation reaction, when conducted in the presence of electron-deficient alkenes, leads to the formation of two types of intermolecular addition products (Scheme 149). The formation of a saturated ketone is explained by the coupling of the product radical and metal radical and the subsequent protonation of the polarized metal−carbon bond of the resulting organometallic species. The formation of an enone-type product may be the

Scheme 147

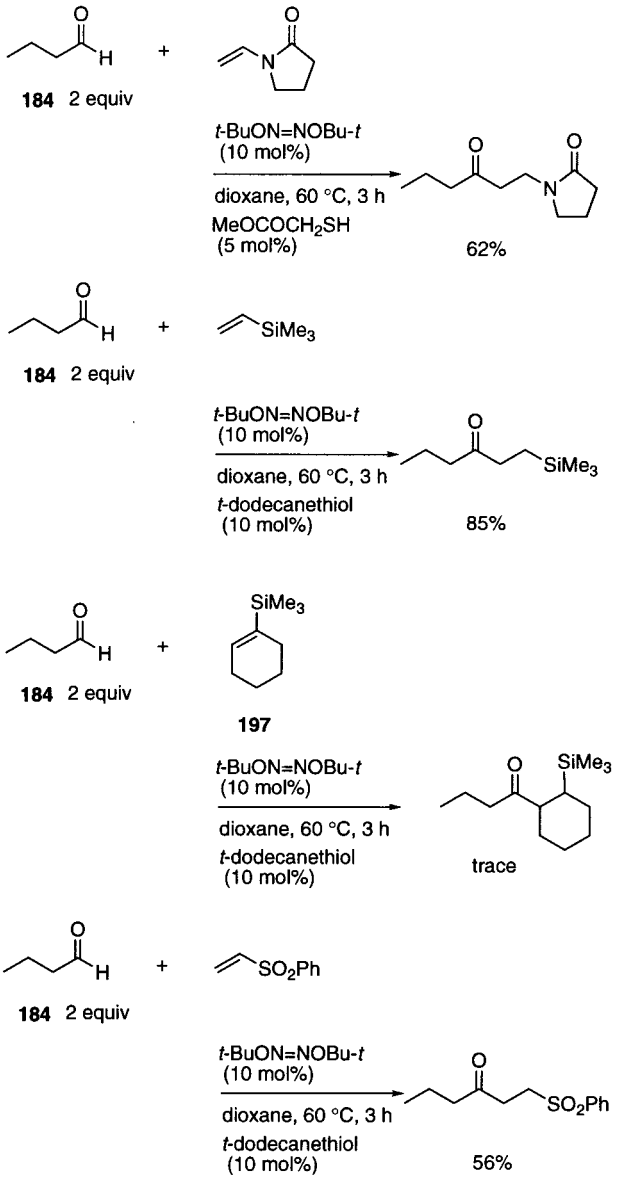


result of β-metal hydride elimination from the same alkylmetal intermediates, which is a familiar reaction course characteristic of transition-metal−alkyl bonds.

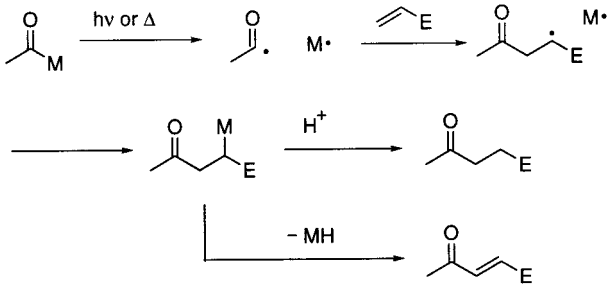
Pattenden and co-workers found that both types of product are formed in the photolysis of acylcobalt-salophen complexes in the presence of alkenes.[215] Thus, the reaction of **198** in the presence of methyl vinyl ketone (**199**) gave a mixture of saturated and unsaturated products **200** and **201** (Scheme 150). A similar photolysis with ethyl acrylate or styrene gave mainly unsaturated products. On the other hand, photolysis with acrylonitrile gave the saturated β-cyanoketone as the predominant product.

Many studies on catalytic epoxidation of alkenes with molecular oxygen use aldehydes as the reaction mediator.[293] It is proposed that the transition-metal complex oxidizes an aldehyde to generate an acyl radical. The so-formed acyl radical adds to molecular oxygen to give an acylperoxy radical, which then undergoes addition to alkenes. Subsequent intra-

Scheme 148

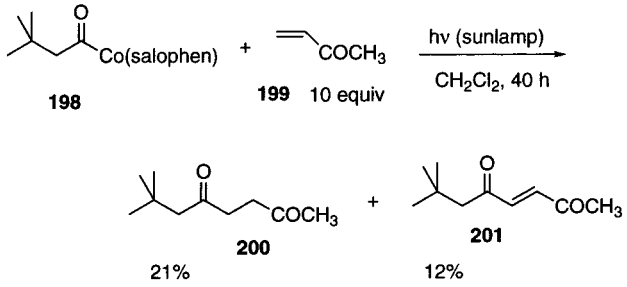


Scheme 149



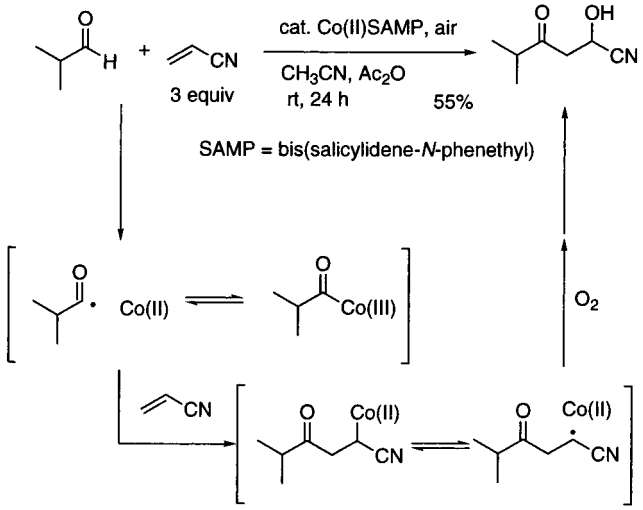
molecular homolytic substitution at oxygen leads to an epoxide. Acylperoxy radicals have an electrophilic nature, and accordingly, the epoxidation process is not smooth for alkenes having electron-withdrawing substituents, whereas acyl radicals have a nucleophilic nature. This may be the subtle point of the work of Iqbal and co-workers, who succeeded in an efficient trapping of acyl radicals by electron-deficient alkenes in the catalytic oxidation system using bis(salicylidene-*N*-phenethyl)cobalt(II) (CoSANP).[294] The

Scheme 150



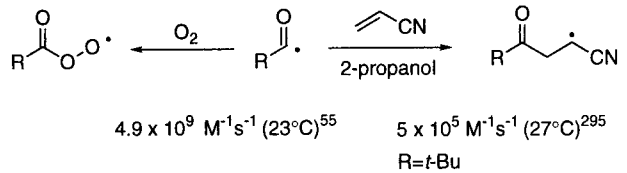
resulting radical is quenched by molecular oxygen to give a β-hydroxy ketone. Scheme 151 illustrates an

Scheme 151



example of such an addition/oxidation sequence leading to a β-hydroxy-β-cyanoketone. It should be noted that, in contrast, efficient conversion of styrene to styrene oxide was performed using a similar set of reaction conditions. Judging from the related kinetic data reported by Ingold's[55] and Fischer's groups,[295] a low concentration of molecular oxygen should be an important factor if the addition of acyl radicals to alkenes is to predominate over the addition to molecular oxygen (Scheme 152).

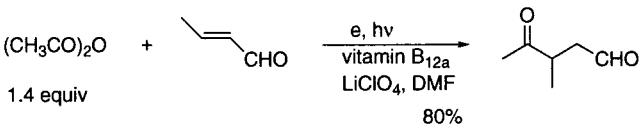
Scheme 152



In 1983, Scheffold and Orlinski reported the one-step synthesis of 1,4-dicarbonyl compounds and 4-oxo nitriles from the corresponding carboxylic acid anhydrides and activated alkenes.[296] The procedure involves the electrochemical reduction of a mixture of anhydrides and alkenes in DMF under irradiation with visible light in the presence of catalytic amounts of vitamin B_{12a} or related cobalt complexes (Scheme 153). It is proposed that irradiation causes homolysis of the Co−C bond of the intermediates.

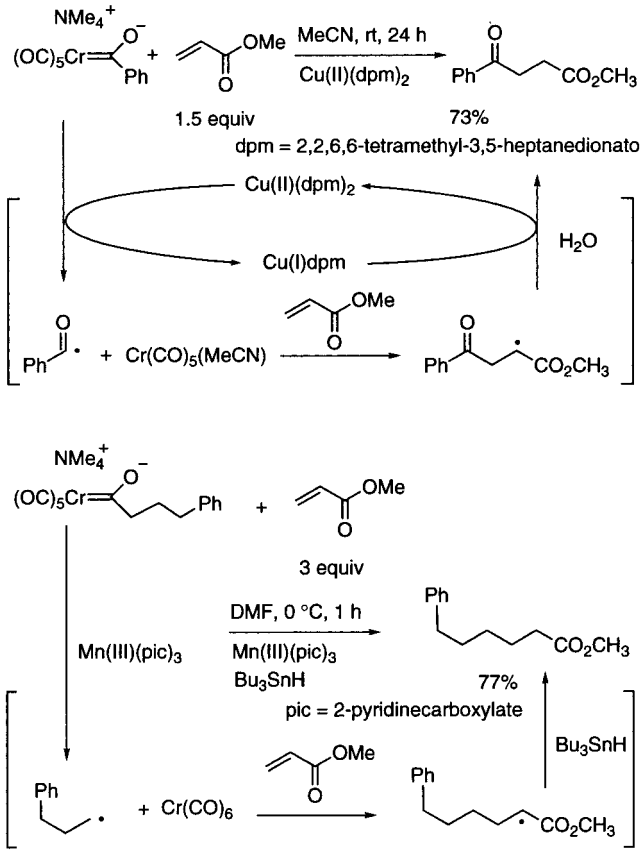
Fischer carbene complexes can serve as acyl radical precursors. Narasaka and Sakurai reported that

Scheme 153



chromium carbene complexes, when exposed to a copper(II) reagent, generate acyl radicals, which then undergo addition to electron-deficient alkenes.[297a] The copper(I) species reduces the resulting radical to an anion, and subsequent protonation leads to the addition product (Scheme 154). This redox-type acyl

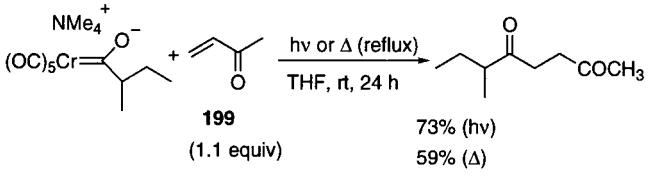
Scheme 154



radical transfer reaction works particularly well for aromatic acyl radical systems. It is interesting to note that if the anionic chromium complexes are oxidized with manganese(III) 2-pyridinecarboxylate, the reaction proceeds along a different course, in which an alkyl radical is formed and trapped via decarbonylation.[297b] The second equation in Scheme 154 shows such an example.

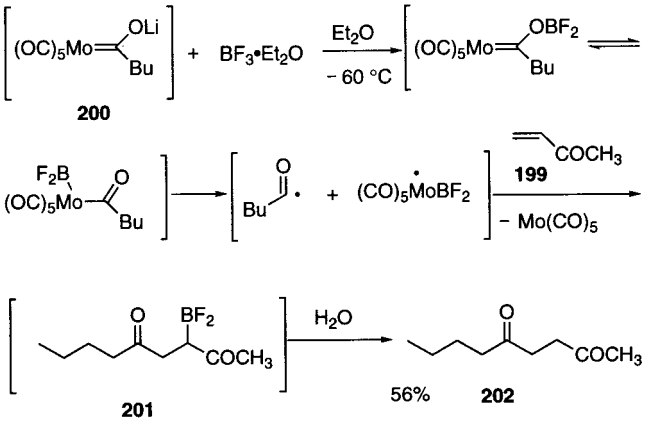
Söderberg and co-workers[298] reported that irradiation and thermal conditions can effect the similar acyl radical transfer reaction without the need for the redox catalyst (Scheme 155).

Scheme 155



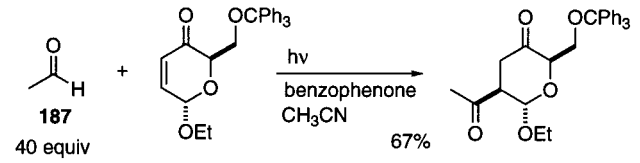
Very recently, Barluenga and co-workers reported that difluoroboroxymolybdenum carbene complexes, which are prepared in situ from pentacarbonyl acyl molybdates and boron trifluoride etherate, undergo spontaneous homolysis upon warming to room temperature, giving 1,2-diketones in good yields (Scheme 21).[152] When the decomposition reaction of complex **200** was conducted in the presence of methyl vinyl ketone (**199**), 1,4-diketone **202** was formed (Scheme 156). Boron enolate **201** is proposed as the precursor for **202**.

Scheme 156



Fraser-Reid and co-workers reported the photochemically induced addition of acetaldehyde (**187**) to enones (Scheme 157).[299] Typically, an acetonitrile

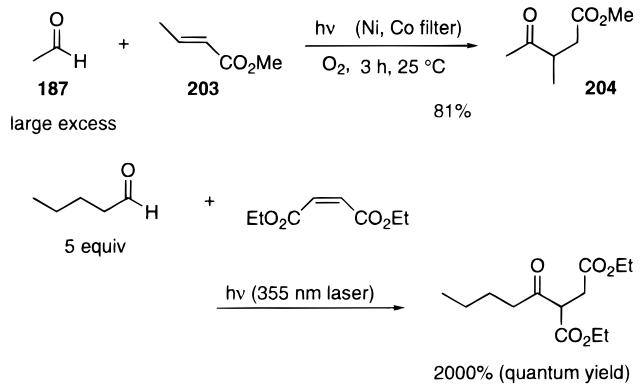
Scheme 157



solution of an enone, a large excess of **187**, and 16 mol % of benzophenone (photosensitizer) were photolyzed for 5 h at 350 nm. After vacuum distillation, the adduct was obtained in 67% yield.

Macias and co-workers reported that photochemical addition of acetaldehyde (**187**) to electron-deficient alkenes in the presence of molecular oxygen provides a mild method for the synthesis of 1,4-difunctionalized compounds.[300] Typically, 5 mmol of an electron-deficient alkene **203** and 100 mL of freshly distilled acetaldehyde (**187**) were irradiated with a medium-pressure mercury lamp through a filter solution ($NiSO_4$ and $CoSO_4$) to give an 81% yield of 4-keto ester **204** (Scheme 158). A similar irradiation experiment under a nitrogen atmosphere was unsuccessful. Molecular oxygen, which was present in the reaction mixture, is thought to operate as a quencher of triplet state of acetaldehyde, converting it to the singlet state. Alternatively, oxygen may serve as a single electron-transfer reagent. Stringat and co-workers reported that 355 nm pulsed laser light can induce a chain addition reaction of pentanal to diethyl maleate (5/1 ratio) with an intensity-dependent quantum yield which can reach 2000% (second example in Scheme 158).[301a] The laser system

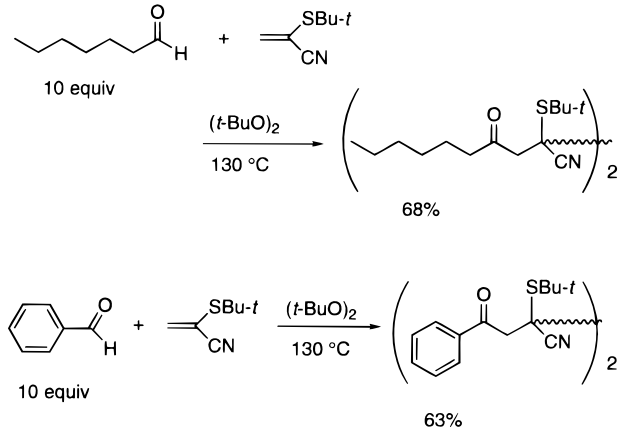
Scheme 158



suppresses the formation of a product from coupling with a hydroxyalkyl radical, which was observed in the irradiation system using a mercury lamp.[301b]

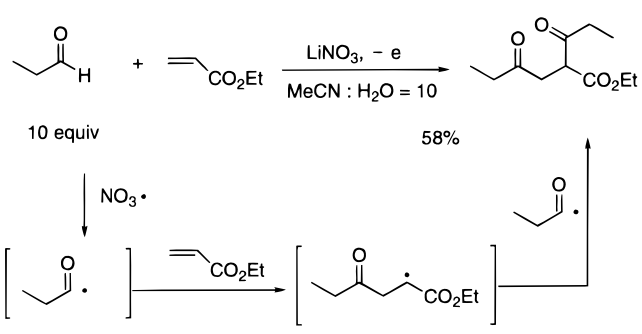
Viehe and co-workers studied the addition of aldehydes to capto-dative alkenes.[302] Since the adduct radical is unable to abstract the aldehydic hydrogen from aldehydes, dimers were obtained in moderate to good yields (Scheme 159).

Scheme 159



Kashimura, Shono, and co-workers found that electrochemically generated $NO_3^{\bullet}$ from NO_3^- abstracts hydrogen from aldehydes to form acyl radicals.[203] Interestingly, in the presence of electron-deficient alkenes, the reaction affords double acylation products in reasonable yields along with a negligible amount of 1 to 1 type product. An example of this double acylation reaction which starts with propanal and methyl acrylate is given in Scheme 160. Since

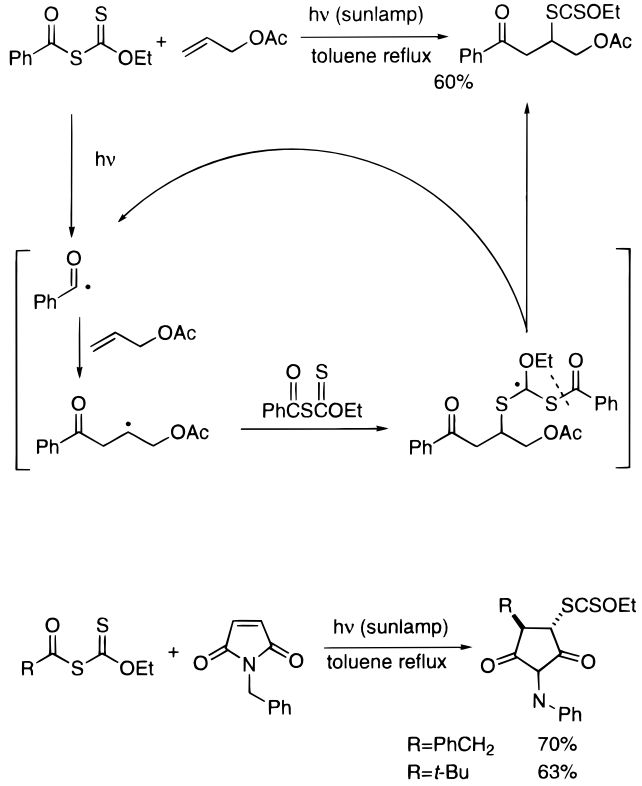
Scheme 160



all the key reactions would take place around the surface of the anode, the local concentration of radical species may be higher than that in the reaction carried out under the nonelectrochemical conditions.

Zard and co-workers reported that acyl radicals, which are generated from *S*-acyl xanthates by photolysis, add to alkenes accompanied with a xanthate group transfer.[131] Examples are given in Scheme 161

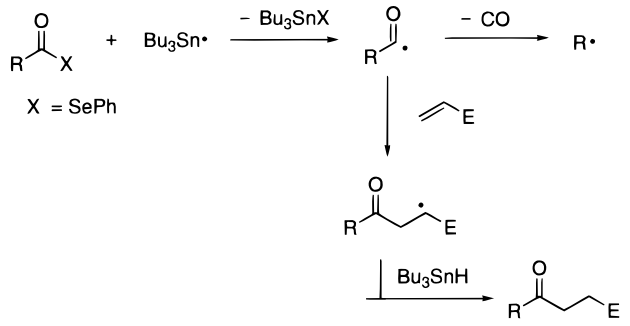
Scheme 161



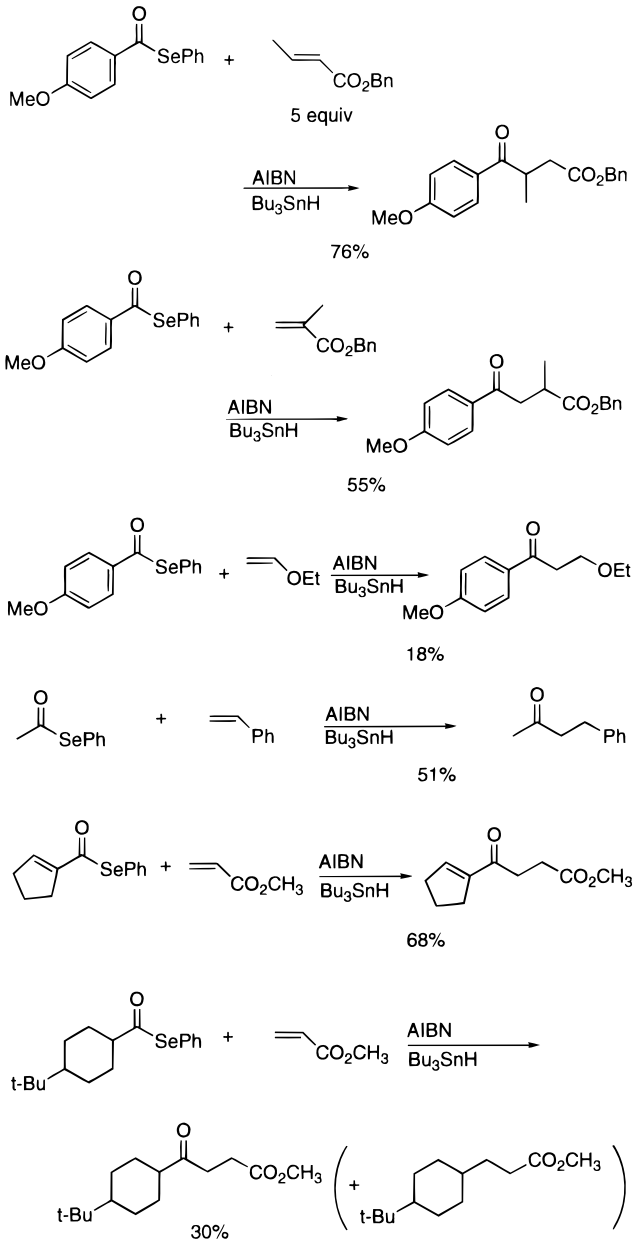
along with the proposed radical chain mechanism. A small amount of the double acylation product was also detected in this reaction. In the cases of the pivaloyl and phenylacetyl radicals (second example in Scheme 161), the decarbonylation reaction of these radicals predominates. As result, the reaction of these *S*-acyl xanthates gave the corresponding *tert*-butyl and benzyl transfer products in good yields.

As emphasized in section IV, acyl selenides are practical precursors for the generation of acyl radicals, since they are readily available and well accommodated to conventional tin radical-mediated reactions. Boger and Mathvink reported a ketone synthesis based on the acyl transfer reaction of acyl selenides to alkenes using tin hydride as a radical mediator.[135,303] The chain mechanism of this reaction is shown in Scheme 162. Among the possible side reactions, decarbonylation may be the most serious. In this regard, aroyl, vinylacyl, and primary alkylacyl radicals are suitable for the reaction but secondary and tertiary acyl radicals are inferior (Scheme 163). The use of excess amounts of alkenes is useful in suppressing both premature quenching and decarbonylation of acyl radicals. While electron-deficient alkenes and styrene work well, electron-rich and ordinary alkenes are not suitable for this ketone synthesis, as shown in the third example of Scheme 163. Unlike the aforementioned case of a thiol-

Scheme 162



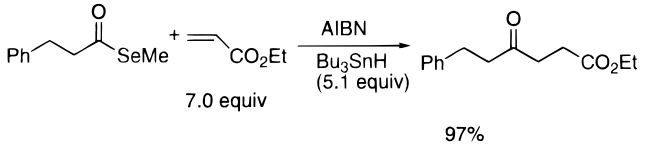
Scheme 163



catalyzed system (Scheme 152), the slow addition of acyl radical to electron-rich alkenes cannot compete effectively with the rapid hydrogen abstraction of acyl radical from the stoichiometric tin hydride.

Curran and Schwarz found optimal conditions for a similar acyl radical transfer reaction from acyl methyl selenide to ethyl acrylate. They discovered that a large excess of tin and olefinic reagent lead to the nearly quantitative formation of the 4-ketoester as illustrated in Scheme 164.[138] The excess reagents

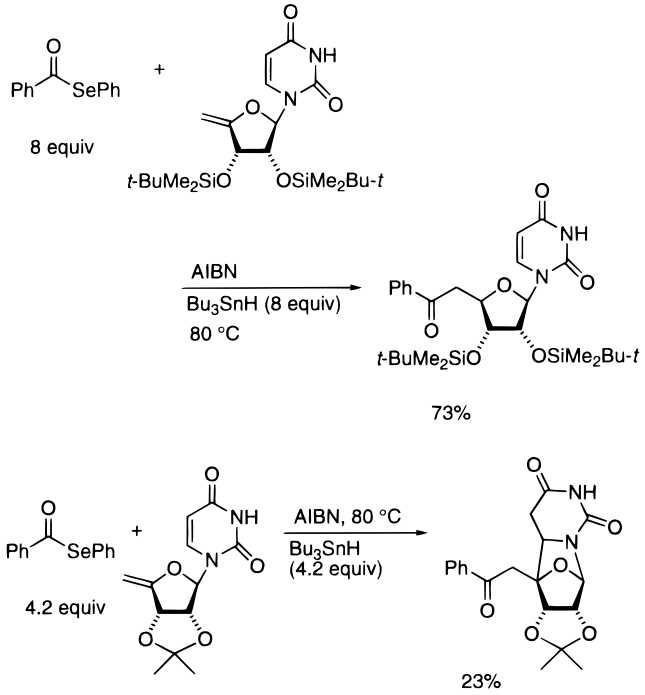
Scheme 164



are needed because of their mutual consumption in a hydrostannylation sequence.

Miyasaka and co-workers reported that acyl radicals generated from acyl selenides add to nucleoside-based enol ethers (Scheme 165).[304] As seen in the first

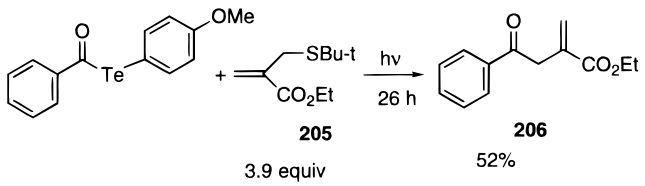
Scheme 165



example, to compensate for the poor reactivity of the alkene, acylating reagents are used in large excess. With a more conformationally rigid substrate having 2,3-acetonide, a second cyclization onto uracil was observed.

Crich and co-workers reported that an aroyl radical, generated from an aromatic acyl telluride by photolysis, adds to nonpolymerizable alkene **205** to form the corresponding addition/elimination product **206** (Scheme 166).[147] The pathway involves an S_H2'-

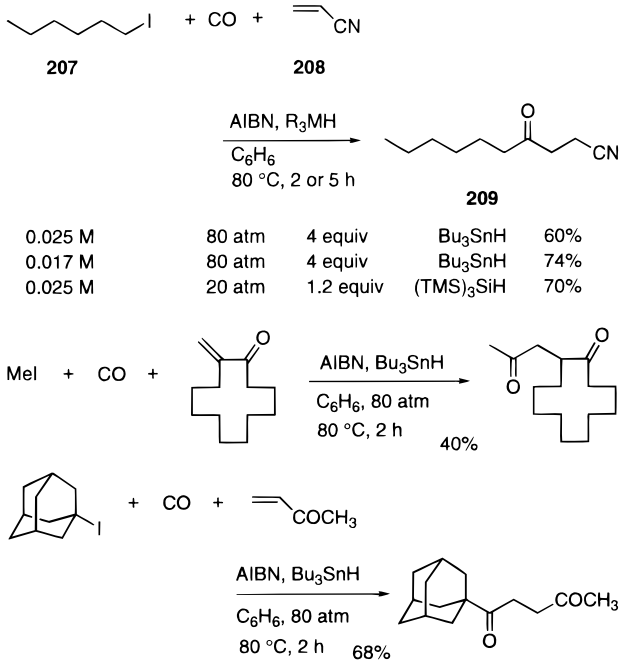
Scheme 166



type reaction with extrusion of a *tert*-butylthiyl radical.

Carbonylation methods can also participate in acyl radical transfer reactions. Ryu, Sonoda, and coworkers reported that in tin hydride-mediated radical chain systems, alkyl and aryl radicals add to carbon monoxide and electron-deficient alkenes sequentially to give the corresponding unsymmetrical ketones in good yields. Interestingly, this reaction sequence represents the double alkylation of carbon monoxide.[305] Scheme 167 shows a three-component coupling

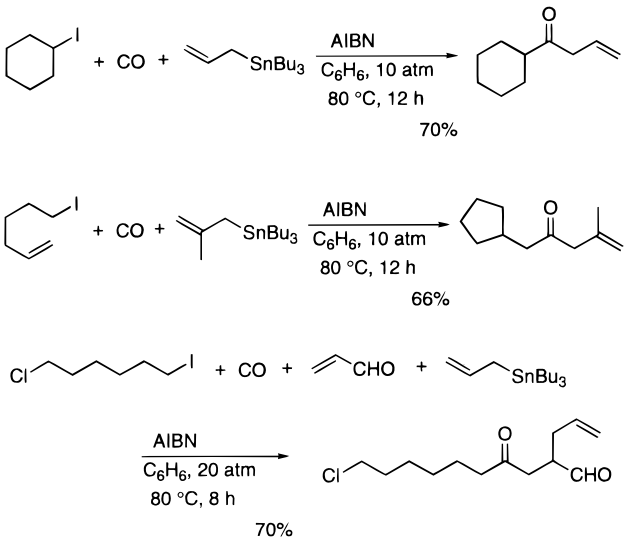
Scheme 167



reaction in which hexyl iodide (**207**), CO, and acrylonitrile (**208**) combine to form a β-cyano ketone **209** under several reaction conditions. The first CO addition step is in competition with the addition to the alkene and the hydrogen abstraction from tin hydride, but a set of higher pressure and dilution conditions enable the carbonylation to predominate over these undesirable reactions. A 4-fold excess of acrylonitrile was used to suppress the formation of heptanal which resulted from premature quenching of the acyl radical by tin hydride. However, the use of $(TMS)_3SiH$, a slower radical mediator than tin hydride, enables the reaction to be carried out with a nearly stoichiometric amount of acrylonitrile.[159] It is also because of this slower reduction that $(TMS)_3SiH$ can mediate carbonylation of free radicals at much lower CO pressures than those needed for the tin hydride system. Some other examples are also shown in Scheme 167.

In general, the use of a slower radical mediator is beneficial if radical carbonylation is to predominate over other undesirable reaction courses. This is also true for the allyltin-mediated radical carbonylation. Because of the slow direct addition of alkyl radicals to allyltin compounds,[306] radical carbonylation with allyltin can be conducted at relatively low CO pressures to give good yields of β,γ-unsaturated ketones.[307] The second example in Scheme 168 shows the cyclization−carbonylation−allylation sequence, in which 5-hexenyl radical cyclization precedes CO

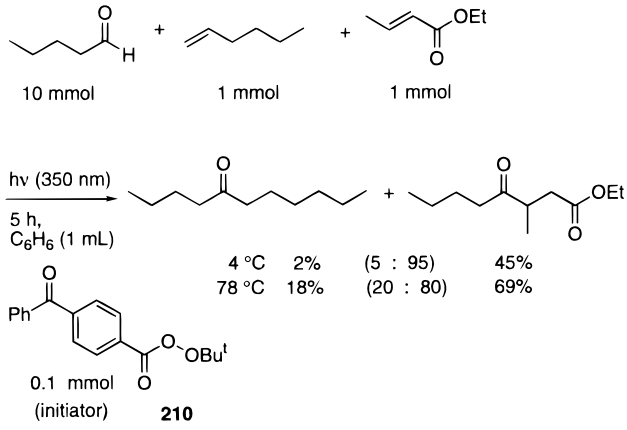
Scheme 168



trapping. In a mixed alkene system comprising electron-deficient alkene and allyltin, acyl radicals favor the electron-deficient alkene and the resulting product radicals then add to allyltin. Thus, a four-component coupling reaction leading to β-functionalized δ,ϵ-unsaturated ketones has been achieved using such a reaction system.[308a] A fluorous version of this chemistry has recently been reported.[308b]

Coupled with an appropriate initiation system, acyl radical addition to alkenes can be carried out at low temperature. This may be especially indispensable when selectivity problems are encountered. Gottschalk and Neckers investigated competition experiments involving acyl radical additions to simple and electron-deficient alkenes by changing the reaction temperature. They employed *tert*-butyl *p*-benzoylperbenzoate (**210**) as the photoinitiator (Scheme 169).[309]

Scheme 169

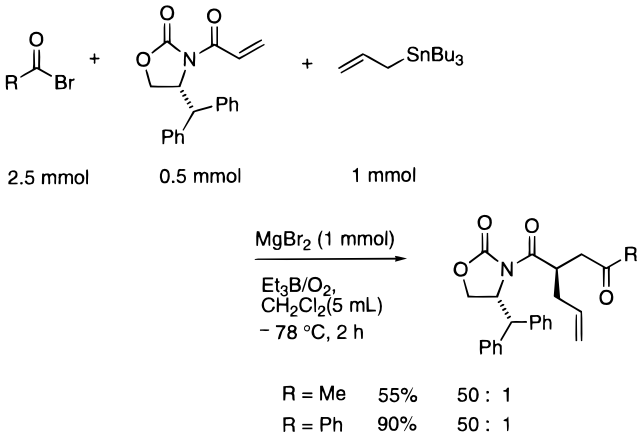


They observed that the preference for addition to electron-deficient alkenes is enhanced at lower temperatures.

Very recently, Sibi and Ji reported that acyl radicals, generated from acyl bromides, can participate in Lewis acid-mediated diastereoselective radical addition reactions.[310] Using triethylborane/O_2 as the radical initiator,[311] the reaction was conducted at −78 °C. The following example represents such a diastereoselective addition/allylation sequence which

uses allyltin, magnesium bromide, and triethylborane as the radical mediator, Lewis acid, and radical initiator, respectively (Scheme 170). The reaction in

Scheme 170

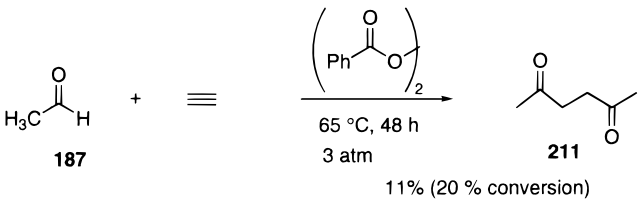


the absence of Lewis acids gave very low diastereoselectivity, and the use of acyl selenides as the acyl radical precursor gave polymeric products. There is little doubt that radical carbonylation can be combined with this stereocontrol system with appropriate low-temperature initiation.

B. Intermolecular Addition to C–C Triple Bonds

Only a restricted number of studies have been reported on the addition of acyl radicals to carbon−carbon triple bonds. Nevertheless, as long ago as 1954, the peroxide-initiated addition of aldehydes to acetylene was described (Scheme 171).[312] Since the

Scheme 171

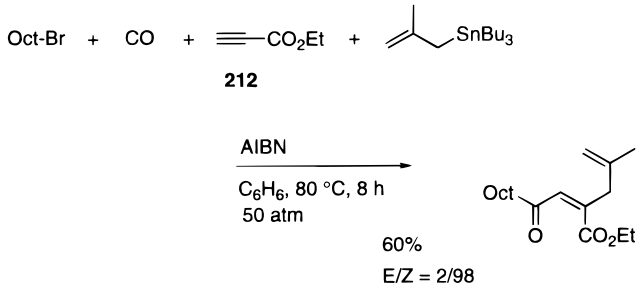


initial product is an α,β-unsaturated ketone, the second addition of aldehyde to this product alkene takes place more easily to give symmetrical 1,4-diketones (**211**). A similar vicinal double addition reaction of aldehydes to dimethyl acetylenedicarboxylate was reported in 1960 by Wiley and Harrell, who used γ-irradiation (^{60}Co) for the initiation.[313] The yields of 2,3-diacylsuccinates ranged up to 31%.

Ryu, Sonoda, and co-workers extended their four-component coupling reaction, which is shown in Scheme 168, to include electron-deficient acetylenes.[314] The following example shows that the reaction proceeds highly stereoselectively with ethyl propiolate (**212**) to give the *Z*-product (Scheme 172). The observed stereoselectivity is explained by assuming that allylation takes place at the least hindered site of the rapidly inverting vinyl radical.

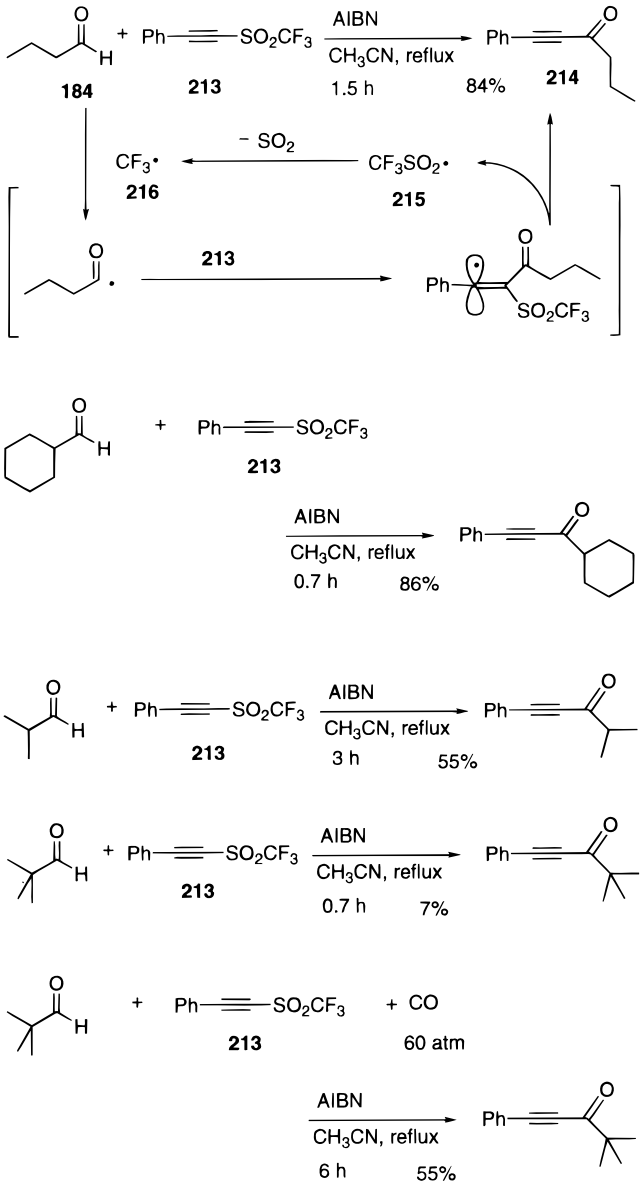
Recently, Fuchs and co-workers reported an interesting acyl radical transfer reaction from aldehydes to acetylenic trifluoromethyl sulfones, which affords

Scheme 172



acetylenic ketones.[315] Two consecutive UMCT (unimolecular chain transfer) processes[316] are involved in the chain propagation sequence (Scheme 173). The

Scheme 173



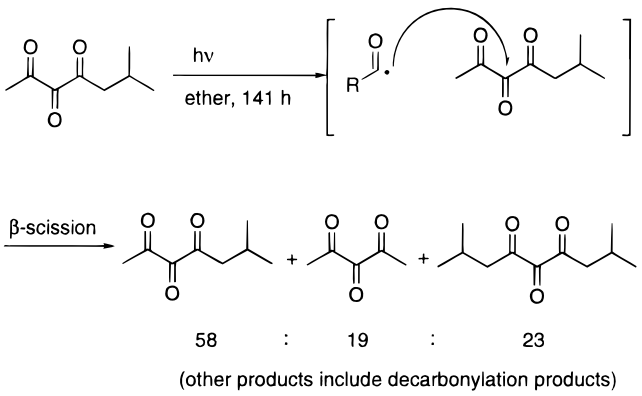
first UMCT is β-scission to form an acetylenic ketone **214** and trifluoromethylsulfonyl radical (**215**), and the second is α-scission of the sulfonyl radical to form the trifluoromethyl radical (**216**) and SO_2. The bond dissociation energy of H−CF_3 is known to be 107 kcal/mol, and the weaker C−H bond (87−88 kcal mol^{-1})

of an aldehyde is a possible target for the trifluoromethyl radical (**216**). Aldehydes are used in a slight excess (1.3−1.5 equiv), and the efficiency of the reaction, which is highly dependent on the structure of aldehydes, is in the order pivaloyl (tertiary) < isopropanoyl (secondary) < butanoyl (primary). This is obviously coupled with the ease of decarbonylation of the corresponding acyl radicals.[75] Indeed, in the case of pivalaldehyde, the major product obtained was that of addition of the *tert*-butyl radical. It is interesting to note that, as shown in the final example of Scheme 173, carrying out the reactions under CO pressures improved the yields of acetylenic ketones. The use of these CO conditions should provide a general solution whenever the decarbonylation course of the acyl radicals seriously competes with the targeted reactions.

C. Intermolecular Addition to Unsaturated Bonds Other than C–C Multiple Bonds

Free-radical additions of acyl radicals to aldehydes are not common. In 1948, Rust and co-workers reported that the reaction of benzaldehyde and di-*tert*-butyl peroxide (130 °C, 30 h) yielded a mixture of meso and racemic 1,2-diphenylethylene glycol dibenzoate. Addition of the benzoyl radical to benzaldehyde was proposed as a key step in the reaction pathway.[317] However, the intermediacy of the benzoyloxybenzyl radical, proposed in this study, was not confirmed by a subsequent, related EPR study.[43] Urry and co-workers reported that irradiation of unsymmetrical vicinal triones induces the acyl exchange reaction (Scheme 174).[318] This disproportion-

Scheme 174

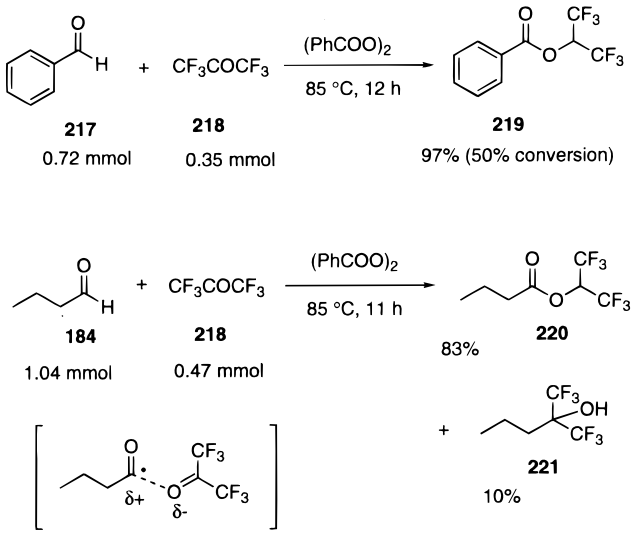


ation-type exchange reaction is most reasonably understood in terms of acyl radical addition onto the central carbonyl group followed by β-scission with extrusion of an acyl radical. In this example, obviously, acyl radical addition takes place in the "carbonphilic" manner.

The formation of esters is frequently observed in the reaction of acyl chlorides with tin hydride and AIBN.[114] When the phenomena was first discovered, it was thought that esters could result from "oxygenphilic" addition of acyl radicals onto the O−C double bond of aldehydes and the subsequent H abstraction of the resulting radical from tin hydride. But, as discussed in section IV.A.2, later work by Ingold and co-workers revealed that the reaction of the over-reduction product (alkoxytin compound) and acyl chloride gives the ester.[190]

Unambiguous examples of the reverse type intermolecular oxygen-philic reaction include acyl radical addition to perfluoro ketones, such as hexafluoroacetone (**218**), trifluoromethyl difluorochloromethyl ketone, etc.[319] The BPO-initiated addition of benzaldehyde (**217**) to **218** gave the *O*-acylated product **219**. Similarly, addition of butanal (**184**) occurs in an oxygen-philic manner to give **220** (Scheme 175). It is

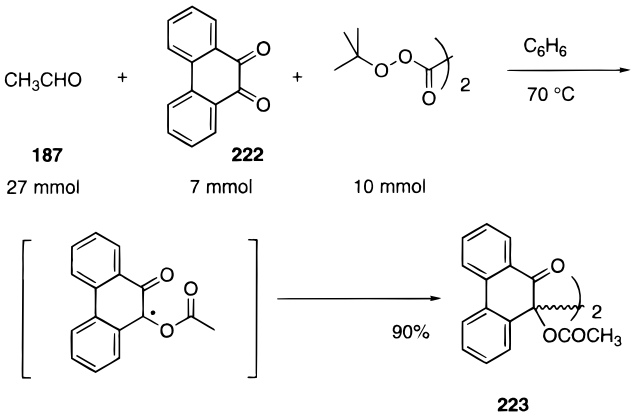
Scheme 175



interesting to note that the addition of a propyl radical, formed by decarbonylation of the acyl radical, to **218** occurs in the carbon-philic manner to give **221**. Polar effects are proposed to account for the oxygenphilic behavior of acyl radicals.

Examples of oxygen-philic addition of acyl radicals are often observed in the photochemical reactions of aldehydes with quinone compounds.[320] Scheme 176

Scheme 176

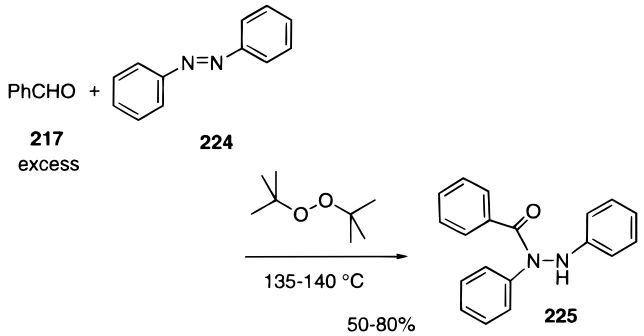


shows an example of the high-yield trapping of the acetyl radical by phenanthraquinone (**222**), which was reported by Maruyama and co-workers.[321] A nonchain radical mechanism which involves oxygenphilic attack of the acetyl radical is proposed for the formation of the dimeric product **223**. A similar reaction under irradiation conditions gave the hydroacylation product rather than the dimer, suggest-

ing a mechanistic difference between two reactions. The photochemical reaction of 1,2-naphthoquinone with aldehydes was studied with emphasis on the mechanistic aspects, and an in-cage mechanism was proposed.[322]

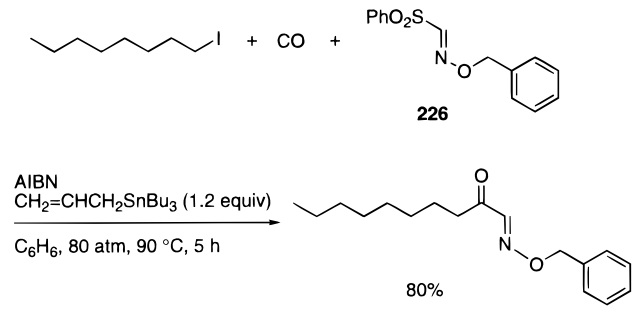
Acyl radicals can also be trapped intermolecularly by N=N double bonds.[323] For example, Kharasch reported that radical chain addition of benzaldehyde (**217**) to azobenzene (**224**) gives good yields of monobenzoylhydrazobenzene **225** (Scheme 177).[323a]

Scheme 177



Intermolecular addition of acyl radicals to C=N double bonds is highly inefficient. However, Kim's sulfonyl oxime ether[324] is a notable exception. For example, radical carbonylation of an alkyl iodide in the presence of sulfonyl oxime **226** gave a new type of three-component coupling product in good yield (Scheme 178).[325] This is a unique transformation,

Scheme 178

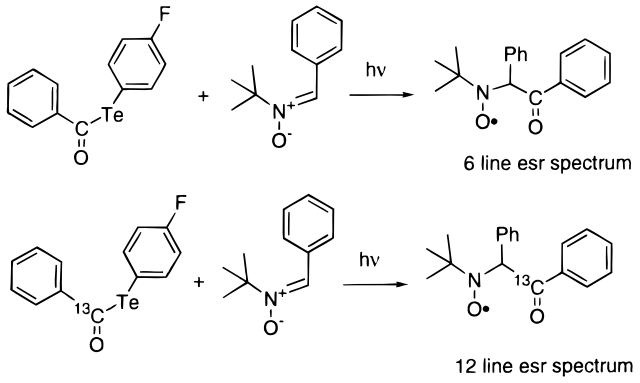


since two representative radical C1 synthons[31] come together to realize the formal double carbonylation reaction of radicals. Such a transformation is not achieved by a double carbonylation of alkyl radical as mentioned above in Scheme 143.

Trapping by nitrones is less efficient but nevertheless takes place with the formation of nitroxyl radicals (section II.B).[53,147] Such a reaction was conducted with a ^{13}C-labeled benzoyl telluride whereby the hyperfine splitting of the resultant nitroxyl in the EPR spectrum was used to confirm the formation of acyl radicals in the photolysis (Scheme 179).[147]

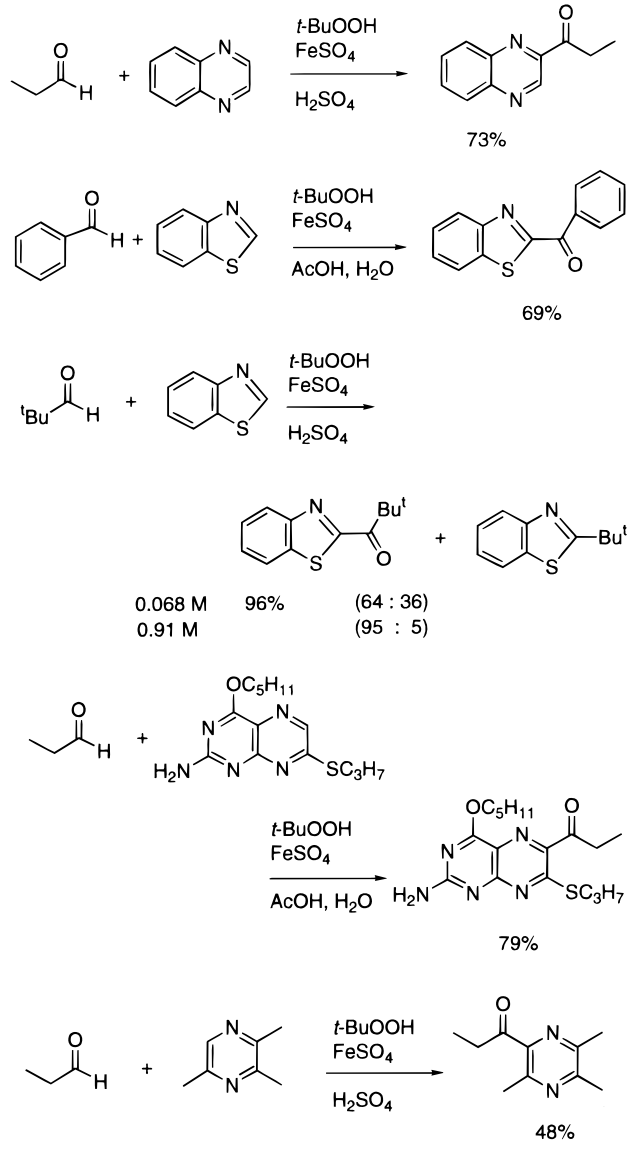
Some of the most useful C−C bond-forming intermolecular processes have been described by the Minisci group who investigated the reaction of aldehydes with protonated heteroaromatic bases under Fenton-type conditions, i.e., with the crucial hydrogen abstraction affected by the electrophilic HO• radical.[326−328] In many cases, excellent yields were obtained, and this is a good preparative method for

Scheme 179



acylated heterocyclic bases. The examples (Scheme 180) nicely illustrate the utility of protonated het-

Scheme 180



erocyclic bases as traps for acyl radicals. The first example illustrates the addition of propanal to quinoxaline.[326] As shown in the third example, the addition reaction of the pivaloyl radical to protonated benzothiazole proceeds at such a rate that decarbon-

ylation is seemingly not a problem, especially when the higher concentration of protonated base was employed.[327] The rate constant for the addition was determined to be 7.1×10^5 mol^{-1} s^{-1} at 5 °C.[327] The last two examples are applications of this Minisci-type homolytic nucleophilic acylation with 7-alkylthiopteridine[329b] and trimethylpyrazine,[329b] respectively. The related acylation reaction starting from α-keto acids is shown in Scheme 33 (section IV.C.2).

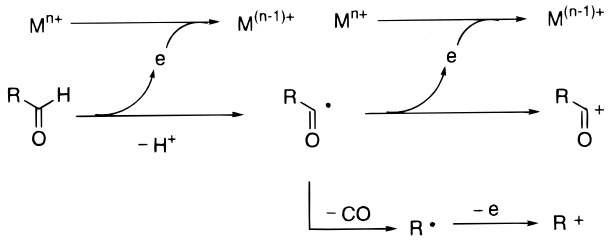
IX. Oxidation and Reduction

A. Oxidation

1. Autoxidation of Aldehydes

The carbon−hydrogen bond in the formyl group of aldehydes is a relatively weak σ bond (section II.A), and a number of one-electron oxidizing reagents have been used to effect the oxidation, including metal species, such as Mn(III), Ce(IV), Co(III), and Fe(III). One-electron oxidation of aldehydes leads to the formation of acyl radicals with liberation of proton (Scheme 181). Thus formed acyl radicals usually

Scheme 181

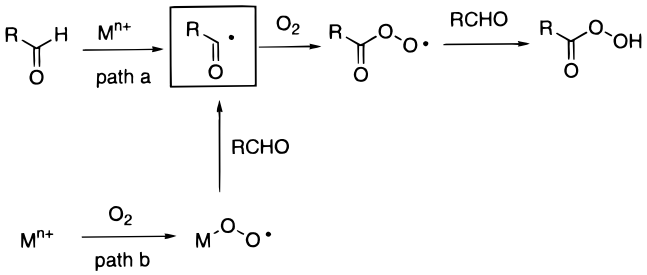


undergo a second one-electron oxidation by another molecule of metal reagents with conversion to acyl cations, but in some cases decarbonylation predominates and the resulting alkyl radicals undergo the one-electron oxidation by metal ions to give alkyl cations. An excellent survey of the initial work in this area is given in two reviews on oxidation[330] and in the earlier reviews on acyl radicals.[4]

As Walling's recent review on autoxidation pointed out,[331] it was recognized more than 150 years ago that aldehydes are prone to facile autoxidation, but the first proposal of the intervention of an acyl radical in the autoxidation system did not surface until the 1930s.[332] Unfortunately, the initiation step of "pure" autoxidation is not yet well understood, since the direct abstraction of hydrogen by oxygen is highly endothermic.

It is well-known that traces of metal salts, such as Fe, Cu, Co, Mn, to mention but a few, catalyze the autoxidation of aldehydes. In such metal-catalyzed aerobic oxidation of aldehydes, the generation of an acyl radical and its conversion to an acyl peroxy radical are thought to be the key and two mechanisms are proposed for this initiation process (Scheme 182). The first mechanism involves the direct interaction of the metal catalyst with the aldehyde to form an acyl radical (path a), which is identical to the first step shown in Scheme 181, and the second involves the binding of oxygen with transition metals to form a metal peroxy radical (path b), which undergos

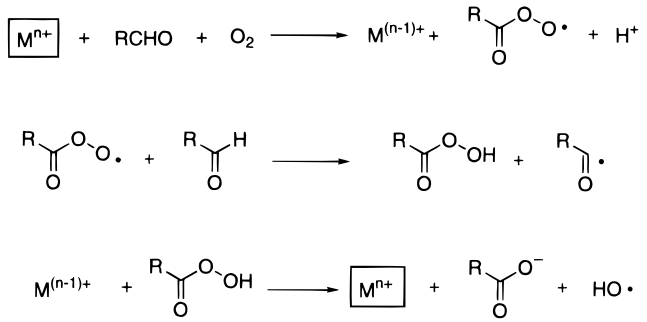
Scheme 182



abstract of hydrogen from the aldehyde to yield an acyl radical.[293,333]

Whatever the case, chain propagation is achieved by H-abstraction from aldehydes by acylperoxy radicals to form peracids and acyl radicals. It is known that the reactivity of acylperoxy radicals is 3−4 orders of magnitude higher than the corresponding reaction of alkylperoxy radicals (section IV, Table 9). Reduced metal species formed during the oxidative initiation step would effect the decomposition of the product peroxides, and through this process they recover the initial oxidation state, thus creating the catalytic oxidation system (Scheme 183). The com-

Scheme 183

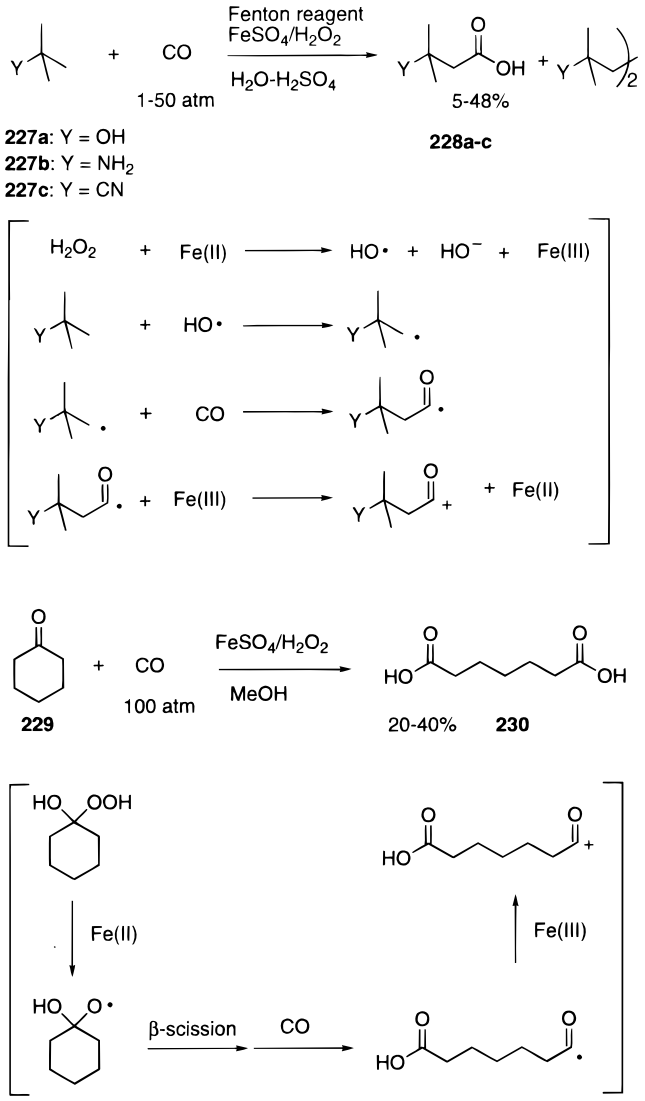


bination of metal species, aldehydes, and molecular oxygen is frequently employed in catalytic oxidations of alkenes, which have considerable synthetic potential but are outside the range of this review.

2. Oxidation of Acyl Radicals by Fenton's Reagent

In the 1950s, two groups independently investigated oxidative radical carbonylation using Fenton's reaction system comprising Fe(II) sulfate and hydrogen peroxide. Coffman and co-workers reported that the combination of Fenton's reagent and carbon monoxide can effect oxidative carbonylation of methyl C−H bonds.[334] The first equation in Scheme 184 summarizes the carboxylation of *tert*-butyl alcohol (**227a**), *tert*-butylamine (**227b**), and pivalonitrile (**227c**) leading to the corresponding carboxylic acids **228a**−**c**. Thus, when these "nine C−H" compounds were exposed to CO (1−50 atm) at room temperature in the presence of hydrogen peroxide−Fe(II)SO_4 (1:1 to 1:0.6) in aqueous sulfuric acid, 5−48% yields of the carboxylated products were formed together with byproducts derived from homocoupling of the parent alkyl radicals. The formation of carboxylic acids can be explained by the redox-type mechanism outlined in Scheme 184, but the use of a 0.6/1 ratio of Fe(II) sulfate to hydrogen peroxide appears far from ideal

Scheme 184



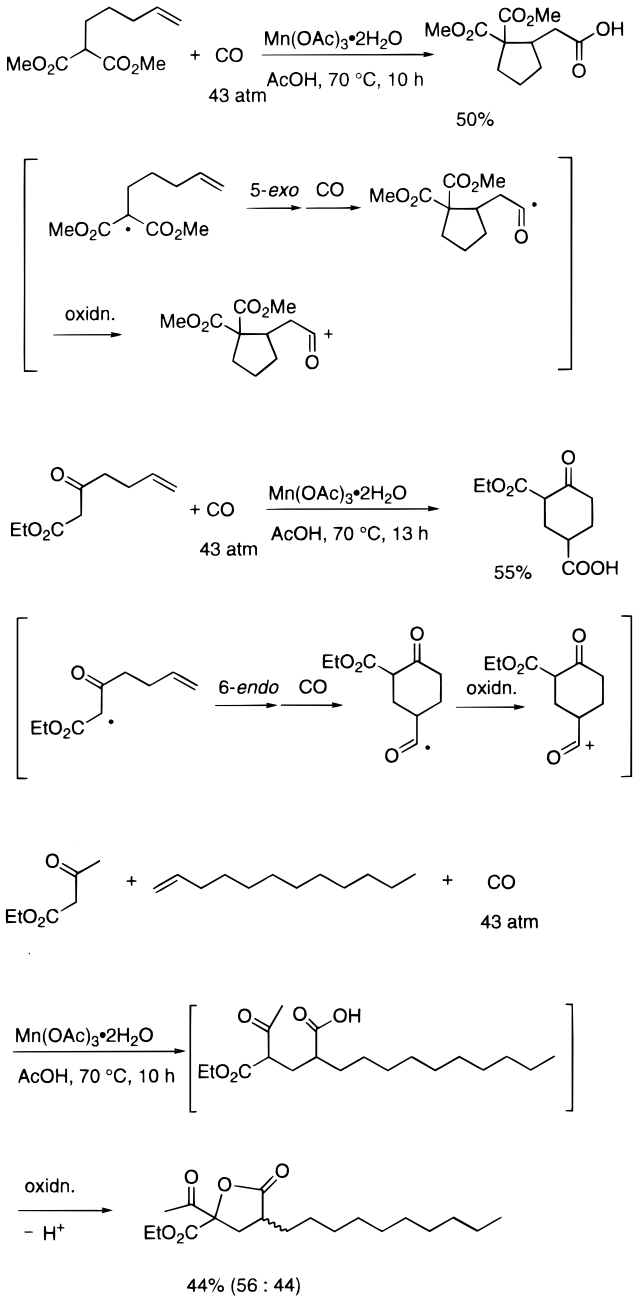
as a practical catalytic process. Furthermore, the severe structural limitation of the substrates in connection with the selectivity in H-abstraction by hydroxyl radical makes this process highly unattractive. Nevertheless, this represents a pioneering effort for the oxidative carbonylation chemistry based on acyl radical species.

Concomitantly, Chiusoli and Minisci reported the use of a Fenton-type redox/CO combination for ring-opening carboxylation of cyclic ketones such as cyclopentanone and cyclohexanone (**229**).[335] Thus, under pressurized conditions of CO, modest yields of pimeric acid (**230**) were obtained from cyclohexanone (**229**) and CO via iron-induced carbonylative decomposition of 1-hydroxycyclohexyl hydroperoxide (the second equation in Scheme 184). In the hands of Coffman and co-workers, the same process, but under only 1 atm of CO, gave only a 4% yield.[334]

3. Oxidation of Acyl Radicals by Manganese(III)

The one-electron oxidation of an acyl radical leading to an acyl cation is expected to be far more facile than the oxidation of primary alkyl, secondary alkyl, and vinyl radicals. The relatively slow oxidation of

Scheme 185



these alkyl and vinyl radicals in manganese(III) oxidation systems allows for the competition of CO trapping by these radicals, followed by smooth one-electron oxidation of the resulting acyl radicals to give carboxylic acids via acyl cations.

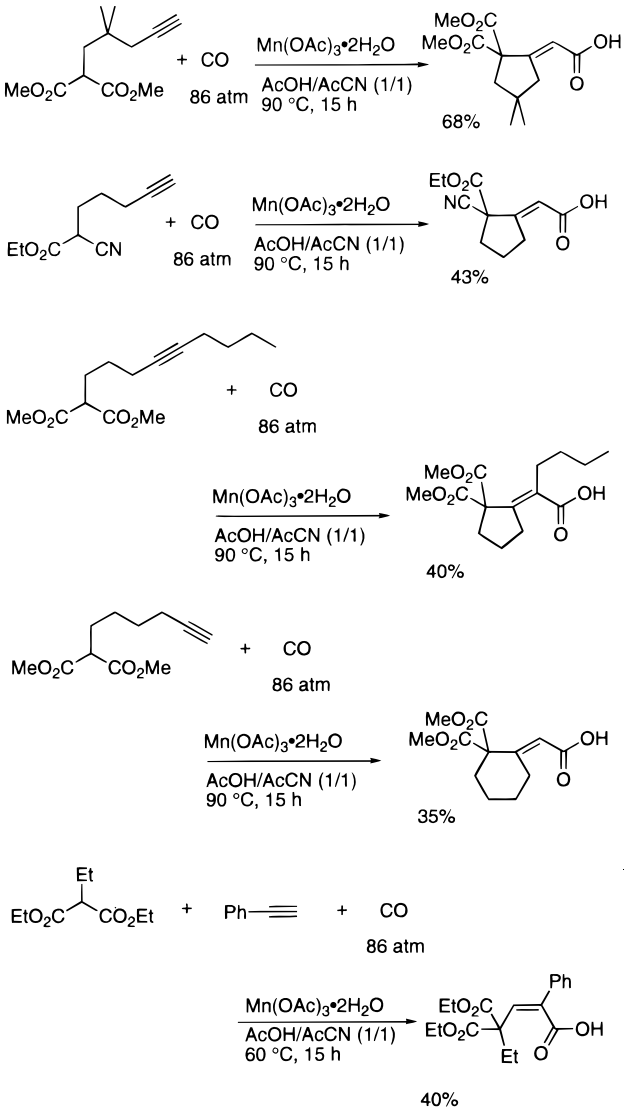
Alper and Ryu reported that acyl radical formation by carbonylation and the subsequent oxidation sequence can be readily achieved in a manganese triacetate-induced oxidation process,[336] which starts with Mn(III)-induced one-electron oxidation of enolizable carbonyl compounds.[3n] The first two examples of Scheme 185 illustrate intramolecular cyclization and oxidative carbonylation. In the first example, a primary radical formed via 5-exo-trig cyclization of a malonyl radical underwent the carbonylation/oxidation sequence. In the second example, a secondary radical formed via 6-endo-trig cyclization takes part in such a reaction sequence. The preferential

formation of a six-membered ring for radicals with a carbonyl group inside the ring is precedented and has been discussed in terms of stereoelectronic effects.[337]

A three-component coupling sequence which involves intermolecular addition of α-ketoalkyl radicals to alkenes and the subsequent carbonylation/oxidation also works well. In the third example of Scheme 185, the initially formed three-component coupling product has an enolic proton, which permits a further manganese(III)-induced oxidative cyclization to take place with formation of a γ-lactone ring as the predominant product.

Alper and Okuro extended the Mn(III)-induced oxidative carbonylation reaction to include alkynes as the substrates, providing a unique synthesis of α,β-unsaturated carboxylic acids (Scheme 186).[338] The

Scheme 186

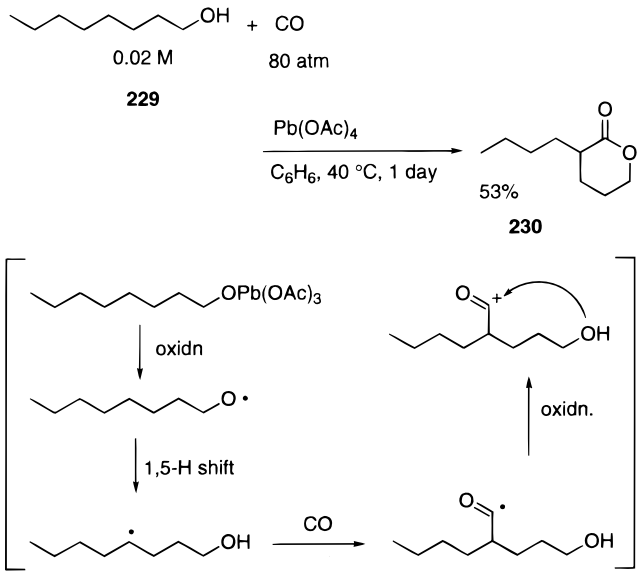


inefficient oxidation of vinyl radicals, which are formed by intra- and intermolecular addition of α-keto radicals to the triple bonds, allows for the successful carbonylation to give α,β-unsaturated acyl radicals. Subsequent oxidation of these radicals leads to α,β-unsaturated acyl cations, which are trapped to give carboxylic acids. Interestingly, the use of a mixed solvent (AcOH−CH_3CN (1:1)) improved the yields of carboxylic acids and in many cases the reaction proceeded stereoselectively.

4. Oxidation of Acyl Radicals by Lead(IV)

Oxidative cyclization of saturated alcohols by lead tetraacetate leading to tetrahydrofuran derivatives was originally discovered in the late 1950s and mainly pursued by Mihailovic and co-workers.[339] Ryu, Tsunoi, and Sonoda reported that the oxidative carbonylation of saturated alcohols leading to δ-lactones can be conveniently achieved with the aid of this one-electron oxidation system.[340] As exemplified by the conversion of 1-octanol (**229**) to δ-lactone **230** in Scheme 187, an acyl radical resulting from carbonylation of the δ-hydroxyalkyl radical, formed by 1,5-radical translocation, undergoes the one-electron oxidation to form an acyl cation. Subsequent deprotonative cyclization of this acyl cation yields the δ-lactone.

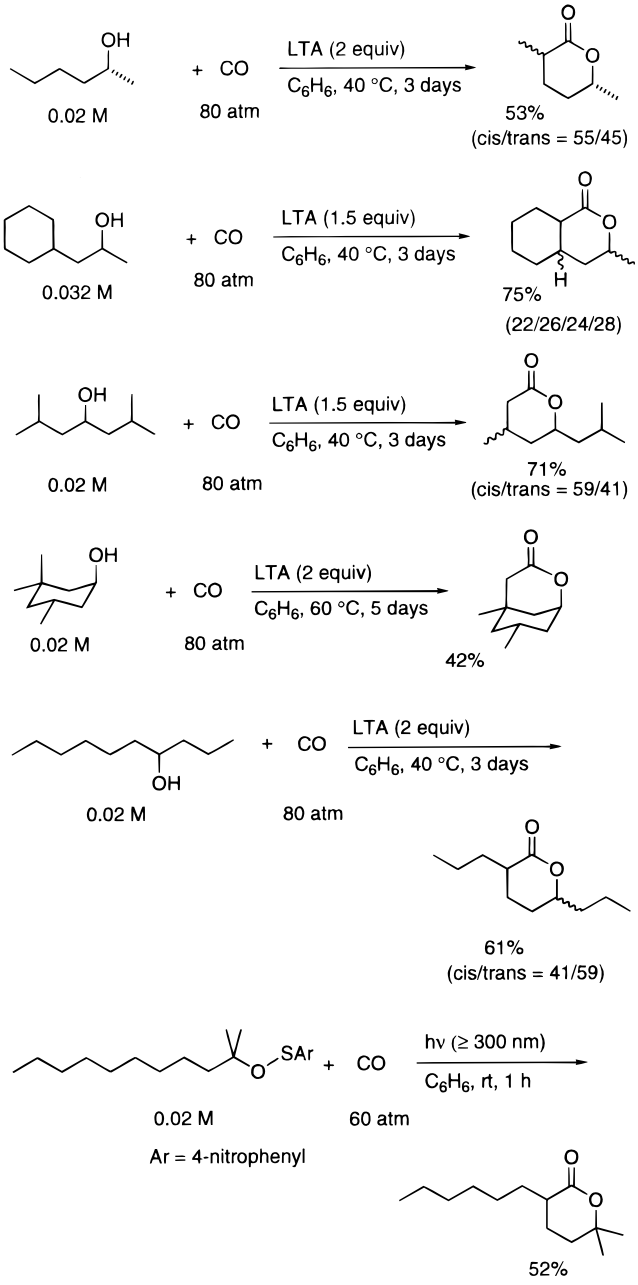
Scheme 187



Thanks to an extensive systematic study,[340] it was revealed that the carbonylation reactions are applicable to primary alcohols having 1° δ-carbons or 2° δ-carbons and secondary alcohols having 1° δ-carbons or 2° δ-carbons, and some of the examples are given in Scheme 188. The relatively low reactivity of the methyl C−H bonds toward hydrogen abstraction by oxygen radical permits the site-selective carbonylation of alcohols at the secondary δ-carbon: the penultimate equation in Scheme 188 demonstrates such an example. Carbonylation of tertiary alcohols was unsuccessful because of the low reactivity of these alcohols to LTA, but a photolytic carbonylation/S_H2 reaction approach via alkyl benzenesulfenates may complement this deficiency in the future.[340b]

The oxidative ring-opening reactions of cyclobutanols by LTA can be combined with a subsequent carbonylation/oxidation sequence (Scheme 189).[341] Interestingly, C1-unsubstituted cyclobutanols **231** and **232** gave δ-lactones **233** and **234** as the products, respectively. This may be understood by assuming intramolecular cyclization of an acyl cation to formyl

Scheme 188

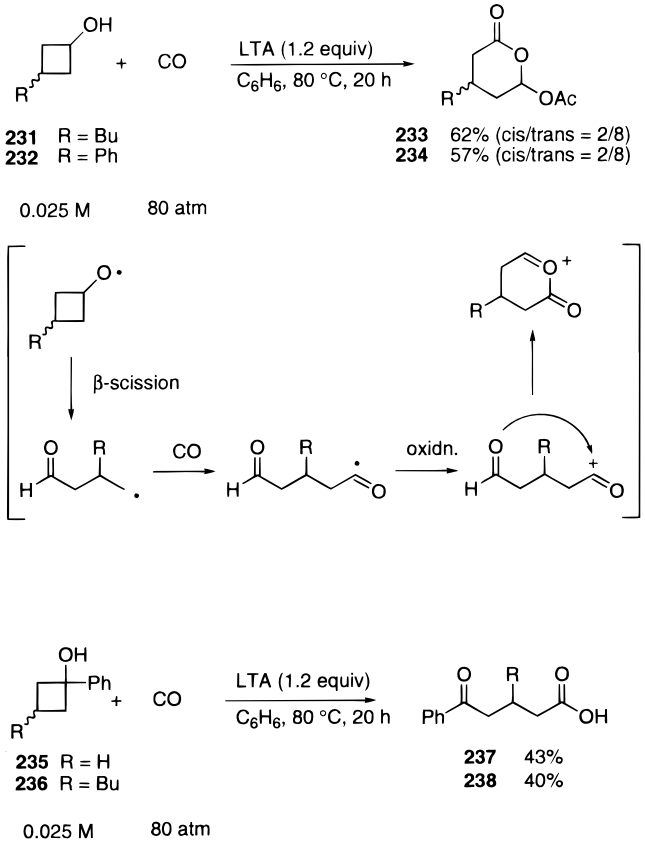


oxygen, followed by acetoxylation with acetic acid, a byproduct of the reaction. In the case of C1-substituted cyclobutanols **235** and **236**, no such product derived via a cationic cyclization onto a ketone carbonyl was observed and, instead, 4-ketocarboxylic acids **237** and **238** were obtained, respectively.

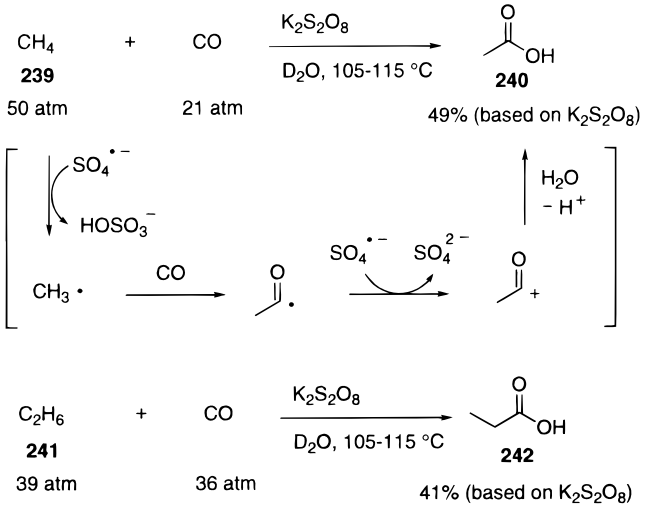
5. Oxidation of Acyl Radicals by Some Other Oxidizing Agents

Peroxydisulfate is a peroxide frequently used as an initiator for radical polymerization in the chemical industry. Lin and Sen reported the successful radical carboxylation of methane (**239**) and ethane (**241**) leading to acetic acid (**240**) and propionic acid (**242**), respectively, using potassium peroxydisulfate as a stoichiometric reagent (Scheme 190).[342] Potassium

Scheme 189



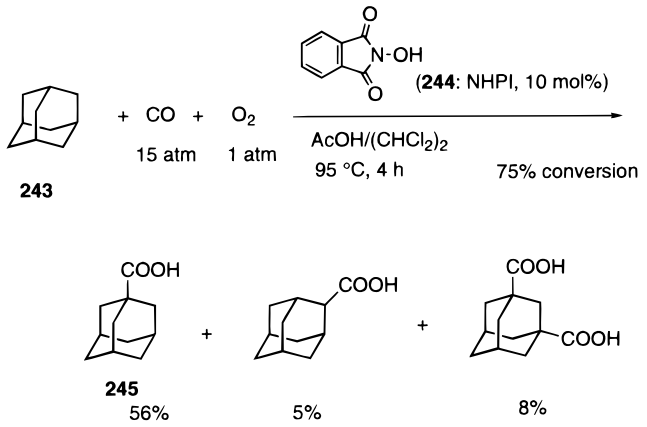
Scheme 190



peroxydisulfate appears to play two roles here: one is as a source of oxygen radical to form methyl and ethyl radicals by H-abstraction and the other is as a one-electron oxidizing reagent to convert acyl radicals, resulting from radical carbonylation, to acyl cations.

Very recently Ishii and co-workers reported an interesting radical carboxylation of adamantane (**243**) using a catalytic amount of NHPI (*N*-hydroxyphthalimide) (**244**), CO, and dioxygen, leading to a reasonable yield of 1-adamantanecarboxylic acid (**245**) (Scheme 191).[343] Although the precise mechanism has not yet been identified because of many alternative reaction courses, the first stage may involve the

Scheme 191



generation of phthalimide-*N*-oxyl (PINO) from NHPI and O_2 and its abstraction of hydrogen from adamantane. The so-formed adamantyl radical would then undergo consecutive addition to CO and O_2 to form the adamantanecarbonylperoxy radical, which would abstract hydrogen from adamantane to form the peracid, a likely precursor for adamantane−carboxylic acid **245**, along with the adamantyl radical.

Russell and co-workers found an example in which a transiently formed acyl radical was oxidized to give a carboxylic acid during the course of their study aiming at intramolecular aromatic alkylation by electron-transfer chain reactions using alkylmercuric halides under photolytic conditions.[344] In the example given in Scheme 192, *tert*-butylmercuric chloride effects one-electron oxidation of an acyl radical leading to an uncyclized carboxylic acid.

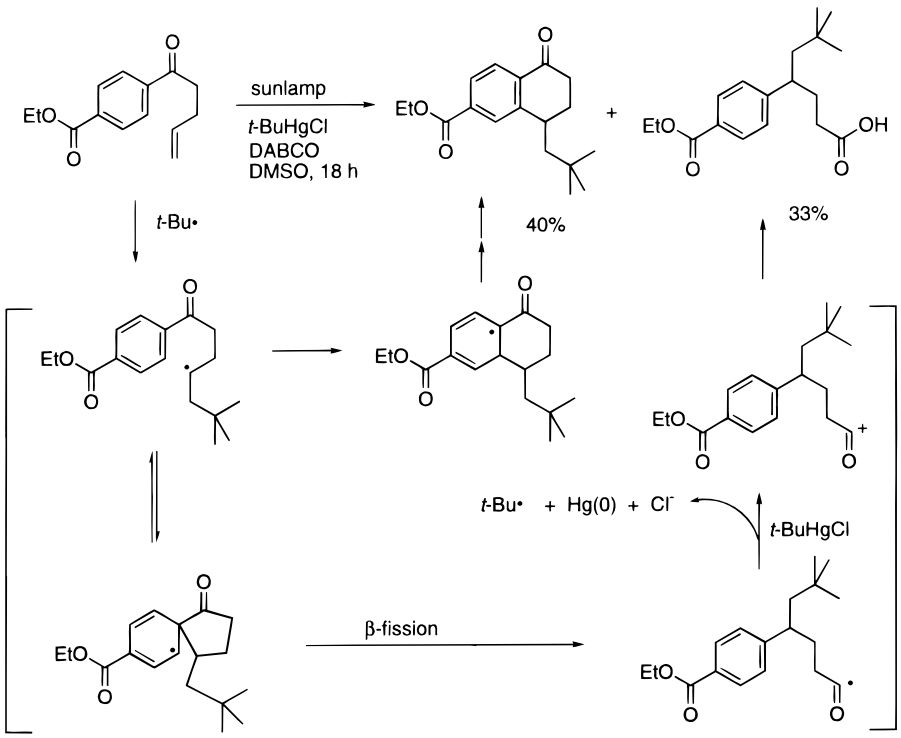
B. Reduction

1. Reduction of Acyl Radicals by Zinc and Samarium Reagents

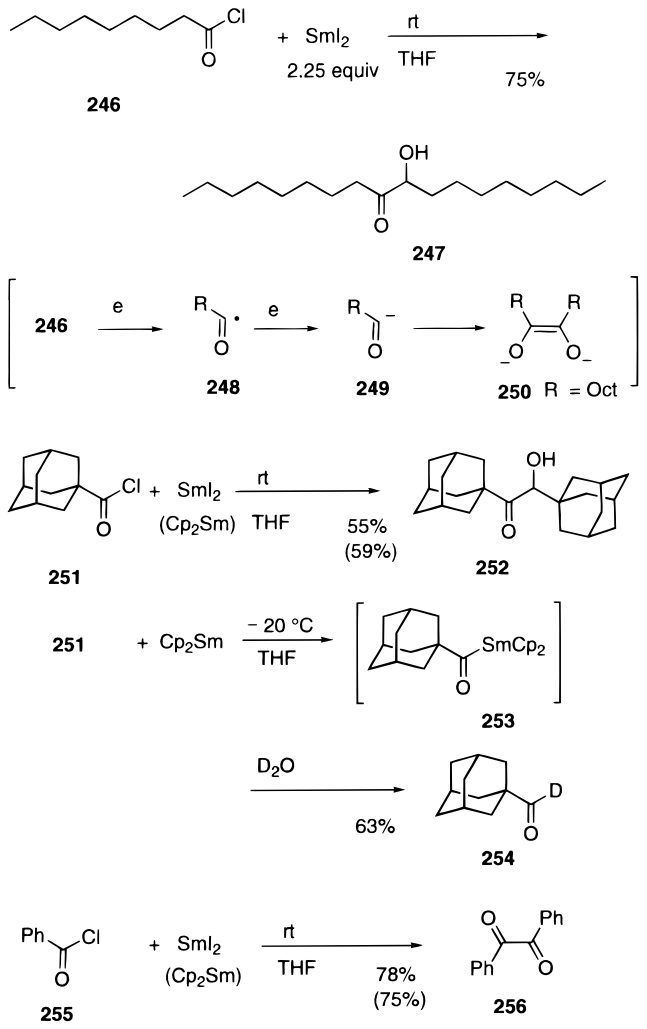
Just as one-electron oxidation of acyl radicals gives acyl cations, one-electron reduction of acyl radicals gives acyl anions. In the following example reported by Kagan and co-workers, nonanoyl chloride (**246**) was reduced by SmI_2 or Cp_2Sm to give a good yield of α-ketol **247** (Scheme 193).[116] Although homocoupling of two molecules of acyl radical **248** followed by repeated one-electron reduction can account for the formation of **247**, one likely alternative mechanism for this reaction involves dimerization of nonanoyl anion **249** arising from two consecutive one-electron reductions of nonanoyl chloride (**246**) by Sm(II). Indeed, the dimerization of acyllithiums is well precedented.[345] A similar Sm(II) reduction of 1-adamantylcarbonyl chloride (**251**) gave the corresponding α-ketol **252** as the main product. In a separate experiment dealing with the reaction of adamantylcarbonyl chloride **251** and Cp_2Sm, a deuterium oxide quench at −20 °C gave a 63% yield of deuterated aldehyde **254**. This supports the intermediacy of an acyl anion **253** for the formation of α-ketol product.

On the other hand, reduction of benzoyl chloride (**255**) by SmI_2 or Cp_2Sm gave a different type of product, α-diketone **256** (Scheme 193).[116] One possible mechanism for this reaction may be the homocoupling of benzoyl radicals arising from one-electron reduction of benzoyl chloride by Sm(II). However, the facts that the use of 2.25 equiv of SmI_2 in this system is sufficient to ensure two-consecutive one-electron transfer processes and the relatively smaller redox potential for the conversion of the benzoyl radical to

Scheme 192



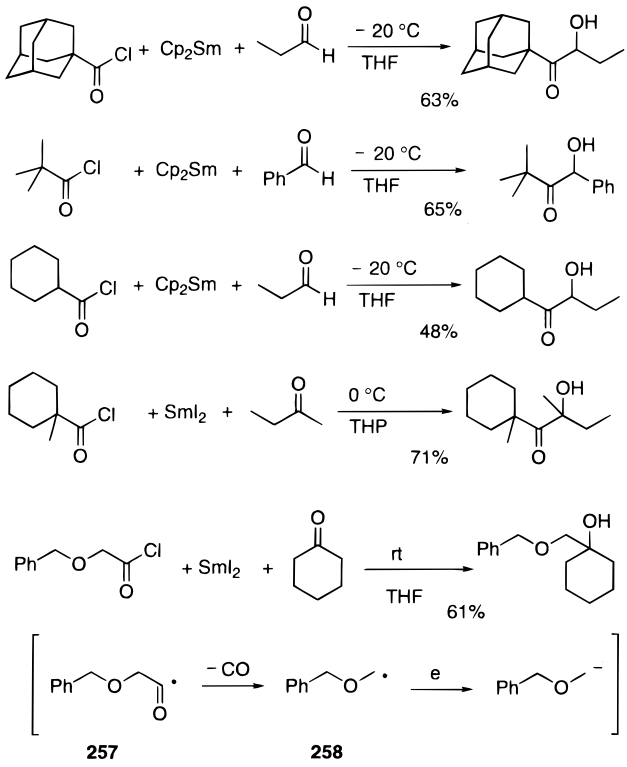
Scheme 193



benzoyl anion in comparison to alkylacyl radicals[346] do not necessarily favor this simple radical/radical coupling mechanism. Since facile air oxidation of a similar benzoyllithium dimer during the workup procedure is known to give a good yield of α-diketone,[347] a related mechanism involving a dimerization/oxidation sequence of benzoylsamarium(III) cannot be excluded.

By the use of a Barbier-type procedure, acylsamarium(III) species generated from acid chlorides and $Cp_2Sm(II)$ can be intermolecularly trapped by aliphatic aldehydes to form α-ketols (Scheme 194). It is well established that SmI_2 is most conveniently generated in THF as the solvent from samarium and 1,2-diiodoethane.[348] However, in this Sm(II)−acyl chloride chemistry, an undesirable THF acylation reaction often lowered the yields of α-ketols. Fortunately, Kagan's recent establishment of a method for the preparation of SmI_2 from samarium and 1,2-diiodoethane in tetrahydropyran (THP) circumvented this dilemma.[349] Thus, as shown in the fourth example of Scheme 194, a good yield of α-ketol was obtained using the SmI_2/THP reagent. The fifth example treats the reaction with an α-alkoxyacyl chloride with accompanying decarbonylation. Perhaps, the rapid decarbonylation of alkoxyacetyl radical **257** to form stable alkoxyalkyl radical **258** is

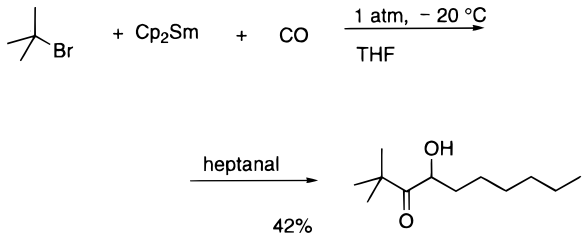
Scheme 194



favored over one-electron reduction of the acyl radical.[350]

Interestingly, Kagan also studied similar reactions starting with *tert*-butyl bromide, CO, and Cp_2Sm (Scheme 195). Unfortunately, the scope and limita-

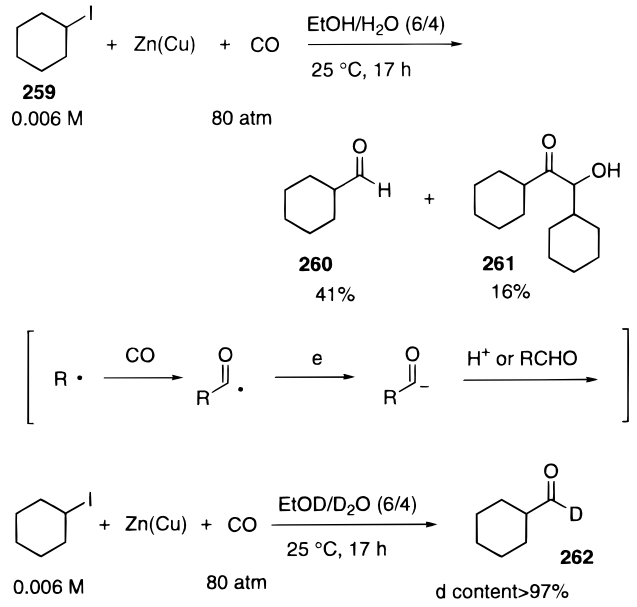
Scheme 195



tions were not examined. Nevertheless, this could be a possible alternative to access similar condensation products. In this case, the acylsamarium is likely formed as the intermediate via radical carbonylation followed by one-electron reduction.[351]

Ryu, Sonoda, and co-workers reported that one-electron reduction of acyl radicals to acyl anions can take place in a zinc-induced carbonylative reduction system of alkyl iodides.[352] For example, treatment of cyclohexyl iodide (**259**) with zinc in a mixed protic solvent (EtOH and H_2O) under CO pressure yielded cyclohexanecarboxaldehyde (**260**) and an α-ketol **261** as the main carbonylation products (Scheme 196). For the formation of the aldehyde, the following reaction mechanism is likely: (i) the cyclohexyl radical is generated by a one-electron reduction of cyclohexyl iodide, (ii) the addition of this radical to CO gives an acyl radical, (iii) one-electron reduction of the acyl radical gives an acyl anion, and (iv) protonation of the acyl anion by the solvent gives

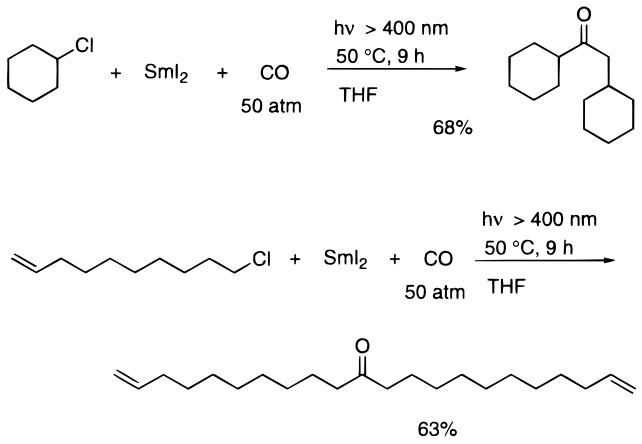
Scheme 196



aldehyde. Indeed, a similar reaction conducted in EtOD−D_2O as the solvent resulted in the formation of RCDO **262** (d-content > 97%), precluding a hydrogen abstraction mechanism by the acyl radical.

More recently, Ogawa, Sonoda, and co-workers reported an interesting carbonylation reaction of organic chlorides with SmI_2 under photoirradiation conditions (Scheme 197).[353] In this reaction, α-ketols

Scheme 197

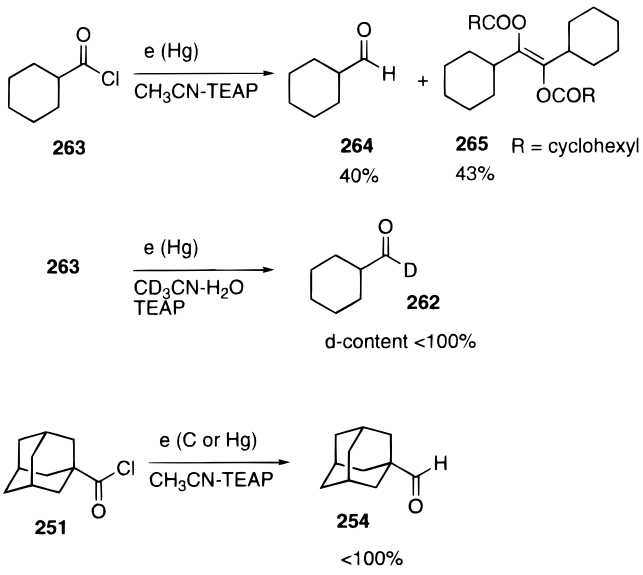


were not usually formed but unsymmmetrical ketones composed of two alkyl units and two CO molecules were obtained in good yields. Interestingly, isolation of an α-ketol by control experiments in the same reaction system was reported. Although the precise mechanism has yet to be elucidated, it may be the case that the unsymmetrical ketones are obtained by further reduction of initially formed α-ketols.

2. Electrochemical Reduction of Acyl Radicals

Several groups studied electrochemical reductions of acid chlorides with a view to generating acyl radicals,[354] but examples which demonstrate the second reduction process from acyl radicals to acyl anions are limited. Recent work of Peters and co-workers aimed at obtaining aldehydes by electrochemical reduction of acyl chlorides, such as benzoyl chloride,[355] heptanoyl chloride,[355] cyclohexanecarbonyl chloride (**263**),[356] and 1-adamantanecarbonyl chloride (**251**).[357] For example, the electrolytic reduction of cyclohexanecarbonyl chloride at mercury cathodes in acetonitrile containing tetraethylammonium perchlorate gave cyclohexanecarboxaldehyde (**264**) in moderate yield along with 1,2-enediol ester **265** (Scheme 198). In an experiment using CD_3CN, they

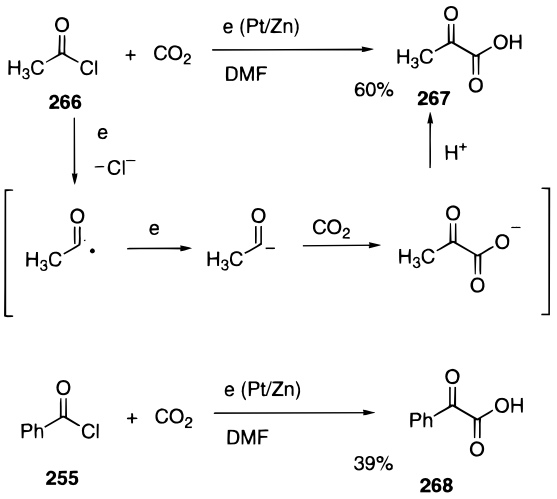
Scheme 198



obtained deuterated aldehyde **262**, confirming that the formyl proton of cyclohexanecarboxaldehyde (**264**) came from acetonitrile. On the other hand, when acetonitrile containing 0.2 M deuterium oxide (mol ratio: $CH_3CN:D_2O$ = 19:1) was used, almost no deuterium incorporation at the formyl position was observed. With these results in hand, the authors favored a mechanism based on the abstraction of hydrogen by acyl radicals from acetonitrile rather than one based on one-electron reduction/protonation of acyl radicals. However, as acyllithiums are known to abstract protons from acetonitrile very smoothly even at −110 °C,[358] the mechanistic ambiguity still remains. The reduction of adamantanecarbonyl chloride (**251**) is noteworthy since 1-adamantanecarboxaldehyde (**254**) was formed in nearly quantitative yield.

Recently, pyruvic acid (**267**) was electrochemically synthesized from acetyl chloride (**266**) and atmospheric CO_2 in an undivided gastight cell with a platinum cathode and a sacrificial zinc anode in DMF containing 0.1 M Bu_4NBF_4 under a potentiostatic regime (Scheme 199).[359] Since the reaction of an acyl radical with carbon dioxide is extremely inefficient,[360] carboxylation of the acyl anion formed by two consecutive one-electron reductions of acetyl chloride may be reasonably suggested as the key step for this pyruvic acid synthesis. Similar cathodic carboxylation of benzoyl chloride (**255**) gave benzoylformic acid (**268**) in 39% yield.

Scheme 199

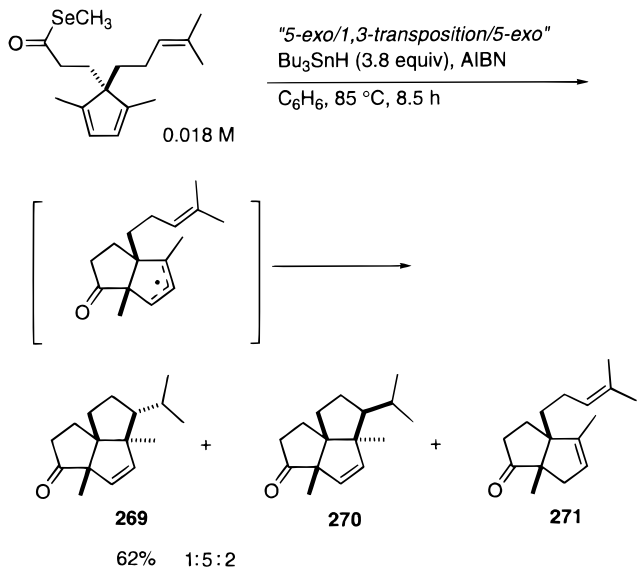


X. Applications to Tandem Reactions

A. Tandem Cyclization Reactions on the Basis of the 5-Exo Mode of Acyl Radical Cyclization

Curran and Scwartz have investigated a tandem 5-exo cyclization reaction of an acyl radicals for the construction of the congested angular triquinane portion (BCD ring) of the tetraquinane *Crinipellin A*.[138] This tandem cyclization strategy is unique in that it involves a 1,4-functionalization of a cyclopentadiene nucleus via 1,3-transposition of an allylic radical resulting from the first 5-exo cyclization (Scheme 200). It produces two diastereomeric tri-

Scheme 200

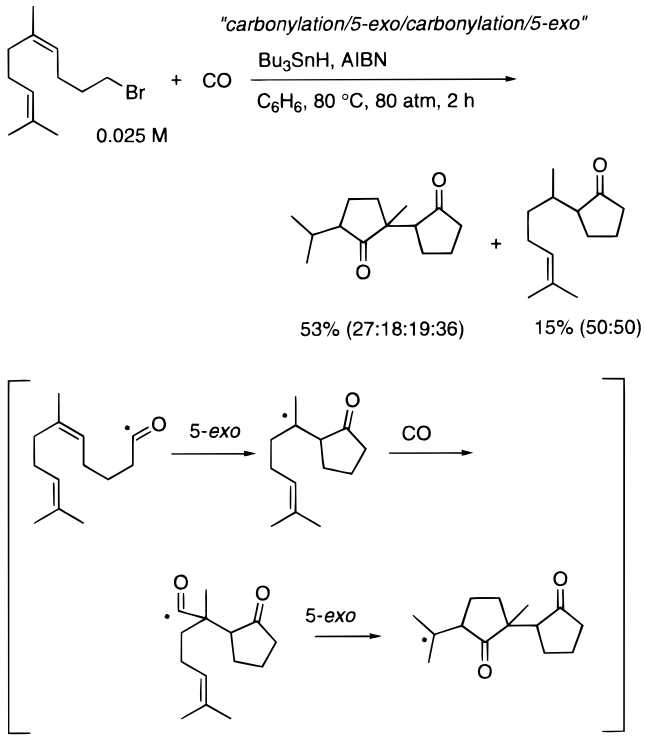


quinanes **269** and **270** in a 1:5.5 ratio along with a bicyclic ketone **271** as a byproduct.

Ryu, Sonoda, and co-workers have observed a double 5-exo cyclization of acyl radicals.[245] In this case, carbonylation was squeezed between two 5-exo acyl radical cyclizations (Scheme 201).

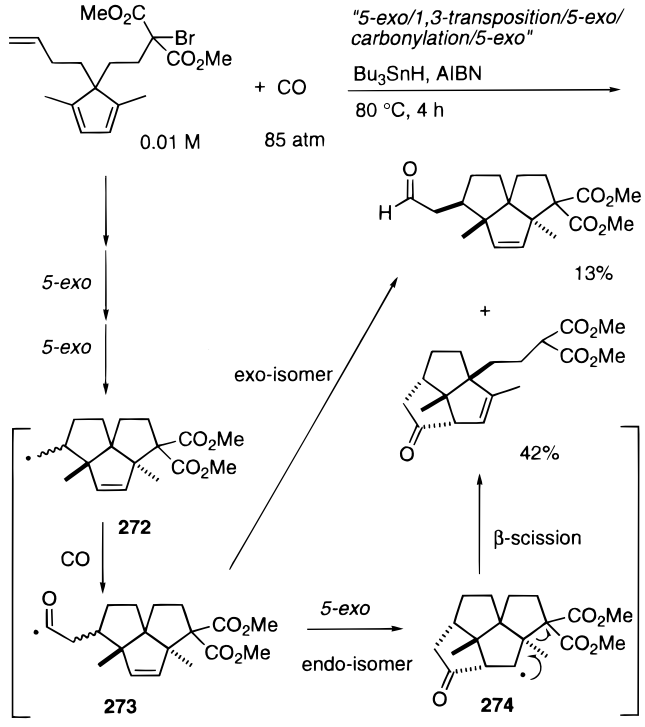
These two groups have jointly pursued the tandem radical cyclization and carbonylative tandem cyclization chemistry, based on Curran's 5,5-disubstituted

Scheme 201



cyclopentadiene system.[361] A malonyl radical is the starting point for this tandem reaction (Scheme 202).

Scheme 202

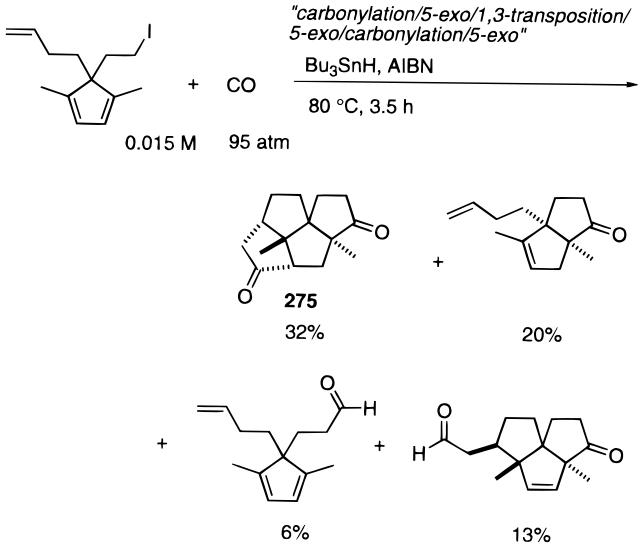


Double 5-exo cyclization beginning with the malonyl radical produces a mixture of endo (major) and exo (minor) radicals **272**, both of which are then carbonylated. Only the endo product radical **273** cyclizes back to the double bond to give a tetracyclic radical **274**, which then undergoes β-fragmentation with expulsion of a malonyl radical and formation of the

final tricyclic ring system. This is an interesting example of a "round trip" radical rearrangement from a malonyl radical to a malonyl radical.

A similar example with incorporation of two molecules of CO is shown in Scheme 203. In this

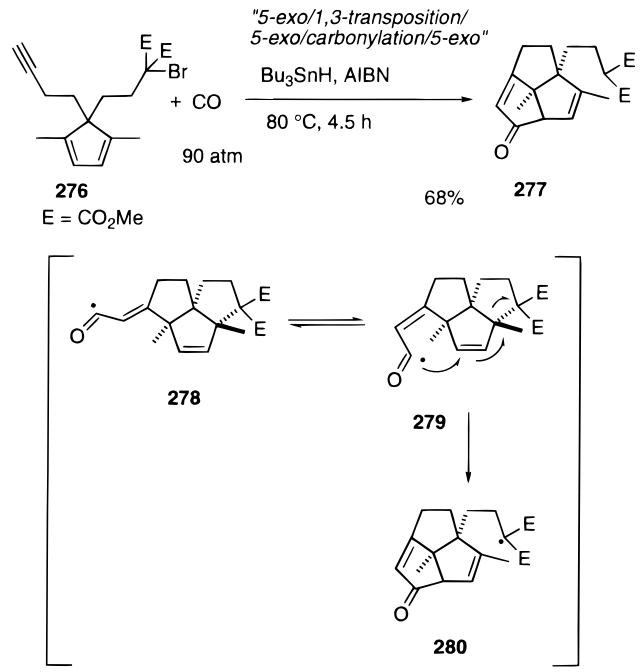
Scheme 203



example, a successful 5-exo/5-exo/carbonylation/5-exo cyclization sequence leads to the tetraquinane product **275**. Remarkably, five C−C bonds were formed in a single procedure.[361]

Carbonylative cyclization of the alkyne analogue **276** provided exclusively the round-trip radical rearrangement product **277** in 68% yield (Scheme 204).[361]

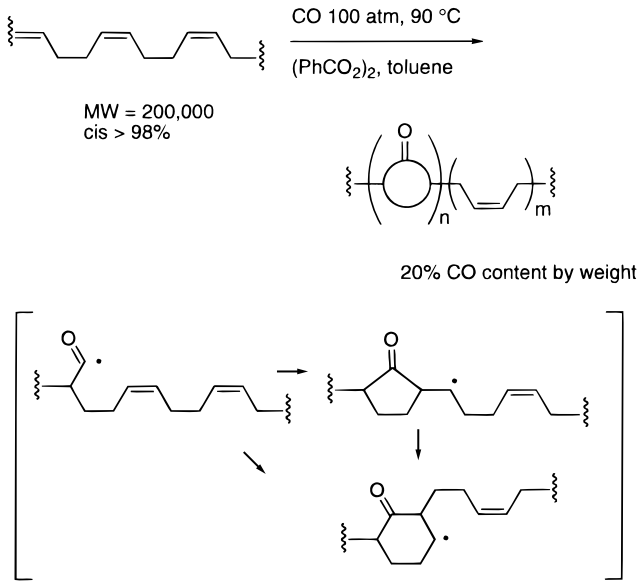
Scheme 204



Interestingly, this is the only product formed that has incorporated CO. In this reaction, initial carbonylation of the vinyl radical produces an equilibrating mixture of *E* and *Z* unsaturated acyl radicals, with the latter **279** undergoing back cyclization and cleavage to provide the product radical **280**.

As is evident from both Schemes 201 and 203, double carbonylation systems provide a unique entry into double acyl radical cyclizations when correctly designed. Chatgilialoglu and co-workers reported a unique polyketone synthesis by radical carbonylation of 1,4-*cis*-polybudadiene.[362] An example is shown in Scheme 205 in which the new polymer contained 20%

Scheme 205



CO by weight. However, the content of carbonyl units as well as the ratio of cyclopentanones/cyclohexanones depended strongly on the experimental conditions.[362a,b] In particular, the formation of six-membered rings is due both to direct 6-endo cyclization and to the expansion of the previously formed five-membered rings (see section VII.A.1).[227]

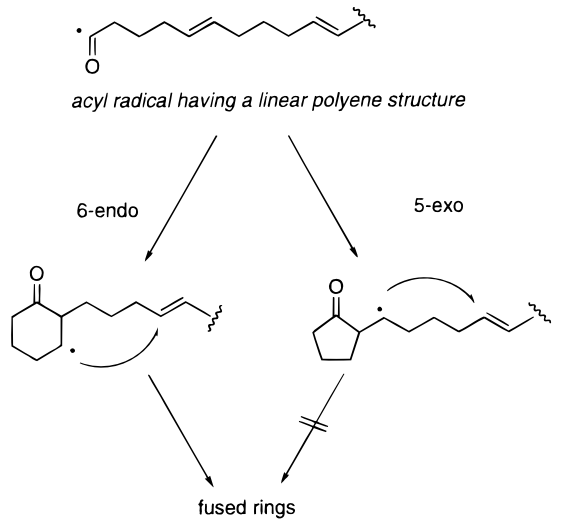
B. Tandem Cyclization Reactions on the Basis of the 6-Endo Mode of Acyl Radical Cyclization

Many more examples of polycyclization reactions of acyl radicals leading to fused polycyclic rings are based on consecutive 6-endo cyclization reactions than on the 5-exo mode. This may be due to the fact that the 6-endo mode of cyclization of acyl radicals having linear polyene structures, unlike the 5-exo mode, can lead to fused polycyclic rings (Scheme 206). In general, acyl radical precursors having linear polyene structures are readily accessible from iterative Wittig-type protocols.

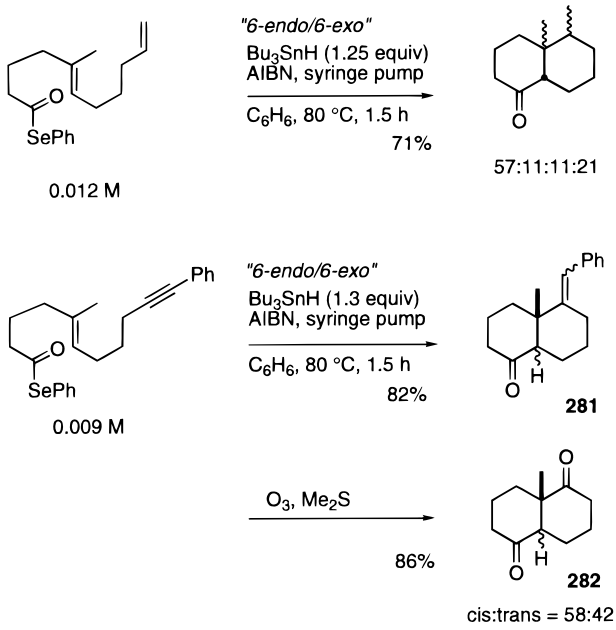
The first equation in Scheme 207, reported by Boger and Mathvink, is an example of forming fused six/six-membered rings by sequential 6-endo-trig/6-exo-trig cyclization reaction.[363] This reaction can be successfully extended to the 6-endo-trig/6-exo-dig mode of cyclization, which provides 9-methyldecalin-1,5-dione (**282**) after ozonolysis of the double cyclized product **281**. This approach, however, suffers from poor stereochemical control at the decalin ring junction.

Pattenden and co-workers have reported the synthesis of 6-methyl-1-decalone (**283**) by a tandem

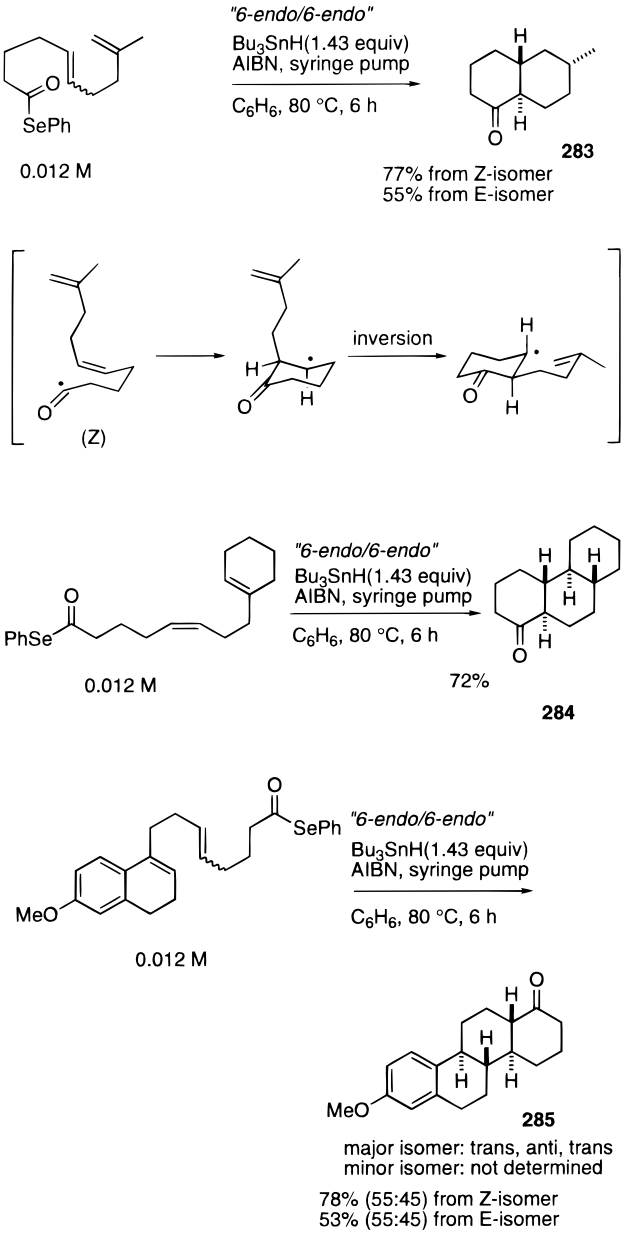
Scheme 206



Scheme 207



Scheme 208

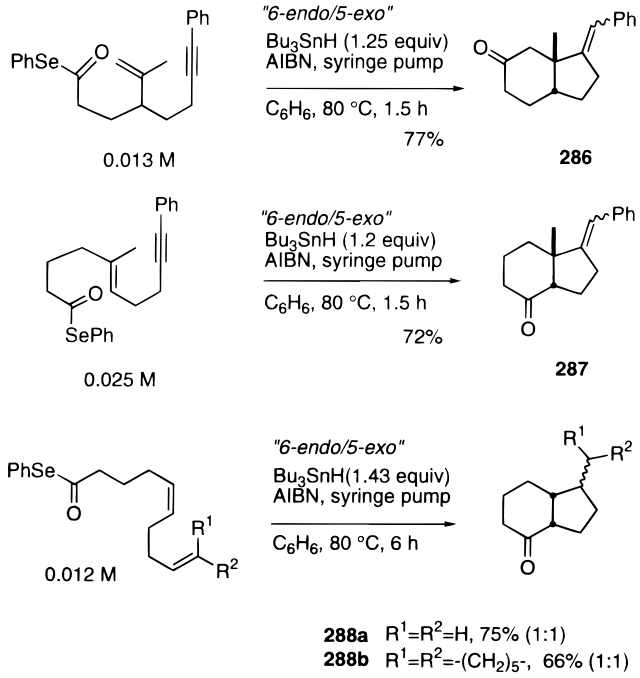


6-endo/6-endo cyclization reaction (Scheme 208).[364] In contrast to the 6-endo/6-exo example shown in Scheme 207, this reaction generates only one diastereomer. Noteworthily, the *E*-isomer underwent a similar stereoselective bicyclization as the *Z* isomer. Rapid inversion of the *β*-keto radical resulting from the first cyclization prior to the second ring-forming reaction may account for the stereochemical outcome. A similar cyclization of a substrate having a terminal cyclohexenyl ring led exclusively to the stereodefined tricycle **284** in good yield. The last example in Scheme 208 demonstrates the synthesis of a tetracyclic compound **285** by a 6-endo/6-endo cyclization. Thus, *E*- and *Z*-acyl selenides attached to a reduced naphthol ring system underwent sequential 6-endo/6-endo cyclizations. Unfortunately, the desired tetracycle **285** was obtained as a 55:45 mixture of diastereomers, irrespective of the *E*/*Z* stereochemistry of the starting substrates.

Tandem 6-endo-trig/5-exo-dig and 6-endo-trig/5-exo-trig cyclization reactions leading to hydrindanones **286**−**288** have also been reported (Scheme 209). In the first two examples from Boger's group,[363] free-radical cyclization followed by ozonolysis permits the convenient preparation of hydrindan-1,6-dione and a 1,4-dione, respectively, with high stereoselectivity (>20 cis:trans). In the third example, reported by Pattenden, the second cyclization to a C−C double bond lacked diastereoselectivity.[364]

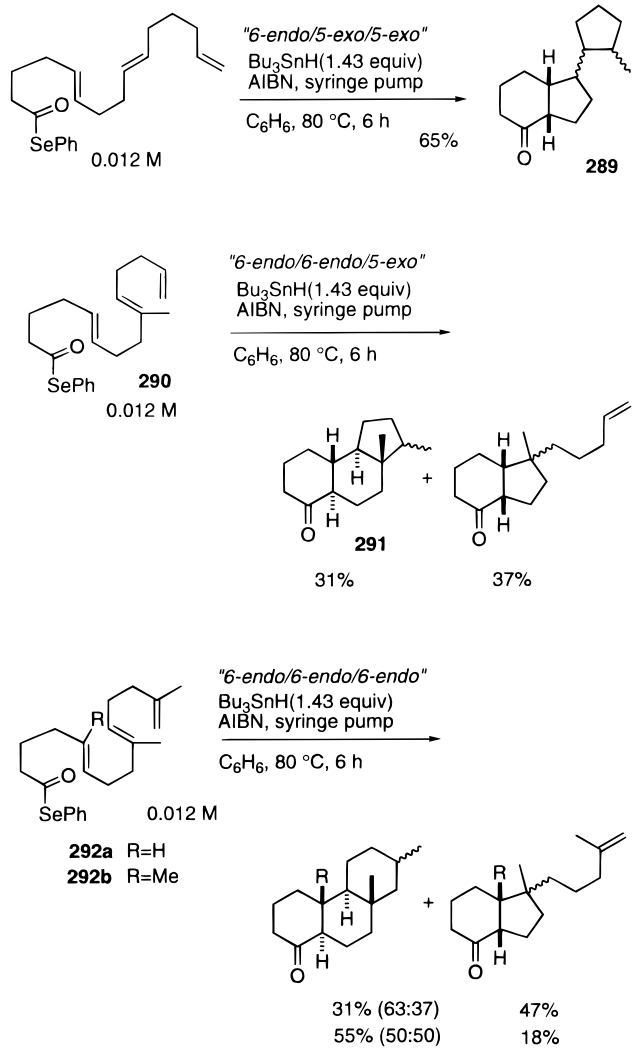
Pattenden's group has attempted triple cyclization reactions using triene systems to form fused tricyclic rings.[365] In the first example shown in Scheme 210, both 6-endo/6-endo/6-exo and 6-endo/5-exo/5-exo cyclizations are possible but the latter mode of cyclization predominated. To favor the second 6-endo cyclization, substitution at the 9-position appears essential. Indeed, the related 9-methyl-substituted trieneselenoate **290** underwent preferential 6-endo/6-endo/5-exo cyclizations leading to the angular fused tricycle **291**. The third example presented in Scheme 210 shows the consecutive triple 6-endo cyclization

Scheme 209



288a $R^1=R^2=H$, 75% (1:1)
288b $R^1=R^2=-(CH_2)_5-$, 66% (1:1)

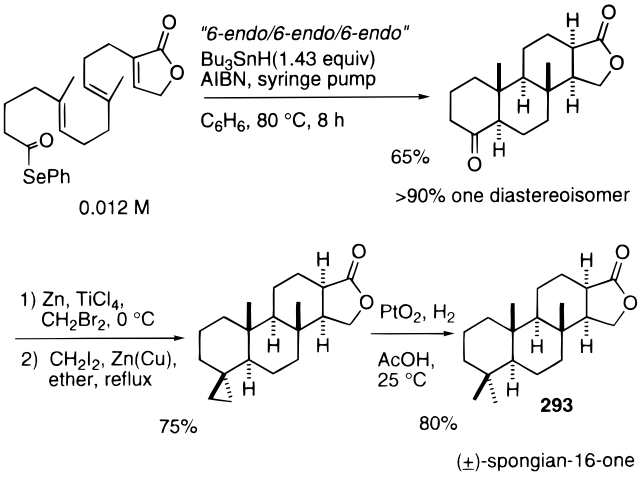
Scheme 210



292a R=H
292b R=Me

which starts with substrates **292a** and **292b** each having a 2-propenyl terminus. In these two cases, byproducts produced via competing 6-endo/5-exo modes of cyclization were also formed. Scheme 211

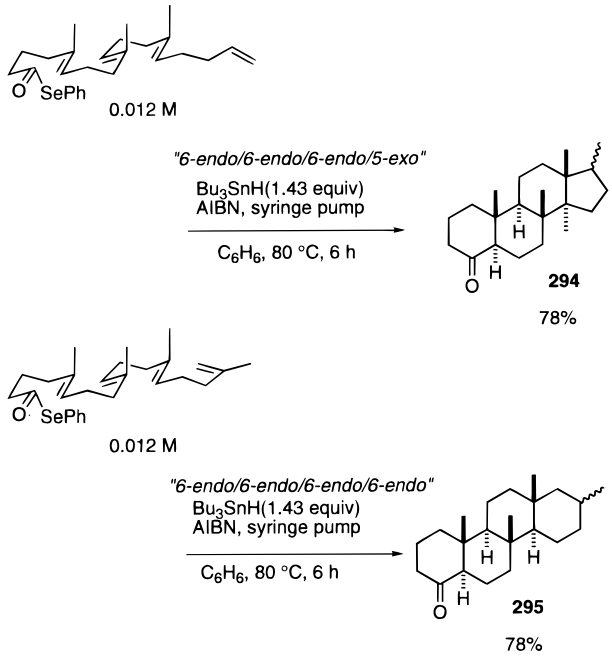
Scheme 211



details an application of the triple 6-endo cyclization by Pattenden to the synthesis of the marine sponge metabolite Spongian-16-one (**293**).[366]

In Scheme 212, two spectacular tetracyclization

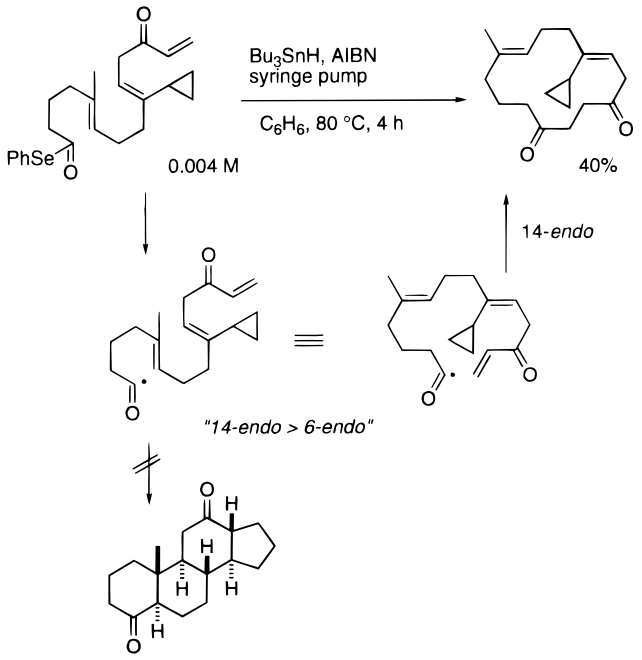
Scheme 212



reactions are shown which proceeded in the 6-endo/6-endo/6-endo/5-exo and 6-endo/6-endo/6-endo/6-endo modes, respectively.[365] Each of the tetracyclic ketones **294** and **295** was produced as a mixture of ring D methyl epimers. However, the first three 6-endo cyclization reactions proceeded with complete regio- and stereocontrol.

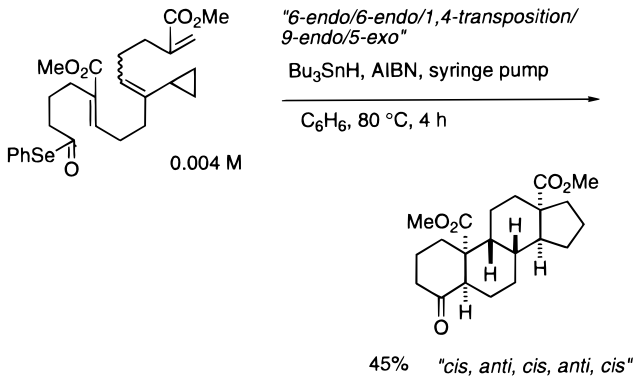
Pattenden and co-workers also reported a new approach to steroid ring construction based on cascades 6-endo-trig cyclization/macrocyclization/transannulation reactions.[367] In the example shown in Scheme 213, the envisaged consecutive 6-endo cyclizations/cyclopropyl carbinyl radical rearrangement/9-endo cyclization/transannular cyclization was un-

Scheme 213



successful due to the efficient 14-endo macrocyclization being more efficient than the 6-endo cascade reactions. However, as shown in the example of Scheme 214, the designed precursor having two carboxylate

Scheme 214

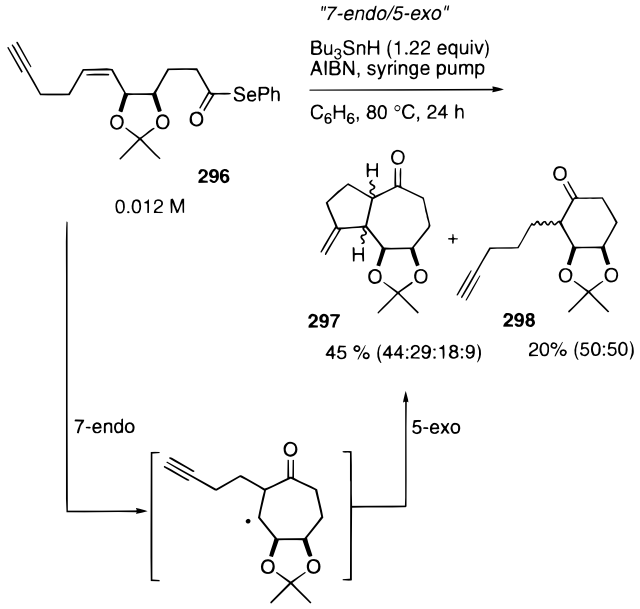


ester moieties led to the formation of tetracyclic steroid ring with success.

C. Tandem Cyclization Reactions on the Basis of the 7-Endo Mode of Acyl Radical Cyclization

Crich and co-workers have reported that 6-heptenoyl radicals bearing either an ethylene ketal or an alkoxy residue at C-5 (allylic position) cyclize preferentially in an endo mode giving substituted cycloheptanones (section VII.A.3, Schemes 113−115).[260] They also investigated tandem 7-endo-trig/5-exo-dig cyclizations starting with enantiomerically pure cyclization precursors, which were obtained from 2,3-*O*-isopropylidene-L-erythro-furanose in four steps. For example, dropwise addition of stannane for 24 h to a dilute solution of substrate **296** provided an isolated yield of approximately 45% of the combined stereoisomers of bicyclo[5.3.0]decan-2-one **297** (Scheme 215).[226,368] The cyclohexanone derivative **298**

Scheme 215

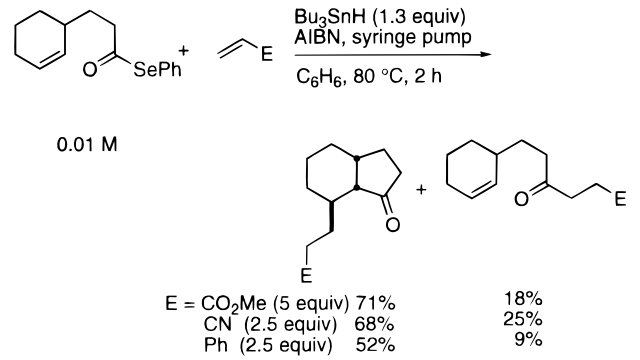


was also isolated from this reaction mixture in 20% yield as a 1:1 mixture of isomers.

D. Cyclization and Intermolecular Addition

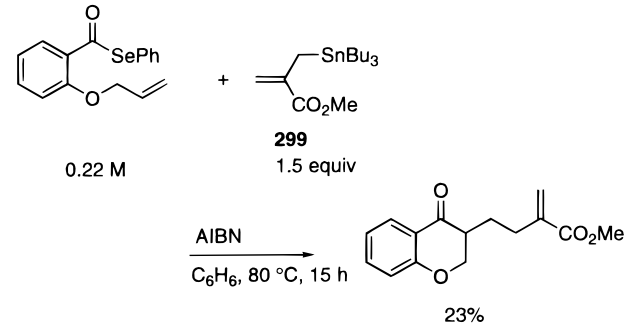
Boger and Mathvink reported that the radicals arising from 5-exo cyclization of acyl radicals can successfully undergo intermolecular addition to electron-deficient alkenes and styrene (Scheme 216).[363]

Scheme 216



Scheme 217 illustrates an interesting example of

Scheme 217

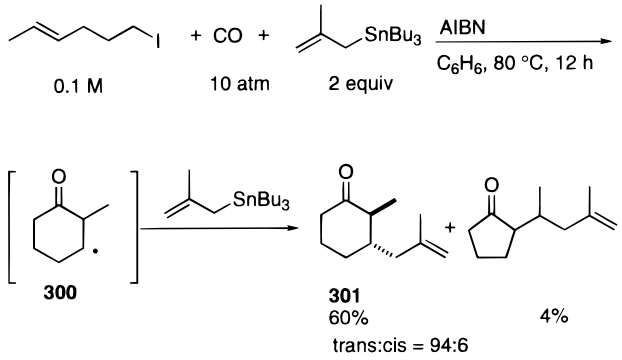


a 6-exo cyclization−intermolecular addition sequence which was reported by Crich and co-workers.[260] In

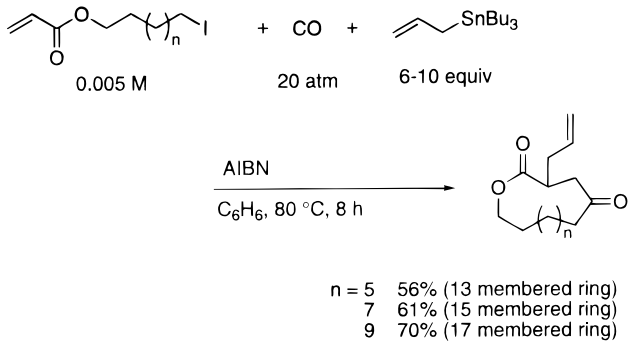
this reaction an activated allyltin **299** was used as an intermolecular trap.

Ryu, Sonoda, and co-workers observed that the 3-oxo-2-methylcyclohexyl radical **300** arising from 6-endo acyl radical cyclization (or from 5-exo cyclization plus isomerization) was trapped by methallyltin to provide 3-methallyl-2-methylcyclohexanone (**301**) as a 94:6 mixture of trans and cis isomers (Scheme 218). The five-membered ring isomer was also obtained in 4% yield.[307] This type of allyltin-mediated radical carbonylation/endo cyclization sequence was successfully extended to the synthesis of allyl-substituted macrolides (Scheme 219).[273]

Scheme 218



Scheme 219

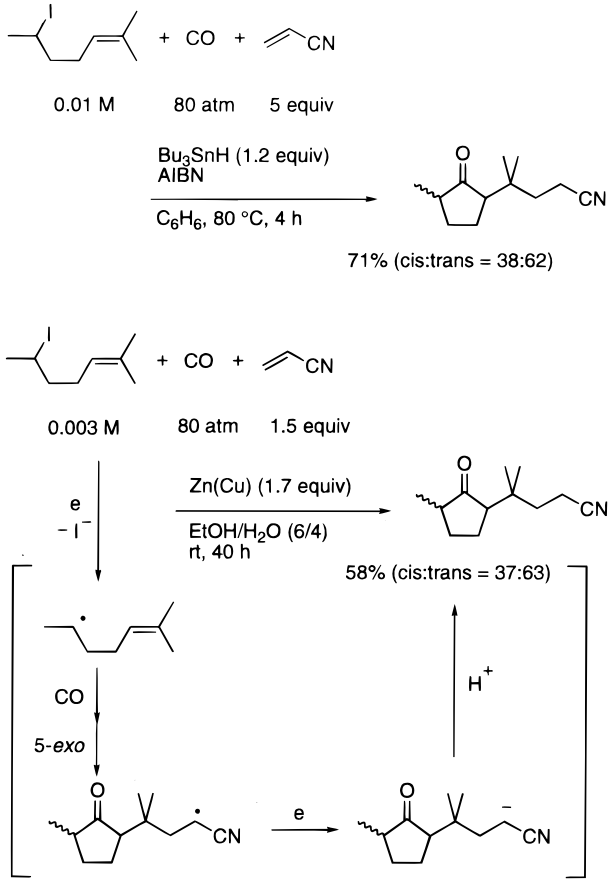


Ryu and co-workers reported a tin hydride-mediated carbonylation−5-exo cyclization sequence with subsequent intermolecular addition of the resulting radical to alkenes (Scheme 220).[352] A similar result was obtained even when the reaction conditions were changed to a nonchain system based on a zinc/aqueous solvent mixture, demonstrating the mechanistic identity of the radical cyclization step.

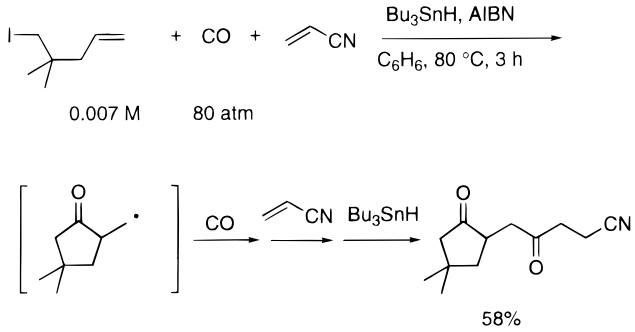
Ryu and co-workers found that 3-oxocyclopentylcarbinyl radicals arising from alkyl radical carbonylation followed by 5-exo cyclization of the resulting acyl radical can be trapped by a second molecule of carbon monoxide and alkenes. The following two tandem reactions in Schemes 221 and 222 represent trapping by CO/acrylonitrile/Bu_3SnH[369] and CO/acrylonitrile/methallyltin,[370] respectively.

In a one-electron reduction system composed of zinc and aprotic solvents, such as THF and acetonitrile, alk-4-enyl iodides react with CO and alkenes to give bicyclo[3.3.0]octan-1-ols and bicyclo[3.2.1]octane-1-ols via radical/anionic dual annulations.[371] Scheme 223 summarizes the concept of this hybrid radical/anionic

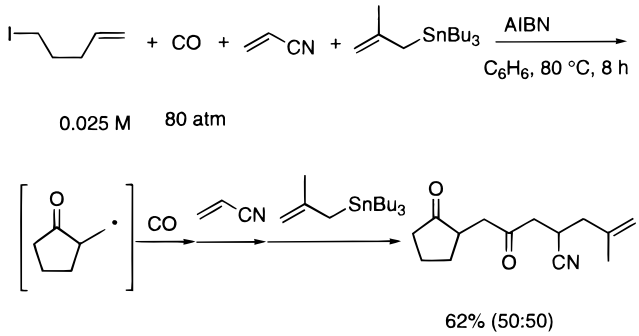
Scheme 220



Scheme 221

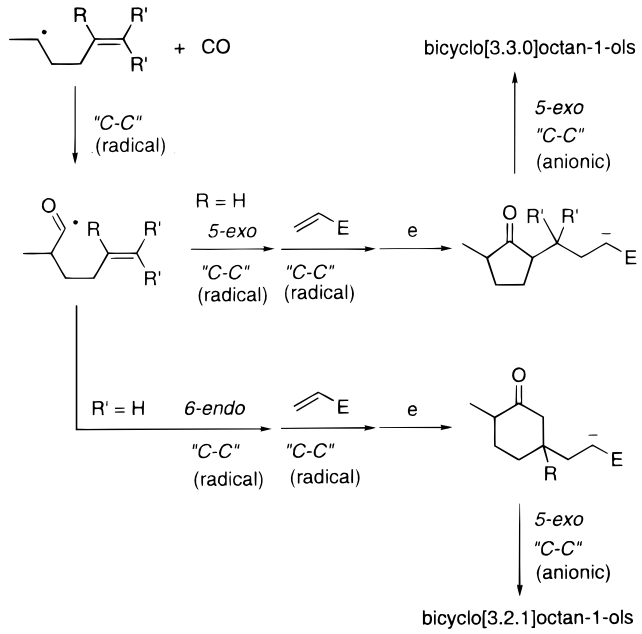


Scheme 222

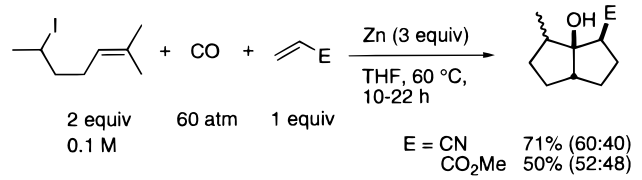


system which remarkably achieves the formation of four C−C bonds by three radical and one anionic reaction. Schemes 224 and 225 provide typical examples of each tandem process. Thus, depending on the substitution pattern of the double bonds in the

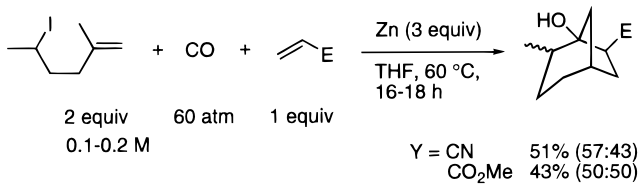
Scheme 223



Scheme 224



Scheme 225



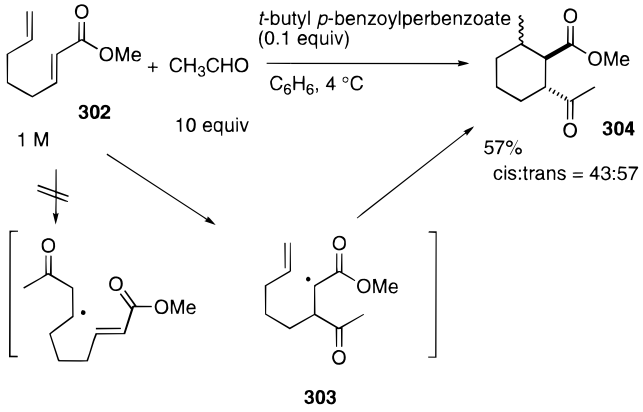
substrate, acyl radical cyclization proceeds in either a 5-exo or 6-endo mode, both leading to a bicyclic compound.

E. Intermolecular Addition and Cyclization

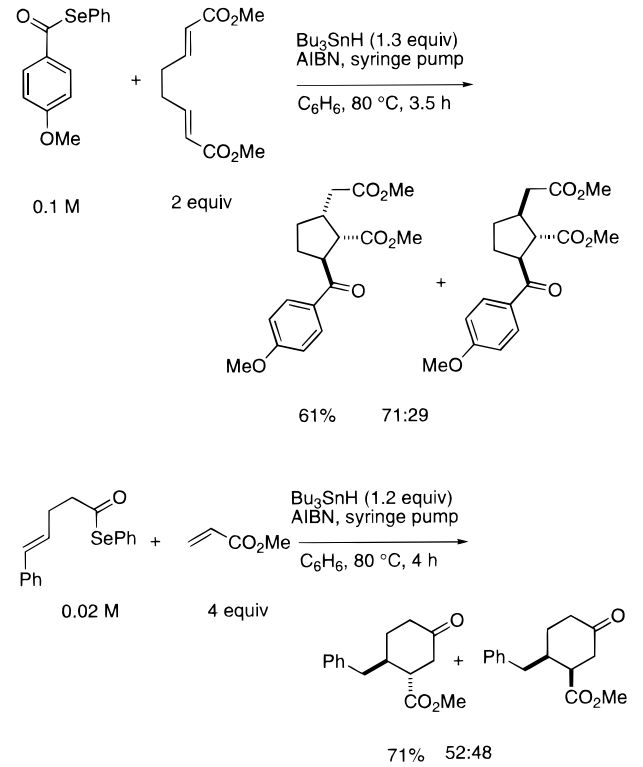
Neckers reported that radical addition of acetaldehyde to methyl octa-2,7-dienoate (**302**) at 4 °C occurs at the inner rather than terminal alkene chemoselectively (Scheme 226).[309] The resulting radical **303** experiences a 6-exo cyclization to form a six-membered ring adduct **304** as a 43:57 mixture of diastereomers. The diastereoselectivity of this reaction was found to be rather insensitive to the reaction temperature in the range from −25 to 78 °C (41:59 to 44:56).

Boger and Mathvink reported on the tin hydride-mediated intermolecular additions of acyl radicals, which are followed by cyclizations.[135,363] The first example presented in Scheme 227 illustrates an acyl radical addition/5-exo cyclization sequence, and the second example is an acyl radical addition/6-exo cyclization sequence.

Scheme 226



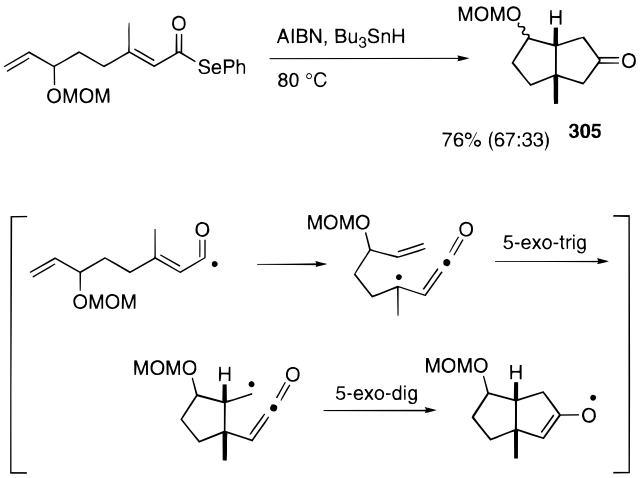
Scheme 227



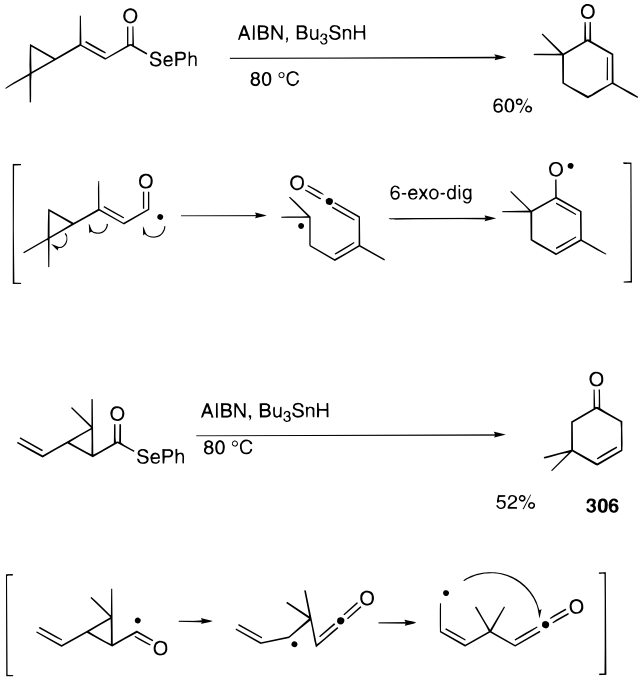
F. Isomerization and Cyclization

As shown in several examples so far, it is likely that *E*- and *Z*-α,β-unsaturated acyl radicals can isomerize via a ketenyl radical, although the intermediacy of ketenyl radicals has yet to be established by spectroscopic studies to our knowledge (section II.B). Recent work by Pattenden demonstrates that the trapping of ketenyl radical isomers is possible by the use of a rationally designed internal C−C double bond system. In the example shown in Scheme 228, Pattenden succeeded in trapping an α-ketene alkyl radical by 5-exo-trig cyclization. The resulting radical then undergoes a 5-exo-dig cyclization back onto the ketene carbonyl, leading to the synthesis of a diquinane **305**.[262] This internal ketone trapping reaction was extended to a sequence involving cyclopropylcarbinyl radical ring opening as the key step shown in the first equation in Scheme 229.[372] Unlike the well-known rapid ring opening of cyclopropylcarbinyl radicals,[3a] cyclopropyl acyl radicals are generally

Scheme 228



Scheme 229



reluctant to undergo a similar ring-opening reaction (section II.B).[373] However, Pattenden reported a rare case in which the formation of an acyl radical is sequenced by the cyclopropylcarbinyl-type radical ring opening. In the second equation shown in Scheme 229, 6-exo-dig cyclization of the resulting allyl radical leads to the formation of the cyclohexenone product **306**.[372] When the terminal alkene had dimethyl substituents, cyclization was retarded and a coupling dimer was formed as the main product. Further related reactions of α-ketenyl radicals, derived from α,*β*-unsaturated selenol and thioesters have recently been described by Pattenden and coworkers.[374]

XI. Related Radicals

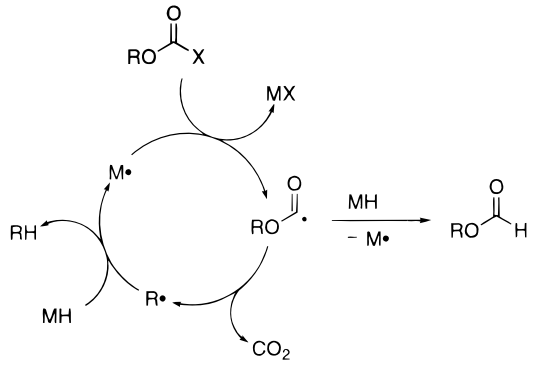
This section is concerned with the chemical reactions of reactive species related to acyl radicals. In particular, the alkoxycarbonyl radicals **307** and carbamoyl radicals **308** are examined. The structural properties of these two species have been discussed in some detail in section II for the purpose of a direct comparison with acyl radicals. Similarly, the rate constant for the reaction of *tert*-butoxy radical with *N*,*N*-dimethyl formamide and ethyl formate are reported in Table 9 and discussed in section IV.A.1.[46] The related radicals in which oxygen in acyl radicals is replaced by heteroatoms, such as imidoyl radicals,[3l,373] are not covered in this review.

307 **308**

A. Alkoxycarbonyl Radicals

Alkoxycarbonyl radicals are important intermediates in one method for the deoxygenation of alcohols. Selenocarbonates can be considered as an alternative to the more popular deoxygenation reaction via thionocarbonates (Barton−McCombie reaction).[375,376] Initial studies showed that benzyl chloroformate is reduced under free-radical conditions to a mixture of toluene and benzyl formate by Bu_3SnH.[113,377] A few years later, Graf et al. reported the reaction of selenocarbonates, readily available from the corresponding alcohols, with Bu_3SnH.[133] The products are the deoxygenated compounds, the alcohol, and the formate ester, depending on the nature of the substrate and the experimental conditions. The mechanism for the formation of deoxygenated products and formates is reported in Scheme 230. On the other hand, the mechanism for the formation of alcohols is not clear.

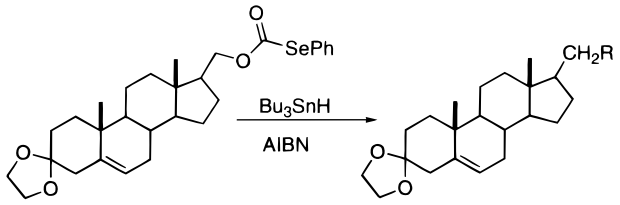
Scheme 230



X = SePh and MH = Bu_3SnH, $(TMS)_3SiH$

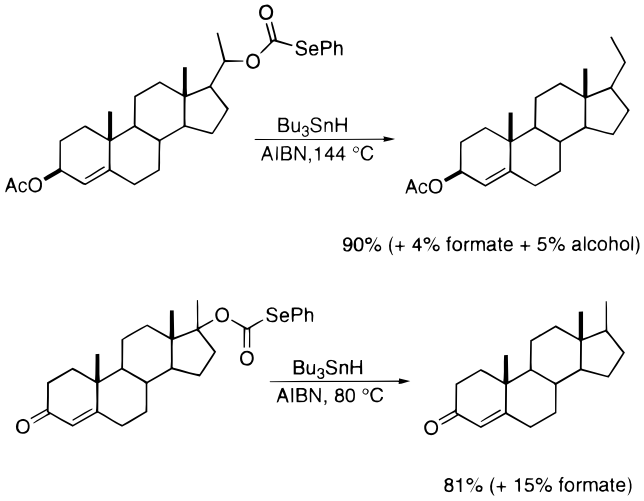
Scheme 231 illustrates this behavior for a selenocarbonate **309** of a primary alcohol. At room temperature, in combination with irradiation for the decomposition of AIBN, the main product is the formate ester **312**, whereas at higher temperatures, such as 164 °C, the deoxygenation product **310** is prevalent.[133] Scheme 232 shows that the secondary alcohol is deoxygenated more easily at 144 °C whereas the tertiary one can be deoxygenated at a moderate temperature (80 °C).[133]

Scheme 231



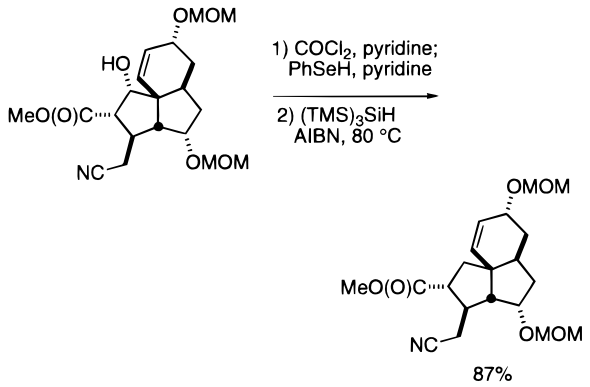
309	310 R = H	311 R=OH	312 R=OC(O)H
rt, hv		19%	81%
80 °C	18%	20%	62%
164 °C	66%	7%	25%

Scheme 232



The removal of hydroxy groups via selenocarbonates has also been achieved using $(TMS)_3SiH$ as the reducing agent. Scheme 233 outlines one such reaction contained in a multistep synthesis of an alkaloid, which was reported by Paquette and co-workers. The deoxygenation was achieved with 87% overall yield for the two steps.[378]

Scheme 233



Photolysis of alkyl(aryltelluro)formates in the presence of diphenyl diselenide afforded the corresponding alkyl(phenylseleno)formates in good yields (Scheme 234).[379] On the other hand, the thermolysis of telluroformates at 160 °C gave alkyl aryl tellurides in excellent yields.

In 1975, Jensen and Moder reported the conversion of alcohols to chlorides in moderate yields via thermal decomposition of *tert*-butyl peroxyglyoxalate in the presence of CCl_4.[380] They proposed the alkoxycarbonyl radicals as intermediates. Later, Barton and Crich[381,382] and Togo and co-workers[383] extended this chemistry to the deoxygenation of tertiary alcohols via derivative **313** of oxalic acid with the desired alcohol and with *N*-hydroxypyridine-2-thione (Scheme 235).[381−383] It was shown that decomposition of this type of ester provides the corresponding R• radical via the alkoxycarbonyl intermediate. The corresponding hydrocarbon was obtained in good yield when a thiol was present in the reaction medium. Newcomb and co-workers also employed these derivatives in order to measure the decarboxylation rate constants by using laser flash photolysis (vide infra).[384]

Scheme 234

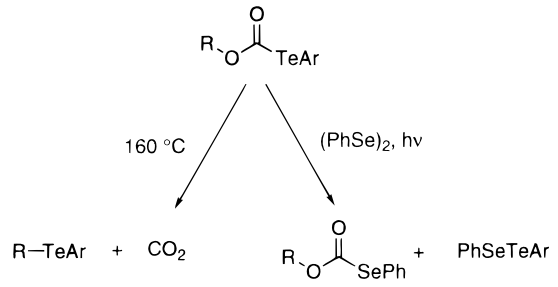
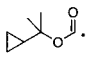
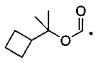
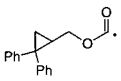
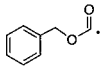
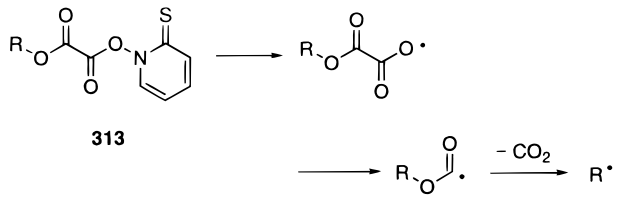


Table 13. Kinetic Data for the Decarboxylation of Alkoxycarbonyl Radicals

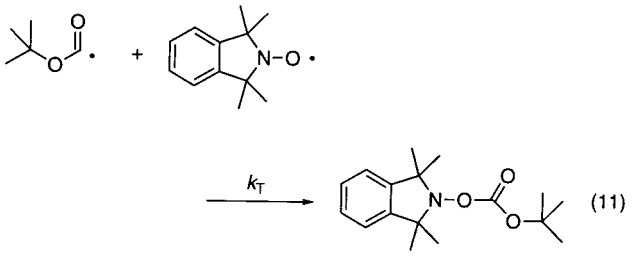
radical	log(A/s^{-1})	E, kcal mol^{-1}	$k_{80\,°C}$, s^{-1}	ref.
	13.8	11.7	3.6×10^6	385
	12.9	7.8	1.2×10^8	387
	13.2	9.8	1.4×10^7	387
	12.2	9.6	1.8×10^6	384
	13	7	5×10^8	384

Scheme 235



The first kinetic data on the decarboxylation of alkoxycarbonyl radicals dates from 1972, when Griller and Roberts measured the activation parameters for the *tert*-butoxycarbonyl radical by a steady-state kinetic EPR technique.[33] In 1986, Rüegge and Fischer looked again at this reaction and provided more reliable data by a time-resolved kinetic EPR method (see Table 13).[385] In 1988, Beckwith and co-workers,[386] using this decarboxylation reaction as a kinetic standard, obtained the Arrhenius expression

$\log(k_T/M^{-1}\ s^{-1}) = 9.5 - 0.3/\theta$, where $\theta = 2.3RT$ kcal mol^{-1}, for reaction of eq 11. Furthermore, they



(11)

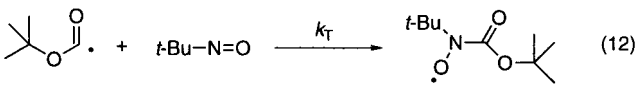
obtained a list of kinetic data of decarboxylation reactions for various ROC(O)• radicals assuming that these species have the same value as k_T derived from the above expression.[387] Some of these data are reported in Table 13. Recently, Newcomb and co-workers, by using oxalate derivatives **313** and laser flash photolysis, obtained the absolute rate constants for the β-cleavage of several alkoxycarbonyl radicals.[384] Some of these values are also collected in Table 13. The kinetic data obtained by these different techniques are in reasonably good agreement.

The data in Table 13 indicate that the decarboxylation of alkoxycarbonyl radicals is assisted by the stabilization of the product radical R•, i.e., primary < secondary < tertiary < benzyl. However, the relief of steric crowding should also play an important role. Furthermore, Table 13 shows that a cyclopropyl or cyclobutyl group adjacent to the radical center of R• also accelerates the rate of decarboxylation. The kinetic accelerations for the cyclopropylcarbinyl cases are in accordance with the stabilization of the radical by the small ring.[388]

The reversible reaction, i.e., the addition of an alkyl radical to the oxygen of carbon dioxide to give an alkoxycarbonyl radical, is expected to be unfavorable with respect to the addition to the carbon, which affords an acyloxyl radical. However, this reaction is well documented with analogous group 14 centered radicals;[360,389a] for example, a variety of silyl radicals were found by EPR to add to CO_2 to give the $R_3SiOC(O)$• radical, and a rate constant of $3.2 \times 10^4\ M^{-1}\ s^{-1}$ was measured for the addition of Me_3Si• radical at −110 °C.[389a]

The kinetic data in Table 13 imply that the deoxygenation of alcohols is an efficient process for tertiary and/or delocalized R• radicals. The unwanted formation of formates in the less efficient deoxygenation of primary alcohols can be circumvented by raising the reaction temperature (cf. Scheme 231), by using a lower stannane concentration, or by using slightly poorer hydrogen donors such as $(TMS)_3SiH$. In this respect, Newcomb has measured the rate of reaction of $RCH_2OC(O)$• radical with Bu_3SnH to be $1.7 \times 10^5\ M^{-1}\ s^{-1}$ at 2 °C.[384]

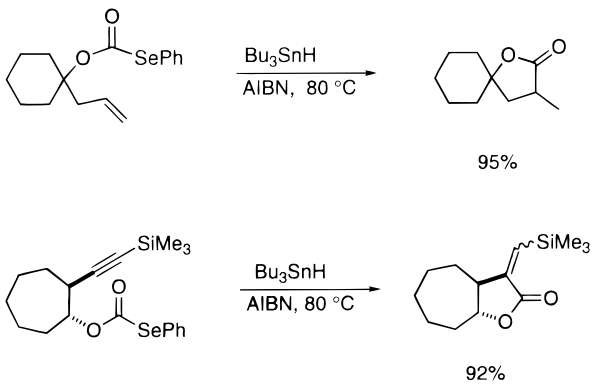
Alkoxycarbonyl radicals add to nitroso derivatives to afford detectable adducts by EPR spectroscopy.[389b] An example is reported in eq 12 in which the rate constant, k_T, relative to the decarboxylation reaction has been measured and found to be $k_T/k = 11\ M^{-1}$. Taking $k = 5.0 \times 10^5\ s^{-1}$ at 40 °C from Table 13, we calculated a $k_T = 5.5 \times 10^6\ M^{-1}\ s^{-1}$ at the same temperature.



(12)

Barton and Crich and Bachi and Bosch have shown that when a multiple bond is properly positioned on the residue R of the ROC(O)• radicals, cyclization reactions can occur efficiently.[381,390,391] Scheme 236

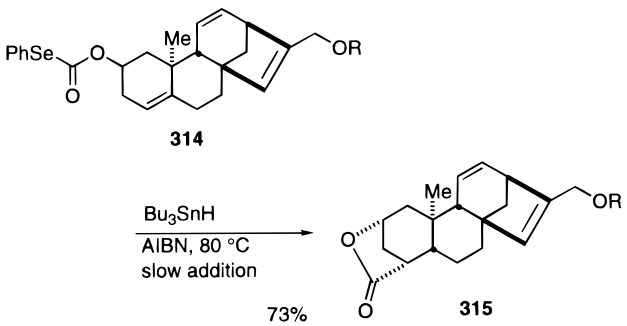
Scheme 236



shows two examples in which the alkoxycarbonyl radical adds intramolecularly to a double or triple bond to provide the γ-lactones in excellent yields.[391] Analogous reactions are also applied to the synthesis of δ-lactones, although activation of the multiple bond is necessary to obtain good yields.

This methodology has also been applied to more complex molecules.[392−394] One particular step of the total synthesis of the diterpenoid atractyligenin, which was reported by Corey and co-workers,[392] is noteworthy in this context. Scheme 237 shows that

Scheme 237

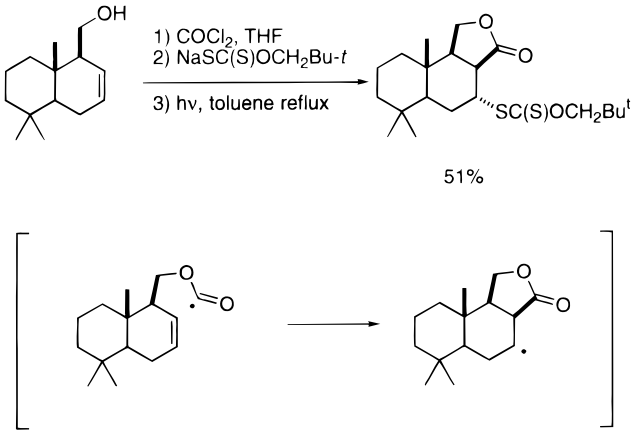


slow addition of the reducing agent over 12 h to a solution of selenocarbonate **314** gives the γ-lactone **315** in a 73% yield.

Saicic and Zard recently described the photolytic transformation of alkoxycarbonyl dithiocarbonates having a double bond in the appropriate position for cyclization.[395] An example is shown in Scheme 238, the key step for the synthesis of (±)-cinnamolide.

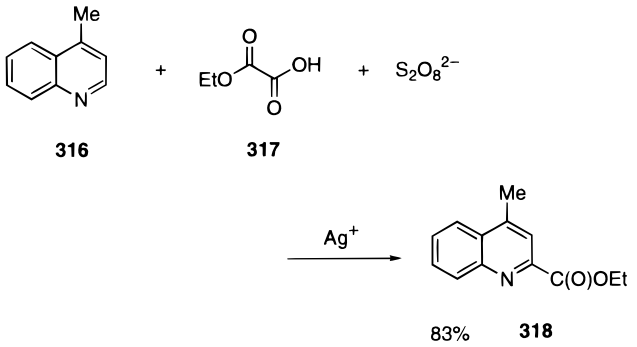
Ethoxycarbonyl radicals, generated from the corresponding selenocarbonate and Bu_3SnH, add intermolecularly to 4′,5′-unsaturated nucleosides to give the expected products in moderate yields (cf. section VIII.A, Scheme 165).[304] The stereochemical outcome of these reactions is strongly dependent on the nature of the protecting groups on the sugar moiety. Minisci and co-workers reported that alkoxycarbonyl radicals

Scheme 238



were also generated by silver-catalyzed decarboxylation of oxalic acid monoesters by $S_2O_8^{2-}$.[396] Radicals generated by this method were used for the alkoxycarbonylation of heteroaromatic bases with a high yield and selectivity in a two-phase system (water and an organic solvent).[396b] Scheme 239 shows an

Scheme 239

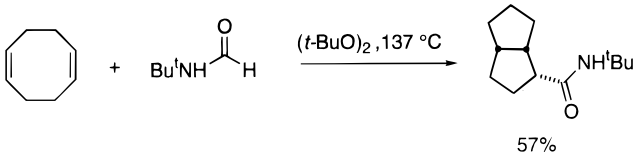


example in which the reaction of monoester **317** from ethanol with lepidine **316** gives substitition at the α-position of the heterocyclic ring to give acylated product **318** in excellent yield. With monoesters of secondary alcohols, this reaction has to compete with the decarboxylation process.

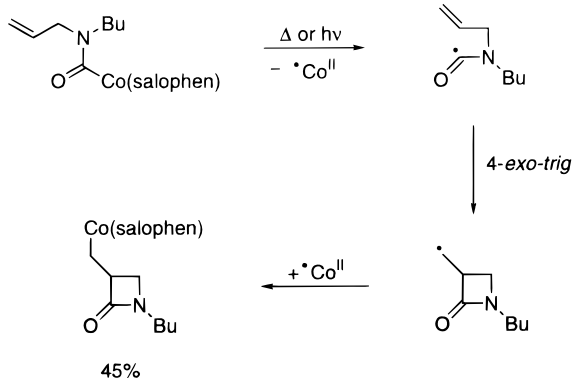
B. Carbamoyl Radicals

Carbamoyl radicals have been explored much less than the analogous alkoxycarbonyl radicals. The photogeneration of carbamoyl radicals from alkyl amides is quite an inefficient process.[397] Early work showed that the addition of carbamoyl radicals, generated by reaction of *tert*-butoxyl radicals with the corresponding formamides, to C−C double bonds is the key step in the transformation depicted in Scheme 240.[398] Pattenden and co-workers reported the generation of carbamoyl radicals by thermal- or light-induced homolysis of carbamoylcobalt salophens

Scheme 240



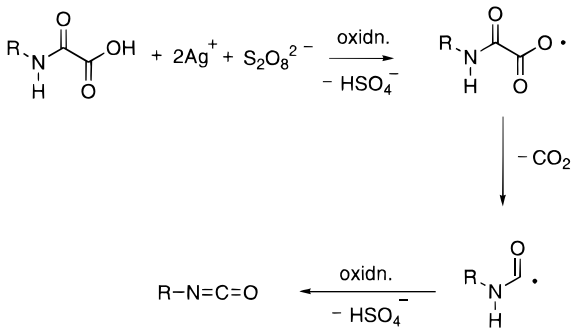
Scheme 241



as well as their intramolecular addition to a C−C double bond properly positioned on the residue R of the amino moiety.[399] Scheme 241 shows an example of a *β*-lactam synthesis in which the carbamoyl radical undergoes a 4-exo-trig cyclization to afford the four-membered ring. With this methodology, *γ*- and *δ*-lactams were also synthesized.

Minisci and co-workers have shown that carbamoylation of heteroaromatic bases by the $NH_2C(O)^{\bullet}$ radical can be achieved in good yields with H_2O_2 and a catalytic amount of Fe(II) salt in formamide at 60−80 °C.[400,401] The Minisci group recently reported a new, general, and simple synthesis of isocyanates based on the intermediacy of carbamoyl radicals.[402] Scheme 242 shows the stoichiometry of these reac-

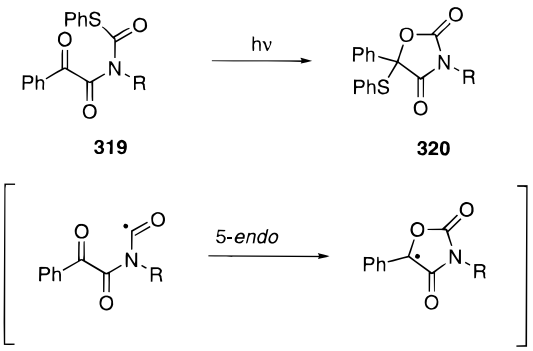
Scheme 242



tions, which were carried out in a two-phase system (water and an organic solvent). The final product is obtained by the oxidation of carbamoyl intermediates, and therefore, the monoalkyl substitution in the starting materials is a necessary condition for a successful reaction. Yields vary from moderate to good. Furthermore, these authors also reported examples of intra- and intermolecular homolytic aromatic carbamoylation.[402]

Sakamoto and co-workers have shown that irradiation of thiocarbamates **319** (R = *p*-tolyl) in solution afforded the racemic cyclic product **320** in 61% yield (Scheme 243). Photolysis of powdered crystals of **319** afforded higher yields (96% yield).[403,404] The reaction mechanism is suggested to occur via the 5-endo cyclization of carbamoyl radical. Interestingly, the solid-state experiment with thiocarbamates **319**, where R = benzyl, afforded **320** in a lower yield but in the enantiomerically enriched form.

Scheme 243



XII. Conclusion

In conclusion, the field of acyl radical chemistry has developed enormously in recent years. With a solid knowledge of the thermodynamic and kinetic parameters which govern their reactivity as well as a considerable range of techniques for their generation at hand, the organic chemist should now be well equipped to take full, controlled advantage of these versatile reactive intermediates in synthesis. We expect that the field will continue to flourish and expand for some years to come.

XIII. Acknowledgments

I.R. thanks Professor Noboru Sonoda for his helpful comments and encouragement and Dr. Shinji Tsunoi for the assistance in the literature searching. D.C. thanks the NSF, NIH, and ACS/PRF for support of his programs in free-radical chemistry and also his research group for their patience.

XIV. References

(1) Kuivila, H. G. *Synthesis* **1970**, 499.
(2) Ryu, I.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1050.
(3) (a) Newcomb, M. *Tetrahedron*, **1993**, *49*, 1151. (b) Ingold, K. U.; Griller, D. *Acc Chem Res.* **1980**, *13*, 317. (c) Chatgilialoglu, C.; Newcomb, M. *Adv. Organomet. Chem.*, in press. (d) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*; Pergamon Press: Oxford, 1986. (e) Curran, D. P. *Synthesis* **1988**, 417 (part 1), 489 (part 2). (f) Motherwell, W. B.; Crich, D. *Free Radical Chain Reactions in Organic Synthesis*; Academic: London, 1992. (g) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 4, Chapters 4.1 and 4.2. (h) Beckwith, A. L. J.; Crich, D.; Duggan, P. J.; Yao, Q. *Chem. Rev.* **1997**, *97*, 3273. (i) Fallis, A. G.; Branza, I. M. *Tetrahedron* **1997**, *53*, 17543. (j) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Free Radical Reactions*; VCH: Weinheim, 1996. (k) Sibi, M. P.; Porter, N. A. *Acc. Chem. Res.*, **1999**, *32*, 163. (l) Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177. (m) Malacria, M. *Chem. Rev.* **1996**, *96*, 289. (n) Snider, B. B. *Chem. Rev.* **1996**, *96*, 339. (o) Parsons, P. J.; Penkett, C. S.; Shell, A. J. *Chem. Rev.* **1996**, *96*, 195. (p) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237.
(4) (a) Vinogradov, M. G.; Nikishin, G. I. *Usp. Khim.* **1971**, *40*, 1960. (b) Caronna, T.; Minisci, F. *Rev. React. Species. Chem.* **1976**, *1*, 263.
(5) Boger, D. L. *Israel J. Chem.* **1997**, *37*, 119.
(6) Crich, D.; Yuan, H. In *Advances in Free Radical Chemistry*; Rawal, V. H., Ed.; JAI Press: New York, 1999; Vol. 2.
(7) O'Neal, H. E.; Benson, S. W. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. 2, Chapter 17.
(8) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493.
(9) Watkins, K. W.; Word, W. W. *Int. J. Chem. Kinet.* **1974**, *6*, 855.
(10) Watkins;, K. W.; Thompson, W. W. *Int. J. Chem. Kinet.* **1973**, *5*, 791.
(11) Alfassi, Z. B.; Golden, D. M. *J. Am. Chem. Soc.* **1973**, *95*, 319.
(12) Solly, R. K.; Benson, S. W. *J. Am. Chem. Soc.* **1971**, *93*, 1592.
(13) Seetula, J. A.; Russell, J. A.; Gutman, D. *J. Am. Chem. Soc.* **1990**, *112*, 1347.
(14) Nicovich, J. M.; Shackelford, C. J.; Wine, P. H. *J. Photochem. Photobiol. A: Chem.* **1990**, *51*, 141.
(15) Niiranen, J. T.; Gutman, D.; Krasnoperov, L. N. *J. Phys. Chem.* **1992**, *96*, 5881.
(16) Bauschlicher, C. W., Jr. *J. Phys. Chem.* **1994**, *98*, 2564.
(17) Griller, D.; Kanabus-Kaminska, J. M. In *Handbook of Organic Photochemistry*; Scaiano, J. C., Ed.; CRC Press: Boca Raton, 1989; Vol. II, Chapter 17.
(18) Gurvich, L. V.; Veyts, I. V.; Alcock, C. B.; Iorish, V. S. *Thermodynamic Properties of Individual Substances*, 4th ed.; Hemisphere: New York, 1991; Vol. 2.
(19) Pedley, J. B.; Naylor, R. D.; Kirby, S. P. *Thermochemical Data of Organic Compounds*, 2nd ed.; Chapman and Hall Ltd.: London, 1986.
(20) (a) Occhialini, D.; Daasbjerg, K.; Lund, H. *Acta Chem. Scand.* **1993**, *47*, 1100. (b) Lund, H.; Daasbjerg, K.; Occhialini, D.; Pedersen, S. U. *Russ. J. Electrochem.* **1995**, *31*, 865.
(21) Seakins, P. W.; Pilling, M. J.; Niiranen, J. T.; Gutman, D.; Krasnoperov, L. N. *J. Phys. Chem.* **1992**, *96*, 9847.
(22) Wiberg, K. B.; Crocker, L. S.; Morgan, K. M. *J. Am. Chem. Soc.* **1991**, *113*, 3447.
(23) Nimlos, M. R.; Soderquist, J. A.; Ellison, G. B. *J. Am. Chem. Soc.* **1989**, *111*, 7675.
(24) Chandrasekhar, J.; Andrade, J. G.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5612.
(25) Winter, P. R.; Rowland, B.; Hess, W. P. Radziszewski, J. G.; Nimlos, M. R.; Ellison, G. B. *J. Phys. Chem. A* **1998**, *102*, 3238.
(26) Traeger, J. C.; McLoughlin, R. G.; Nicholson, A. J. *J. Am. Chem. Soc.* **1982**, *104*, 5318.
(27) Traeger, J. C. *Org. Mass Spectrom.* **1985**, *20*, 223.
(28) Fischer, H.; Paul, H. In *Landolt-Börnstein: Magnetic Properties of Free Radical*; Fischer, H., Hellwege, K.-H., Eds.; Springer-Verlag: Berlin, 1977; Vol 9, Part b, pp 318−324.
(29) Neugebauer, F. A. In *Landolt-Börnstein: Magnetic Properties of Free Radical*; Fischer, H., Ed.; Springer-Verlag: Berlin: 1987; Vol 17, Part b, pp 512−529.
(30) Adrian, F. J.; Kim, B. F.; Bohandy, J. *J. Chem. Phys.* **1985**, *82*, 1804.
(31) Bennett, J. E.; Mile, B. *Trans. Faraday Soc.* **1971**, *67*, 1587.
(32) Bower, H.; McRae, J.; Symons, M. C. R. *J. Chem. Soc. A* **1971**, 2400.
(33) Griller, D.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 2* **1972**, 747.
(34) Cochran, E. L.; Adrian, F. J.; Bowers, V. A. *J. Chem. Phys.* **1966**, *44*, 4626.
(35) Guerra, M. *J. Chem. Soc., Perkin Trans. 2* **1996**, 779.
(36) Paul, H.; Fischer, H. *Helv. Chim. Acta* **1973**, *56*, 1575.
(37) (a) Davies, A. G.; Sutcliffe, R. *J. Chem. Soc., Perkin Trans. 2* **1980**, 819. (b) Davies, A. G.; Sutcliffe, R. *J. Chem. Soc., Chem. Commun.* **1979**, 473.
(38) Krusic, P. J.; Chen, K. S.; Meakin, P.; Kochi, J. K. *J. Phys. Chem.* **1974**, *78*, 2036.
(39) (a) Davies, A. G.; Sutcliffe, R. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1483. (b) Blum, P. M.; Davies, A. G.; Sutcliffe, R. *J. Chem. Soc., Chem. Commun.* **1979**, 217.
(40) Davies, A. G.; Hawari, J. A.-A.; Muggleton, B.; Tse, M.-W. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1132.
(41) Korth, H.-G.; Lusztyk, J.; Ingold, K. U. *J. Chem. Soc., Perkin Trans. 2* **1990**, 1997.
(42) Pawar, D. M.; Noe, E. A. *J. Org. Chem.* **1998**, *63*, 2850.
(43) Krusic, P. J.; Rettig, T. A. *J. Am. Chem. Soc.* **1970**, *92*, 722.
(44) Grossi, L.; Placucci, G. *J. Chem. Soc., Chem Commun.* **1985**, 943.
(45) Casarini, D.; Grossi, L.; Placucci, G. *J. Chem. Soc., Perkin Trans. 2* **1986**, 599.
(46) Chatgilialoglu, C.; Lunazzi, L.; Macciantelli, D.; Placucci, G. *J. Am. Chem. Soc.* **1984**, *106*, 5252.
(47) (a) Yonezawa, T.; Noda, I.; Kawamura, T. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 766. (b) Yonezawa, T.; Noda, I.; Kawamura, T. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 650.
(48) Hefter, H.; Fischer, H. *Ber. Bunsen-Ges. Phys. Chem.* **1970**, *74*, 493.
(49) (a) Sutcliffe, R.; Ingold, K. U. *J. Am. Chem. Soc.* **1981**, *103*, 7686. (b) Grossi, L. *J. Chem. Soc., Chem Commun.* **1989**, 1248.
(50) Baban, J. A.; Roberts, B. P. *J. Chem. Soc., Chem Commun.* **1979**, 537.
(51) (a) Sevilla, M D.; Sutyanarayana, D.; Morehouse, K. M. *J. Phys. Chem.* **1981**, *85*, 1027. (b) Sevilla, M D.; Becker, D.; Sevilla, C. L.; Swarts, S. *J. Phys. Chem.* **1985**, *89*, 633.
(52) Turro, N. J.; Paczkowski, M. A.; Wan, P. *J. Org. Chem.* **1985**, *50*, 1399.
(53) (a) Janzen, E. G.; Davis, E. R. Dubose, C. M. *Magn. Reson. Chem.* **1995**, *33*, S166. (b) Mackor, A.; Wajer, Th. A. J. M.; De Boer, Th. J. *Tetrahedron Lett.* **1968**, 1623. (c) Grossi, L. *Tetrahedron* **1997**, *53*, 3205. (d) Grossi, L. *Tetrahedron* **1997**, *53*, 6401.
(54) Neville, A. G.; Brown, C. E.; Rayner, D. M.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1991**, *113*, 1869.

(55) Brown, C. E.; Neville, A. G.; Rayner, D. M.; Ingold, K. U.; Lusztyk, J. *Aust. J. Chem.* **1995**, *48*, 363.
(56) (a) Jacox, M. E. *Chem. Phys.* **1982**, *69*, 407. (b) Shirk, D. J.; Pimentel, G. C. *J. Am. Chem. Soc.* **1968**, *90*, 3349.
(57) Jacox, M. E. *J. Chem. Phys.* **1988**, *88*, 4598.
(58) For HC(O)• in the gas-phase, see: McKellar, A. R. W.; Burkholder, J. B.; Orlando, J. J.; Howard, C. J. *J. Mol. Spectrosc.* **1988**, *130*, 445.
(59) (a) Basco, N.; Parmar, S. S. *Int. J. Chem. Kinet.* **1985**, *17*, 891. (b) Parkes, D. A. *Chem. Phys. Lett.* **1981**, *77*, 527. (c) Adachi, H.; Basco, N.; James, D. G. L. *Chem. Phys. Lett.* **1978**, *59*, 502.
(60) Tsentalovich, Y. P.; Fischer, H. *J. Chem. Soc., Perkin Trans. 2* **1994**, 729.
(61) Noda, S.; Fueki, K.; Kuri, Z. *J. Chem. Phys.* **1969**, *49*, 3287.
(62) Huggenberger, C.; Lipscher, J.; Fischer, H. *J. Phys. Chem.* **1980**, *84*, 3467.
(63) Fischer, H.; Baer, R.; Hany, R.; Verhoolen, I.; Walbiner, M. *J. Chem. Soc., Perkin Trans. 2* **1990**, 787.
(64) Roberts, B. P.; Scaiano, J. C. *J. Chem. Soc., Perkin Trans. 2* **1981**, 905.
(65) (a) Bakac, A.; Espenson, J. H. *J. Chem. Soc., Chem. Commun.* **1991**, 1497. (b) Bakac, A.; Espenson, J. H.; Young, V. G., Jr. *Inorg. Chem.* **1992**, *31*, 4959.
(66) Nagahara, K.; Ryu, I.; Kambe, N.; Komatsu, M.; Sonoda, N. *J. Org. Chem.* **1995**, *60*, 7384.
(67) Boese, W. T.; Goldman, A. S. *Tetrahedron Lett.* **1992**, *33*, 2119.
(68) Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley: New York, 1976.
(69) Gorin, E. *J. Phys. Chem.* **1939**, *7*, 256.
(70) Herr, D. S.; Noyes, W. A., Jr. *J. Am. Chem. Soc.* **1940**, *62*, 2052.
(71) Fischer, H.; Paul, H. *Acc. Chem. Res.* **1987**, *20*, 200.
(72) Vollenweider, J.-K.; Paul, H. *Int. J. Chem. Kinet.* **1986**, *18*, 791.
(73) Kerr, J. A.; Lloyd, A. C. *Trans. Faraday Soc.* **1967**, *63*, 2480.
(74) Chatgilialoglu, C.; Lucarini, M. *Tetrahedron Lett.* **1995**, *36*, 1299.
(75) Chatgilialoglu, C.; Ferreri, C.; Lucarini, M.; Pedrielli, P.; Pedulli, G. F. *Organometallics* **1995**, *14*, 2672.
(76) Applequist, D. E.; Kaplan, L. *J. Am. Chem. Soc.* **1965**, *87*, 2194.
(77) Applequist, D. E.; Klug, J. H. *J. Org. Chem.* **1978**, *43*, 1729.
(78) Semenov, N. *Some Problems of Chemical Kinetics and Reactivity*; Pergamon: New York, 1958; Vol. I.
(79) Lunazzi, L.; Ingold, K. U.; Scaiano, J. C. *J. Phys. Chem.* **1983**, *87*, 529.
(80) Turro, N. J.; Gould, I. R.; Baretz, B. H. *J. Phys. Chem.* **1983**, *87*, 531.
(81) Maouf, A.; Lemmetyinen, H.; Koskikallio, *Acta Chem. Scand.* **1990**, *44*, 336.
(82) Cozens, F. L.; Scaiano, J. C. *J. Am. Chem. Soc.* **1993**, *115*, 5204.
(83) Kerr, J. A.; Wright, J. P. *J. Chem. Soc., Faraday Trans.* **1985**, *81*, 1471.
(84) Maricq, M. M.; Szente, J. J.; Khitrov, G. A.; Dibble, T. S.; Fransisco, S. J. *J. Phys. Chem.* **1993**, *99*, 11875.
(85) Fransisco, S. J. *Chem. Phys. Lett.* **1992**, *191*, 7.
(86) Lehni, M.; Fischer, H. *Int. J. Chem. Kinet.* **1983**, *15*, 733.
(87) Harris, E. F. P.; Waters, W. A. *Discus. Faraday Soc.* **1953**, *14*, 221.
(88) Harris, E. F. P.; Waters, W. A. *Nature* **1952**, *170*, 212.
(89) Berman, J. D.; Stanley, J. H.; Sherman, W. V.; Cohen, S. G. *J. Am. Chem. Soc.* **1963**, *85*, 4010.
(90) Julia, M.; Maumy, M.; Mion, L. *Bull. Soc. Chim. Fr.* **1967**, 2641.
(91) Julia, M.; Maumy, M. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 5.
(92) Tanner, D. D.; Law, F. C. *J. Am. Chem. Soc.* **1969**, *91*, 7535.
(93) Barclay, L. R. C.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 1793.
(94) Kerr, J. A.; Trotman-Dickenson, A. F. *J. Chem. Soc.* **1960**, 1611.
(95) (a) Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 2674. (b) Beckwith, A. L. J.; Raner, K. D. *J. Org. Chem.* **1992**, *57*, 4954.
(96) Wisniewski Grissom, J.; Klingberg, D.; Megenburg, S.; Stallman, B. L. *J. Org. Chem.* **1994**, *59*, 7876.
(97) Asmus, K.-D.; Bonifacic, M. In *Landolt-Börnstein*: *Radical Reaction Rates in Liquids*; Fischer, H., Ed.; Springer-Verlag: Berlin, 1984, Vol. II/13b, p 198.
(98) Weldon, D.; Holland, S.; Scaiano, J. C. *J. Org. Chem.* **1996**, *61*, 8544.
(99) (a) Marko, I. E.; Mekhalfia, A. *Tetrahedron Lett.* **1990**, *31*, 7237. (b) Marko, I. E.; Mekhalfia, A.; Ollis, W. D. *Synlett* **1990**, 347.
(100) Walling, C.; Mintz, M. J. *J. Am. Chem. Soc.* **1967**, *89*, 1515.
(101) Kim, S. S.; Sohn, S. C. *Tetrahedron Lett.* **1982**, *23*, 3703.
(102) Kim, S. S.; Koo, H. M.; Choi, S. Y. *Tetrahedron Lett.* **1985**, *26*, 891.
(103) Niki, E.; Ukegawa, K.; Kamiya, Y. *Kogyo Kagaku Zasshi* **1971**, *74*, 1354; *Chem. Abstr.* **1971**, *75*, 76328 g.
(104) Howard, J. A.; Korcek, S. *Can. J. Chem.* **1970**, *48*, 2165.
(105) Zaikov, G. E.; Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1969**, *47*, 3017.
(106) Tavadyn, L. A.; Mardoyan, V. A.; Musaelyan, M. V. *Int. J. Chem. Kinet.* **1996**, *28*, 555.
(107) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic: New York, 1981.
(108) Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519.
(109) van der Kerk, G. J. M.; Noltes, J. G.; Luijten, J. G. A. *J. Appl. Chem.* **1957**, *7*, 356.
(110) Kuivila, H. G. *Adv. Organomet. Chem.* **1964**, *1*, 47.
(111) Kupchik, E. J.; Kiesel, R. J. *J. Org. Chem.* **1966**, *29*, 3690.
(112) Kupchik, E. J.; Kiesel, R. J. *J. Org. Chem.* **1968**, *31*, 456.
(113) Kuivila, H. G.; Walsh, E. J., Jr. *J. Am. Chem. Soc.* **1966**, *88*, 571.
(114) Walsh, E. J., Jr.; Kuivila, H. G. *J. Am. Chem. Soc.* **1966**, *88*, 576.
(115) Lusztyk, J.; Lusztyk, E.; Maillard, B.; Lunazzi, L.; Ingold, K. U. *J. Am. Chem. Soc.* **1983**, *105*, 4475.
(116) Collin, J.; Namy, J.-L.; Dallemer, F.; Kagan, H. B. *J. Org. Chem.* **1991**, *56*, 3118.
(117) Sasaki, M.; Collin, J.; Kagan, H. B. *Tetrahedron Lett.* **1988**, *29*, 6105.
(118) Barton, D. H. R.; Jasberenyi, J. C.; Morrell, A. I. *Tetrahedron Lett.* **1991**, *32*, 311.
(119) Maeda, H.; Maki, T.; Ohmori, H. *Tetrahedron Lett.* **1992**, *33*, 1347.
(120) Grunwell, J. R.; Marron, N. A.; Hanhan, S. I. *J. Org. Chem.* **1973**, *38*, 1559.
(121) Tomioka, H.; Takimoto, Y.; Kawabata, M.; Harada, M.; Fouassier, J.-P.; Ruhlmann, D. *J. Photochem. Photobiol. A.* **1990**, *53*, 359.
(122) Gaber, A. E. M. *Phosphorus, Sulfur, Silicon, Relat. Elements* **1991**, *55*, 211.
(123) Penn, J. H.; Liu, F. *J. Org. Chem.* **1994**, *59*, 2608.
(124) Boger, D. L.; Mathvink, R. J. *J. Org. Chem.* **1988**, *53*, 3377.
(125) Crich, D.; Fortt, S. M. *Tetrahedron* **1989**, *45*, 6581.
(126) Beckwith, A. L. J.; Duggan, S. A. M. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1509.
(127) Tada, M.; Nakagiri, H. *Tetrahedron Lett.* **1992**, *33*, 6657.
(128) Crich, D.; Hao, X. *J. Org. Chem.* **1997**, *62*, 5982.
(129) Barton, D. H. R.; George, M. V.; Tomoeda, M. *J. Chem. Soc.* **1962**, 1967.
(130) Zard, S. Z. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 672.
(131) Delduc, P.; Tailhan, C.; Zard, S. Z. *J. Chem. Soc., Chem. Commun.* **1988**, 308.
(132) Webster, R. D.; Bond, A. M. *J. Org. Chem.* **1997**, *62*, 1779.
(133) (a) Pfenninger, J.; Henberger, C.; Graf, W. *Helv. Chim. Acta* **1980**, *63*, 2328. (b) Pfenninger, J.; Graf, W. *Helv. Chim. Acta* **1980**, *63*, 1562.
(134) (a) Bates, G. S.; Diakur, J.; Masamune, S. *Tetrahedron Lett.* **1976**, 4423. (b) Gais, H.-J. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 244.
(135) Boger, D. L.; Mathvink, R. J. *J. Org. Chem.* **1992**, *57*, 1429.
(136) Masamune, S.; Hayase, Y.; Schilling, W.; Chan, W. K.; Bates, G. S. *J. Am. Chem. Soc.* **1977**, *99*, 6756.
(137) Zhang, Y.; Yu, Y.; Lin, R. *Synth. Commun.* **1993**, *23*, 189.
(138) Schwartz, C. E.; Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 9272.
(139) (a) Kozikowski, A. P.; Ames, A. P. *J. Org. Chem.* **1978**, *43*, 2735. (b) Kozikowski, A. P.; Ames, A. P. *Tetrahedron* **1985**, *41*, 4821.
(140) (a) Grieco, P. A.; Jaw, J. Y.; Claremon, D. A.; Nicolaou, K. C. *J. Org. Chem.* **1981**, *46*, 1215. (b) Grieco, P. A.; Yokoyama, Y.; Williams, E. *J. Org. Chem.* **1978**, *43*, 1283.
(141) Batty, D.; Crich, D. *Synthesis* **1990**, 273.
(142) Ghosh, S. K.; Singh, U.; Mamdapur, V. R. *Tetrahedron Lett.* **1992**, *33*, 805.
(143) (a) Inoue, T.; Takeda, T.; Kambe, N.; Ogawa, A.; Ryu, I.; Sonoda, N. *J. Org. Chem.* **1994**, *59*, 5824. (b) Tingoli, M.; Temperini, A.; Testaferri, L.; Tiecco, M. *Synlett* **1995**, 1129.
(144) Byeon, C.-H.; Chen, C.-Y.; Ellis, D. A.; Hart, D. J.; Li, J. *Synlett* **1998**, 596.
(145) Chen, C.; Crich, D. *Tetrahedron Lett.* **1993**, *34*, 1545.
(146) Chen, C.; Crich, D.; Papadatos, A. *J. Am. Chem. Soc.* **1992**, *114*, 8313.
(147) Crich, D.; Chen, C.; Hwang, J.-T.; Yuan, H.; Papadatos, A.; Walter, R. I. *J. Am. Chem. Soc.* **1994**, *116*, 8937.
(148) Schiesser, C. H.; Skidmore, M. A. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2689.
(149) Patel, V. F.; Pattenden, G.; Thompson, D. M. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2729.
(150) Pattenden, G.; Tankard, M. *J. Organomet. Chem.* **1993**, *460*, 237.
(151) Simunic, J. L.; Pinhas, A. R. *Inorg. Chem.* **1989**, *28*, 2400.
(152) Barluenga, J.; Rodríguez, F.; Fañanás, F. J. *Organometallics* **1997**, *16*, 5384.
(153) Sumiyoshi, T.; Schnabel, W.; Henne, A.; Lechtken, P. *Polymer* **1985**, *26*, 141.
(154) Jacobi, M.; Henne, A. *J. Radiat. Curing* **1983**, *10*, 16.
(155) Sluggett, G. W.; Turro, C.; George, M. W.; Koptyug, I. V.; Turro, N. J. *J. Am. Chem. Soc.* **1995**, *117*, 5148.
(156) Jockusch, S.; Koptyug, I. V.; McGarry, P. F.; Sluggett, G. W.; Turro, N. J.; Watkins, D. M. *J. Am. Chem. Soc.* **1997**, *119*, 11495.
(157) Faltings, K. *Ber.* **1939**, *72B*, 1207.
(158) Ryu, I.; Kusano, K.; Ogawa, N.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1990**, *112*, 1295.

(159) Ryu, I.; Hasegawa, M.; Kurihara, A.; Ogawa, A.; Tsunoi, S. *Synlett* **1993**, 143.
(160) Gupta, V.; Kahne, D. *Tetrahedron Lett.* **1993**, *34*, 591.
(161) Ryu, I.; Niguma, T.; Minakata, S.; Komatsu, M.; Hadida, S.; Curran, D. P. *Tetrahedron Lett.* **1997**, *38*, 7883.
(162) Nakatani, S.; Yoshida, J.; Isoe, S. *J. Chem. Soc., Chem. Commun.* **1992**, 880.
(163) Chatgilialoglu, C.; Ferreri, C. In *Supplement C2: The Chemistry of Triple Bonded Functional Groups*; Patai, S., Ed.; Wiley: Chichester, 1994; Chapter 16, pp 917−944.
(164) (a) Sauer, J. C. *J. Am. Chem. Soc.* **1957**, *79*, 5314. (b) Foster, R. E.; Larchar, A. W.; Lipscomb, R. D.; McKusick, B. C. *J. Am. Chem. Soc.* **1956**, *78*, 5606.
(165) Ryu, I.; Kurihara, A.; Muraoka, H.; Tsunoi, S.; Kambe, N.; Sonoda, N. *J. Org. Chem.* **1994**, *59*, 7570.
(166) Tsunoi, S.; Ryu, I.; Muraoka, H.; Tanaka, M.; Komatsu, M.; Sonoda, N. *Tetrahedron Lett.* **1996**, *37*, 6729.
(167) Fujiwara, Y.; Takaki, K.; Taniguchi, Y. *Synlett* **1996**, 591.
(168) Lin, M.; Sen, A. *J. Chem. Soc., Chem. Commun.* **1992**, 892.
(169) Lin, M.; Sen, A. *Nature* **1994**, *368*, 613.
(170) Kurioka, M.; Nakata, K.; Jintoku, T.; Taniguchi, Y.; Takaki, K.; Fujiwara, Y. *Chem. Lett.* **1995**, 244.
(171) Ferguson, R. R.; Crabtree, R. H. *J. Org. Chem.* **1991**, *56*, 5503.
(172) Jaynes, B. S.; Hill, C. L. *J. Am. Chem. Soc.* **1995**, *117*, 4704.
(173) Boese, W. T.; Goldman, A. S. *Tetrahedron Lett.* **1992**, *33*, 2119.
(174) Kräutler, B. *Helv. Chim. Acta* **1984**, *67*, 1053.
(175) Turro, N. J. *Modern Molecular Photochemistry*; Benjamin/Cummings: Menlo Park, 1978.
(176) (a) Jackson, W. M.; Okabe, H. *Adv. Photochem.* **1986**, *13*, 1. (b) *Handbook of Organic Photochemistry and Photobiology*; Horsepool, W. M., Ed.; CRC Press: New York, 1994; pp 416−429.
(177) (a) Weiss, D. S. In *Organic Photochemistry*; Padwa, A., Ed.; Dekker: New York, 1981; Vol. 5. (b) Chapman, O. L.; Weiss, D. S. In *Organic Photochemistry*; Chapman, O. L., Ed.; Dekker: New York, 1973; Vol. 2.
(178) Monroe, B. M. In *Advances in Photochemistry*; Pitts, J. N., Hammond, G. S., Noyes, W. A., Eds.; Wiley: New York, 1971; Vol. 8, pp 77−108.
(179) de la Fuente, J.; Lissi, E. A.; Rozas, R. *Can. J. Chem.* **1984**, *62*, 2117.
(180) (a) Caronna, T.; Fronza, G.; Minisci, F.; Porta, O. *J. Chem. Soc., Perkin Trans. 2* **1971**, 2035. (b) Caronna, T.; Fronza, G.; Minisci, F.; Porta, O. *J. Chem. Soc., Perkin Trans. 2* **1972**, 1477.
(181) Fontana, F.; Minisci, F.; Barbosa, M. C. N.; Vismara, E. *J. Org. Chem.* **1991**, *56*, 2866.
(182) For a mechanistic study, see: (a) Sawaki, Y.; Ogata, Y. *J. Am. Chem. Soc.* **1976**, *98*, 7324. (b) Sawaki, Y.; Ogata, Y. *J. Org. Chem.* **1976**, *41*, 2340. Also see references cited therein.
(183) Bentrude, W. G.; Darnall, K. R. *J. Am. Chem. Soc.* **1968**, *90*, 3588.
(184) Murphy, J. A.; Patterson, C. W.; Wooster, N. F. *Tetrahedron Lett.* **1988**, *29*, 955.
(185) Anson, M. S.; Montana, J. G. *Synlett* **1994**, 219.
(186) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901.
(187) Billingham, N. C.; Jackson, R. A.; Malek, F. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1137.
(188) Oka, K.; Nakao, R.; Abe, Y.; Dohmaru, T. *J. Organomet. Chem.* **1990**, *381*, 155.
(189) Ballestri, M.; Chatgilialoglu, C.; Cardi, N.; Sommazzi, A. *Tetrahedron Lett.* **1992**, *33*, 1787.
(190) Lusztyk, J.; Lusztyk, E.; Maillard, B.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 2923.
(191) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188.
(192) Chatgilialoglu, C.; Ferreri, C.; Gimisis, T. In *The Chemistry of Organic Silicon Compounds*; Rappoport, S., Apelog, Y., Eds; Wiley: London, 1998; Vol. 2, Chapter 25, pp 1539−1579.
(193) Ireland, R. E.; Norbeck, D. W.; Mandel, S. G.; Mandel, N. S. *J. Am. Chem. Soc.* **1985**, *107*, 3285.
(194) Crich, D.; Eustace, K. A.; Ritchie, T. J. *Heterocycles* **1989**, *28*, 67.
(195) Quirante, J.; Escolano, C.; Bonjock, J. *Synlett* **1997**, 179.
(196) Stojanovic, A.; Renaud, P. *Synlett* **1997**, 181.
(197) Alcaide, B.; Rodriguez-Vicente, A.; Sierra, M. A. *Tetrahedron Lett.* **1998**, *39*, 163.
(198) Crich, D.; Yao, Q. *J. Org. Chem.* **1996**, *61*, 3566.
(199) Crich, D.; Hwang, J.-T.; Yuan, H. *J. Org. Chem.* **1996**, *61*, 6189.
(200) Giese, B.; Erdmann, P.; Giraud, L.; Göbel, T.; Petretta, M.; Schäfer, T.; von Raumer, M. *Tetrahedron Lett.* **1994**, *35*, 2683.
(201) Crich, D.; Yao, Q. *Tetrahedron* **1998**, *54*, 305.
(202) (a) Punniyamurthy, T.; Kalra, S. J. S.; Iqbal, J. *Tetrahedron Lett.* **1994**, *35*, 2959. (b) Pimpim, R. S.; Rubega, C. C. C.; de Bravo, R. V. F.; Kascheres, C. *Synth. Commun.* **1997**, *27*, 811.
(203) Shono, T.; Soejima, T.; Takigawa, K.; Yamaguchi, Y.; Maekawa, H.; Kashimura, S. *Tetrahedron Lett.* **1994**, *35*, 4161.
(204) Goldberg, K. I.; Bergman, R. G. *J. Am. Chem. Soc.* **1989**, *111*, 1285.
(205) Algarra, F.; Baldovî, M. V.; Garcîa, H.; Miranda, M. A.; Primo, J. *Tetrahedron* **1993**, *49*, 10897.
(206) Winstein, S.; Seubold, F. H. *J. Am. Chem. Soc.* **1947**, *69*, 2916.
(207) Ginsburg, D. *J. Am. Chem. Soc.* **1951**, *73*, 702.
(208) Foster, R. E.; Larchar, A. W.; Lipscomb, R. D.; McKusick, B. C. *J. Am. Chem. Soc.* **1956**, *78*, 5606.
(209) Suzuki, T.; Tsuji, J. *J. Org. Chem.* **1970**, *35*, 2982.
(210) Walling, C.; Savas, E. S. *J. Am. Chem. Soc.* **1960**, *82*, 1738.
(211) (a) Thaler, W. A. *J. Am. Chem. Soc.* **1966**, *88*, 4278. (b) Thaler, W. A. *J. Am. Chem. Soc.* **1967**, *89*, 1902.
(212) Nagahara, K.; Ryu, I.; Komatsu, M.; Sonoda, N. *J. Am. Chem. Soc.* **1997**, *119*, 5465.
(213) Ryu, I.; Nagahara, K.; Kambe, N.; Sonoda, N.; Kreimerman, S.; Komatsu, M. *Chem. Commun.* **1998**, 1953.
(214) (a) Walling, C.; Basedow, O. H.; Savas, E. S. *J. Am. Chem. Soc.* **1960**, *82*, 2181. (b) Takagi, M.; Goto, S.; Tazaki, M.; Matsuda, T. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1982.
(215) Coveney, D. J.; Patel, V. F.; Pattenden, G.; Thompson, D. M. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2721.
(216) Ryu, I.; Okuda, T.; Nagahara, K.; Kambe, N.; Komatsu, M.; Sonoda, N. *J. Org. Chem.* **1997**, *62*, 7550.
(217) Adams, R. D.; Huang, M.; Huang, W. *Organometallics* **1997**, *16*, 4479.
(218) Ryu, I.; Muraoka, H.; Kambe, N.; Komatsu, M.; Sonoda, N. *J. Org. Chem.* **1996**, *61*, 6396.
(219) (a) Wiberg, K. B.; Waddell, S. T.; Laidig, K. *Tetrahedron Lett.* **1986**, 27, 1553. (b) Wiberg, K. B.; Waddell, S. T. *J. Am. Chem. Soc.* **1990**, *112*, 2194.
(220) (a) Kaszynski, P.; Michl, J. *J. Org. Chem.* **1988**, *53*, 4593. (b) Kaszynski, P.; Friedli, A. C.; Michl, J. *J. Am. Chem. Soc.* **1991**, *114*, 601.
(221) Riemann, H.; Capomaggi, A. S.; Strauss, T.; Olivetto, E. P.; Barton, D. H. R. *J. Am. Chem. Soc.* **1961**, *83*, 4481.
(222) Dowd, P.; Choi, S. C. *J. Am. Chem. Soc.* **1987**, *109*, 3493.
(223) Beckwith, A. L. B.; O'Shea, D. M.; Gerba, S.; Westwood, S. W. *J. Chem. Soc., Chem. Commun.* **1987**, 666.
(224) Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091.
(225) Chatgilialoglu, C.; Timokhin, V. I.; Ballestri, M. *J. Org. Chem.* **1998**, *63*, 1327.
(226) Crich, D.; Batty, D. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3193.
(227) Chatgilialoglu, C.; Ferreri, C.; Luarini, M.; Venturini, A.; Zavitsas, A. A. *Chem. Eur. J.* **1997**, *3*, 376.
(228) Wang, C.; Gu, X.; Yu, M. S.; Curran, D. P. *Tetrahedron* **1998**, *54*, 8355.
(229) Ryu, I.; Fukushima, H.; Okuda, T.; Matsu, K.; Kambe, N.; Sonoda, N.; Komatsu, M. *Synlett* **1997**, 1265.
(230) Cf.: Giese, B.; Heinrich, N.; Horler, H.; Koch, W.; Schwarz, H. *Chem. Ber.* **1986**, *119*, 3528.
(231) Ito, Y.; Fujii, S.; Saegusa, T. *J. Org. Chem.* **1976**, *41*, 2073.
(232) Ito, Y.; Sugaya, T.; Nakatsuka, M.; Saegusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 8366.
(233) Booker-Milburn, K. I. *Synlett* **1992**, 809.
(234) Booker-Milburn, K. I.; Thompson, D. F. *Synlett* **1993**, 592.
(235) (a) Iwasawa, N.; Hayakawa, S.; Isobe, K.; Narasaka, K. *Chem. Lett.* **1991**, 1193. (b) Iwasawa, N.; Hayakawa, S.; Funahashi, M.; Isobe, K.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 879.
(236) (a) Iwasawa, N.; Funahashi, M.; Hayakawa, S.; Narasaka, K. *Chem. Lett.* **1993**, 545. (b) Iwasawa, N.; Funahashi, M.; Narasaka, K. *Chem. Lett.* **1994**, 1697.
(237) Blanco, L.; Mansouri, A. *Tetrahedron Lett.* **1988**, *29*, 3239.
(238) Cekovic, Z. *Tetrahedron Lett.* **1972**, 749.
(239) Walsh, E. J.; Messinger, J. M.; Grudloski, D. A.; Allchin, C. A. *Tetrahedron Lett.* **1980**, 4409.
(240) Green, S. P.; Whiting, D. A. *J. Chem. Soc., Chem. Commun.* **1992**, 1753.
(241) Fernandez-Mateos, A.; Coca, C. P.; Gonzalez, R. R.; Hernandez, C. T. *Tetrahedron* **1996**, *52*, 4817.
(242) Evans, P. A.; Manangan, T. *Tetrahedron Lett.* **1997**, *38*, 8165.
(243) Evans, P. A.; Roseman, J. D. *J. Org. Chem.* **1996**, *61*, 2252.
(244) Evans, P. A.; Roseman, J. D. *Tetrahedron Lett.* **1995**, *36*, 31.
(245) Ryu, I.; Kusano, K.; Hasegawa, M.; Kambe, N.; Sonoda, N. *J. Chem. Soc., Chem. Commun.* **1991**, 1018.
(246) Cf.: Curran, D. P.; Liu, H. *J. Am. Chem. Soc.* **1991**, *113*, 2127.
(247) Tsunoi, S.; Ryu, I.; Yamasaki, S.; Fukushima, H.; Tanaka, M.; Komatsu, M.; Sonoda, N. *J. Am. Chem. Soc.* **1996**, *118*, 10670.
(248) Ryu, I.; Nagahara, K.; Kurihara, A.; Komatsu, M.; Sonoda, N. *J. Organomet. Chem.* **1997**, *548*, 105.
(249) Denney, D. B.; Klemchuk, P. P. *J. Am. Chem. Soc.* **1958**, *80*, 3289.
(250) Curtin, D. Y.; Kauer, J. C. *J. Org. Chem.* **1960**, *25*, 880.
(251) Urry, W. H.; Trecker, D. J.; Hartzler, H. D. *J. Org. Chem.* **1964**, *29*, 1663.
(252) Chatzopoulus, M.; Montheard, J.-P. *C. R. Acad. Sci., Ser. C* **1975**, *280*, 29.
(253) Montheard, J.-P. *C. R. Acad. Sci., Ser. C* **1967**, *260*, 570.
(254) Julia, M.; Maumy, M. *Bull. Soc. Chim. Fr.* **1969**, 2415.
(255) Julia, M.; Maumy, M.; Mion, L. *Bull. Soc. Chim. Fr.* **1967**, 2641.
(256) Barton, D. H. R.; Clive, D. L. J.; Magnus, P. D.; Smith, G. *J. Chem. Soc. C* **1971**, 2193.
(257) Bachi, M. D.; Denenmark, D. *Heterocycles* **1989**, *28*, 583.

(258) Kampmeier, J. A.; Harris, S. H.; Wedegaertner, D. K. *J. Org. Chem.* **1980**, *45*, 315.
(259) Dang, H.-S.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 67.
(260) Crich, D.; Eustace, K. A.; Fortt, S. M.; Ritchie, T. J. *Tetrahedron* **1990**, *46*, 2135.
(261) Sasaki, M.; Collin, J.; Kagan, H. B. *Tetrahedron* **1988**, *29*, 6105.
(262) Hayes, C. J.; Pattenden, G. *Tetrahedron Lett.* **1996**, *37*, 271.
(263) Batty, D.; Crich, D.; Fortt, S. M. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2875.
(264) Ohtsuka, M.; Takekawa, Y.; Shishido, K. *Tetrahedron Lett.* **1998**, *39*, 5803.
(265) Evans, P. A.; Roseman, J. D.; Garber, L. T. *J. Org. Chem.* **1996**, *61*, 4880.
(266) Evans, P. A.; Roseman, J. D. *Tetrahedron Lett.* **1997**, *38*, 5249.
(267) Hanessian, S.; Dhanoa, D. S.; Beaulieu, P. L. *Can. J. Chem.* **1987**, *65*, 1859.
(268) Crich, D.; Fortt, S. M. *Tetrahedron Lett.* **1988**, *29*, 2585.
(269) Bachi, M. D.; Bosch, E. *J. Org. Chem.* **1992**, *57*, 4696.
(270) Boger, D. L.; Mathvink, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 4008.
(271) Astley, M. P.; Pattenden, G. *Synlett* **1992**, 101.
(272) Ryu, I.; Nagahara, K.; Yamazaki, H.; Tsunoi, S.; Sonoda, N. *Synlett* **1994**, 643.
(273) Nagahara, K.; Ryu, I.; Yamazaki, H.; Kambe, N.; Komatsu, M.; Sonoda, N.; Baba, A. *Tetrahedron* **1997**, *53*, 14615.
(274) Baldwin, J. E.; Adlington, R. M.; Robertson, J. *Tetrahedron* **1991**, *47*, 6795.
(275) Barton, D. H. R.; George, M. V.; Tomoeda, M. *J. Chem. Soc.* **1962**, 1967.
(276) (a) Harrison, D. A.; Schwartz, R. N.; Kagan, J. *J. Am. Chem. Soc.* **1970**, *92*, 5793. Also see: (b) Kende, A. S.; Belletire, J. L. *Tetrahedron Lett.* **1972**, 2145. (c) Praefcke, K. *Tetrahedron Lett.* **1973**, 973.
(277) Mendenhall, G. D.; Protasiewicz, J. D.; Brown, C. E.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1994**, *116*, 1718.
(278) Janzen, E. G.; Oehler, U. M. *Tetrahedron Lett.* **1983**, *24*, 669.
(279) Yamamoto, Y.; Ohno, M.; Eguchi, S. *J. Am. Chem. Soc.* **1995**, *117*, 9653.
(280) Yamamoto, Y.; Ohno, M.; Eguchi, S. *J. Org. Chem.* **1996**, *61*, 9264.
(281) Brinza, I. M.; Fallis, A. G. *J. Org. Chem.* **1996**, *61*, 3580.
(282) Ryu, I.; Matsu, K.; Minakata, S.; Komatsu, M. *J. Am. Chem. Soc.* **1998**, *120*, 5838.
(283) Ryu, I.; Ogura, S.; Minakata, S.; Komatsu, M. *Tetrahedron Lett.* **1999**, *40*, 1515.
(284) Walling, C. *Free Radicals in Solution*; Wiley: New York, 1957.
(285) Kharasch, M. S.; Urry, W. H.; Kuderna, B. M. *J. Org. Chem.* **1949**, *14*, 248.
(286) (a) Coffman, D. D.; Pinkney, P. S.; Wall, W. H.; Young, H. S. *J. Am. Chem. Soc.* **1952**, *74*, 3391. (b) Brubaker, M. M.; Coffman, D. D.; Hoehn, H. H. *J. Am. Chem. Soc.* **1952**, *74*, 1509.
(287) Brubaker, M. M. U.S. Patent 2,680,763; *Chem. Abstr.* **1955**, *49*, 6691.
(288) (a) Patrick, T. M., Jr. *J. Org. Chem.* **1952**, *17*, 1009, 1269. (b) Huang, R. L. *J. Chem. Soc.* **1956**, 1749.
(289) Stockman, H. *J. Org. Chem.* **1964**, *29*, 245.
(290) van der Linde, L. M.; van der Weerdt, A. J. A. *Tetrahedron Lett.* **1984**, *25*, 1201.
(291) (a) Dowbenko, R. *J. Am. Chem. Soc.* **1964**, *86*, 946. (b) Friedman, L. *J. Am. Chem. Soc.* **1964**, *86*, 1885.
(292) (a) LaZerte, J. D.; Koshar, R. J. *J. Am. Chem. Soc.* **1955**, *77*, 910. (b) Muramatsu, H.; Inukai, K. *J. Org. Chem.* **1962**, *27*, 1572.
(293) Nam, W.; Kim, H. J.; Kim, S. H.; Ho, R. Y. N.; Valentine, J. S. *Inorg. Chem.* **1996**, *35*, 1045 and references therein.
(294) (a) Punniyamurthy, T.; Bhatia, B.; Iqbal, J. *J. Org. Chem.* **1994**, *59*, 850. (b) Bhatia, S.; Punniyamurthy, T.; Bhatia, B.; Iqbal, J. *Tetrahedron* **1993**, *49*, 6101.
(295) Jent, F.; Paul, H.; Roduner, E.; Heming, M.; Fischer, H. *Int. J. Chem. Kinet.* **1986**, *18*, 1113.
(296) Scheffold, R.; Orlinski, R. *J. Am. Chem. Soc.* **1983**, *105*, 7200.
(297) (a) Sakurai, H.; Narasaka, K. *Chem. Lett.* **1994**, 2017. (b) Narasaka, K.; Sakurai, H. *Chem. Lett.* **1993**, 1269.
(298) Söderberg, B. C.; York, D. C.; Harriston, E. A.; Caprara, H. J.; Flurry, A. H. *Organometallics* **1995**, *14*, 3712.
(299) Fraser-Reid, B.; Anderson, R. C.; Hicks, D. R.; Walker, D. L. *Can. J. Chem.* **1977**, *55*, 3986.
(300) (a) Macias, F. A.; Molinillo, J. M. G.; Collado, I. G.; Massanet, G. M.; Rodriguez-Luis, F. *Tetrahedron Lett.* **1990**, *31*, 3063. (b) Macias, F. A.; Molinillo, J. M. G.; Massanet, G. M.; Rodriguez-Luis, F. *Tetrahedron Lett.* **1992**, *48*, 3345.
(301) (a) Stringat, R.; Fabre, G.; Fellous, R.; Paquet, P. *Tetrahedron Lett.* **1992**, *33*, 4303. (b) Kawenoki, L.; Maurel, D.; Kossanyi, J. *Bull. Soc. Chim. Fr.* **1982**, 385.
(302) Mignani, S.; Beaujean, M.; Janousek, Z.; Merenyi, R.; Viehe, H. G. *Tetrahedron* **1981**, *37*, 111.
(303) Boger, D. L.; Mathvink, R. J. *J. Org. Chem.* **1989**, *54*, 1777.
(304) Haraguchi, K.; Tanaka, H.; Miyasaka, T. *Tetrahedron Lett.* **1990**, *31*, 227.
(305) Ryu, I.; Kusano, K.; Yamazaki, H.; Sonoda, N. *J. Org. Chem.*, **1991,** *56*, 5003.
(306) (a) Keck, G.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079. (b) Curran, D. P.; van Elburg, P. A.; Giese, B.; Gilges, S. *Tetrahedron Lett.* **1990**, *31*, 2861.
(307) Ryu, I.; Yamazaki, H.; Kusano, K.; Ogawa, A.; Sonoda, N. *J. Am. Chem. Soc.* **1991**, *113*, 8558.
(308) (a) Ryu, I.; Yamazaki, H.; Ogawa, A.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1993**, *115*, 1187. (b) Ryu, I.; Niguma, T.; Minakata, S.; Komatsu, M.; Luo, Z.; Curran, D. P. *Tetrahedron Lett.* **1999**, *40*, 2367.
(309) Gottschalk, P.; Neckers, D. C. *J. Org. Chem.* **1985**, *50*, 3498.
(310) Sibi, M. P.; Ji, J. *J. Org. Chem.* **1996**, *61*, 6090.
(311) Nozaki, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1987**, *109*, 2547.
(312) Schlubach, H. H.; Franzen, V.; Dehl, E. *Liebigs Ann. Chem.* **1954**, *587*, 124.
(313) Wiley, R. H.; Harrel, J. R. *J. Org. Chem.* **1960**, *25*, 903.
(314) Ryu, I.; Yamazaki, H.; Fukushima, H.; Sonoda, N. Unpublished results.
(315) Gong, J.; Fuchs, P. L. *Tetrahedron Lett.* **1997**, *38*, 787.
(316) Curran, D. P.; Xu, J.; Lazzarini, E. *J. Chem. Soc., Perkin Trans. 1* **1995**, 3049.
(317) Rust, F. F.; Seubold, F. H.; Vaughan, W. E. *J. Am. Chem. Soc.* **1948**, *70*, 3258.
(318) Urry, W. H.; Pai, M. H.; Chen, C. Y. *J. Am. Chem. Soc.* **1964**, *86*, 5342.
(319) Urry, W. H.; Nishihara, A.; Niu, J. H. Y. *J. Org. Chem.* **1967**, *32*, 347.
(320) Bruce, J. M.; Creed, D.; Ellis, J. N. *J. Chem. Soc. C* **1967**, 1486 and references therein.
(321) Maruyama, K.; Sakurai, H.; Otsuki, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2777.
(322) (a) Maruyama, K.; Takuwa, A.; Matsukiyo, S.; Soga, O. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1414. (b) Takuwa, A.; Soga, O. *J. Chem. Soc., Perkin Trans. 2* **1985**, 409.
(323) (a) Kharasch, M. S.; Zimmermann, M.; Zimmt, W.; Nudenberg, W. *J. Org. Chem.* **1953**, *18*, 1045. (b) Horner, L.; Naumann, W. *Liebigs Ann. Chem.* **1954**, *587*, 81. (c) Huisgen, R.; Jakob, F. *Liebigs Ann. Chem.* **1954**, *590*, 37.
(324) (a) Kim, S.; Lee, I. Y.; Yoon, J-. Y.; Oh, D. H. *J. Am. Chem. Soc.* **1996**, *118*, 5138. (b) Kim, S.; Lee, I. Y.; Yoon, J-.Y. *J. Am. Chem. Soc.* **1997**, *119*, 5982.
(325) Ryu, I.; Kuriyama, H.; Komatsu, M.; Yoon, J.-Y.; Kim, S. Unpublished work.
(326) Gardini, G. P.; Minisci, F. *J. Chem. Soc. C* **1970**, 929.
(327) Belatti, M.; Caronna, T.; Citterio, A.; Minisci, F. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1835.
(328) (a) Minisci, F.; Porta, *Adv. Heterocycl. Chem.* **1974**, *16*, 123. (b) Minisci, F.; Vismara, E.; Fontana, F. *Heterocycles* **1989**, *28*, 489.
(329) (a) Baur, R.; Sugimoto, T.; Pfleiderer, W. *Helv. Chim. Acta* **1988**, *71*, 531. (b) Houminer, Y.; Southwick, E. W.; Williams, D. L. *J. Heterocycl. Chem.* **1986**, *23*, 497.
(330) (a) Kochi, J. K. *Organometallic Mechanisms and Catalysis*; Academic Press: New York, 1978; pp 97−99. (b) *Metal-Catalyzed Oxidations of Organic Compounds*; Shelddon, R. A., Kochi, J. K., Eds.; Academic Press: New York, 1981; pp 140−143, 359−363.
(331) Walling, C. In *Active Oxygen in Chemistry*; Foote, C. S., Valentine, J. S., Greenberg, A., Liebman, J. F., Eds.; Blackie Academic & Professional: London, 1995; pp 24−65.
(332) Bäckström, H. L. J. *Z. Phys. Chem.* **1934**, *B25*, 99.
(333) (a) Murahashi, S.-I. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2443. (b) Strukul, G. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1198. (c) Nam, W.; Baeg, S. J.; Lee, K. A.; Ahn, B. T.; Muller, J. G.; Burrows, C. J.; Valentine, J. S. *Inorg. Chem.* **1996**, *35*, 6632. (d) Wentzel, B. B.; Gosling, P. A.; Feiters, M. C.; Nolte, R. J. M. *J. Chem. Soc., Dalton Trans.* **1998**, 2241.
(334) Coffman, D. D.; Cramer, R.; Mochel, W. E. *J. Am. Chem. Soc.* **1958**, *80*, 2882.
(335) Chiusoli, G. P.; Minisci, F. *Gazz. Chim. Ital.* **1958**, *88*, 43.
(336) Ryu, I.; Alper, H. *J. Am. Chem. Soc.* **1993**, *115*, 7543.
(337) Curran, D. P.; Chang, C. -T. *J. Org. Chem.* **1989**, *54*, 3140.
(338) Okuro, K.; Alper, H. *J. Org. Chem.* **1996**, *61*, 5312.
(339) For reviews, see: (a) Mihailovic, M. L.; Cekovic, Z.; Lorenc, L. In *Organic Syntheses by Oxidation with Metal Compounds*; Mijs, W. J., de Jonge, C. R. H. I., Eds.; Plenum Press: New York, 1986; Chapter 14. (b) Majetich, G.; Wheless, K. *Tetrahedron* **1995**, *51*, 7095.
(340) (a) Tsunoi, S.; Ryu, I.; Sonoda, N. *J. Am. Chem. Soc.* **1994**, *116*, 5473. (b) Tsunoi, S.; Ryu, I.; Okuda, T.; Tanaka, M.; Komatsu, M.; Sonoda, N. *J. Am. Chem. Soc.* **1998**, *120*, 8692.
(341) Tsunoi, S.; Ryu, I.; Tamura, Y.; Yamasaki, S.; Sonoda, N. *Synlett* **1994**, 1009.
(342) Lin, M.; Sen, A. *J. Chem. Soc., Chem. Commun.* **1992**, 892.
(343) Kato, S.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1998**, *63*, 222.
(344) Russel, G. A.; Chen, P.; Kim, B. H.; Rajaratnam, R. *J. Org. Chem.* **1997**, *119*, 8795.

(345) (a) Nudelman, N. S.; Outumuro, P. *J. Org. Chem.* **1982**, *47*, 4347. (b) Murai, S.; Ryu, I.; Iriguchi, J.; Sonoda, N. *J. Am. Chem. Soc.* **1984**, *106*, 2440.
(346) Occhialini, D.; Daasbjerg, K.; Lund, H. *Acta Chem. Scand.* **1993**, *47*, 1100.
(347) Nudelman, N. S.; Vitale, A. A. *J. Org. Chem.* **1981**, *46*, 4625.
(348) Namy, J.-L.; Girard, P.; Kagan, H. B. *New J. Chem.* **1977**, *1*, 5.
(349) Namy, J.-L.; Colomb, M.; Kagan, H. B. *Tetrahedron Lett.* **1994**, *35*, 1723.
(350) Sasaki, M.; Collin, J.; Kagan, H. B. *Tetrahedron Lett.* **1988**, *29*, 4847.
(351) Collin, J.; Kagan, H. B. *Tetrahedron Lett.* **1988**, *29*, 6097.
(352) Tsunoi, S.; Ryu, I.; Fukushima, H.; Tanaka, M.; Komatsu, M.; Sonoda, N. *Synlett* **1995**, 1249.
(353) Ogawa, A.; Sumino, Y.; Nanke, T.; Ohya, S.; Sonoda, N.; Hirao, T. *J. Am. Chem. Soc.* **1997**, *119*, 2745.
(354) (a) Guirado, A.; Barba, F.; Manzanera, C.; Velasco, M. D. *J. Org. Chem.* **1982**, *47*, 142. (b) Guirado, A.; Barba, F.; Martin, J. *Synth. Commun.* **1983**, *13*, 327. (c) Cheek, G. T.; Horine, P. A. *J. Electrochem. Soc.* **1984**, *131*, 1796.
(355) Urove, G. A.; Peters, D. G.; Mubarak, M. S. *J. Org. Chem.* **1992**, *57*, 786.
(356) Urove, G. A.; Peters, D. G. *J. Electrochem. Soc.* **1993**, *140*, 932.
(357) Mubarak, M. S.; Peters, D. G. *J. Electrochem. Soc.* **1995**, *142*, 713.
(358) Li, N.-M.; Yu, S.; Kabalka, G. W. *J. Org. Chem.* **1995**, *60*, 5973.
(359) Pokhodenko, V. D.; Koshechko, V.; Titov, V. E.; Lopushanskaja, V. A. *Tetrahedron Lett.* **1995**, *36*, 3277.
(360) Hadida, S.; Super, M. S.; Beckman, E. J.; Curran, D. P. *J. Am. Chem. Soc.* **1997**, *119*, 7406.
(361) Curran, D. P.; Sisko, J.; Balog, A.; Sonoda, N.; Nagahara, K.; Ryu, I. *J. Chem. Soc., Perkin. Trans. 1* **1998**, 1591.
(362) (a) Chatgilialoglu, C.; Ferreri, C.; Sommazzi, A. *J. Am. Chem. Soc.* **1996**, *118*, 7223. (b) Sommazzi, A.; Cardi, N.; Garbassi, F.; Chatgilialoglu, C. U.S. Patent 5,1994,369, 187. (c) Chatgilialoglu, C. In *Chemical Synthesis: Gnosis to Prognosis*; Chatgilialoglu, C., Snieckus, V., Eds.; Kluwer: Dordrecht, 1996; pp 263−276.
(363) Boger, D. L.; Mathvink, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 4003.
(364) Chen, L.; Gill, G. B.; Pattenden, G.; Simonian, H. *J. Chem. Soc., Perkin Trans. 1* **1996**, 31.
(365) Batsanov, A.; Chen, L.; Gill, G. B.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1996**, 45.
(366) (a) Pattenden, G.; Roberts, L. *Tetrahedron Lett.* **1996**, *37*, 4191. (b) Pattenden, G.; Roberts, L.; Blake, A. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 863.
(367) Handa, S.; Pattenden, G.; Li, W.-S. *Chem. Commun.* **1998**, 311.
(368) Batty, D.; Crich, D. *Tetrahedron Lett.* **1992**, *33*, 875.
(369) Ryu, I.; Fukushima, H.; Tsunoi, S.; Sonoda, N. Unpublished work.
(370) Ryu, I.; Yamazaki, H.; Nagahara, K.; Tsunoi, S.; Sonoda, N. Unpublished work.
(371) Tsunoi, S.; Ryu, I.; Yamasaki, S.; Tanaka, M.; Sonoda, N.; Komatsu, M. *Chem. Commun.* **1997**, 1889.
(372) Herbert, N.; Pattenden, G. *Synlett* **1997**, 69.
(373) Bachi, M. D.; Balanov, A.; Bar-Ner, N.; Bosch, E.; Denenmark, D.; Mizhiritskii, M. *Pure Appl. Chem.* **1993**, 65, 595.
(374) (a) Boeck, B. D.; Herbert, N.; Pattenden, G. *Tetrahedron Lett.* **1998**, *39*, 6971. (b) Boeck, B. D.; Pattenden, G. *Tetrahedron Lett.* **1998**, *39*, 6975.
(375) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.
(376) Chatgilialoglu, C.; Ferreri, C. *Res. Chem. Intermed.* **1993**, *19*, 755.
(377) Beak, P.; Mojé, S. W. *J. Org. Chem.* **1974**, *39*, 1320 and references therein.
(378) Paquette, L. A.; Friedrich, D.; Panard, E.; Williams, J. P.; Laurent, D. St.; Roden, B. A. *J. Am. Chem. Soc.* **1993**, *115*, 4377.
(379) Lucas, M. A.; Schiesser, C. H. *J. Org. Chem.* **1996**, *61*, 5754.
(380) Jensen, F. R.; Moder T. I. *J. Am. Chem. Soc.* **1975**, *97*, 2281.
(381) Barton, D. H. R.; Crich, D. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1603.
(382) Crich, D.; Fortt, S. M. *Synthesis* **1987**, 35.
(383) Togo, H.; Fujii, M.; Yokoyama, M. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 57.
(384) Simakov, P. A.; Martinez, F. N.; Horner, J. H.; Newcomb, M. *J. Org. Chem.* **1998**, *63*, 1226.
(385) Rüegge, D.; Fischer, H. *Int. J. Chem. Kinet.* **1986**, *18*, 145.
(386) Beckwith, A. L.; Bowry, V. W.; Moad, G. *J. Org. Chem.* **1988**, *53*, 1632.
(387) Beckwith, A. L.; Bowry, V. W. *J. Am. Chem. Soc.* **1994**, *116*, 2710.
(388) Walton, J. C. *Magn. Reson. Chem.* **1987**, *25*, 998.
(389) (a) Johnson, K. M.; Roberts, B. P. *J. Chem. Res. (S)* **1989**, 352. (b) Perkins, M. J.; Roberts, B. P. *J. Chem. Soc., Perkin II* **1974**, 297.
(390) (a) Bachi, M. D.; Bosch, E. *Tetrahedron, Lett.* **1986**, *27*, 641. (b) Bachi, M. D.; Bosch, E. *Heterocycles* **1989**, *28*, 579.
(391) Bachi, M. D.; Bosch, E. *J. Org. Chem.* **1992**, *57*, 4696.
(392) Singh, A. K.; Bakshi, R. K.; Corey, E. J. *J. Am. Chem. Soc.* **1987**, *109*, 6187.
(393) Clive, D. L. J.; Manning, H. W.; Boivin, T. L. B.; Postema, M. H. D. *J. Org. Chem.* **1993**, *58*, 6857.
(394) Evans, P. A.; Murthy, V. S. *Tetrahedron Lett.* **1998**, *39*, 9627.
(395) Saicic, R. N.; Zard, S. Z. *Chem. Commun.* **1996**, 1631.
(396) (a) Minisci, F. *Top. Curr. Chem.* **1976**, *62*, 41. (b) Coppa, F.; Fontana, F.; Lazzarini, E.; Minisci, F.; Pianese, G.; Zhao, L. *Tetrahedron Lett.* **1992**, *33*, 3057.
(397) Mazzocchi, P. H.; Bowen, M. *J. Org. Chem.* **1976**, *41*, 1279.
(398) Friedma, L. *J. Am. Chem. Soc.* **1964**, *86*, 1885.
(399) Gill, G. B.; Pattenden, G.; Reynolds, S. J. *Tetrahedron Lett.* **1989**, *30*, 3229.
(400) Minisci, F.; Citterio, A.; Vismara, E.; Giordano, C. *Tetrahedron* **1985**, *41*, 4157.
(401) Minisci, F. *Synthesis* **1973**, 1.
(402) Minisci, F.; Fontana, F.; Coppa, F.; Yan, Y. M. *J. Org. Chem.* **1995**, *60*, 5430.
(403) Sakamoto, M.; Takahashi, M.; Fujita, T.; Nishio, T.; Iida, I.; Watanabe, S. *J. Org. Chem.* **1995**, *60*, 4683.
(404) For a related review, see: Ito, Y. *Synlett* **1998**, 26.

CR9601425