Bull Soc Chim Fr (1996) 133, 15-24

Hydroxylation of carbanions with lithium *tert*-butyl peroxide acting as an oxenoid

Marc Julia*, Virginie Pfeuty-Saint Jalmes, Karen Plé, Jean-Noël Verpeaux, in part G Hollingworth

Département de chimie, ENS, 24, rue Lhomond, 75231 Paris Cedex 05, France

(Received 31 July 1995; accepted 2 November 1995)

Summary – The lithium salt of *tert*-butyl hydroperoxide can convert alkyl, vinyl, aryl carbanions, acetylides and various enolates into the corresponding hydroxylated derivatives in good yields and under mild conditions.

carbanion / oxenoid / phenol / ynolate / hydroxyacid / hydroxyamide

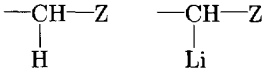
Résumé – Hydroxylation de carbanions par l'hydroperoxyde de *tert*-butyle lithié jouant le rôle d'oxénoïde. *L'hydroperoxyde de* tert*-butyle lithié est un agent d'hydroxylation électrophile des carbanions* sp_3, sp_2 *ou* sp*: les alkyl lithiens et les énolates sont transformés en alcools correspondants, les carbanions aromatiques en phénols et les acétylures conduisent aux ynolates. Les conditions sont douces et les rendements sont généralement élevés.*

carbanion / oxenoïde / phénol / ynolate / hydroxyacide / hydroxyamide

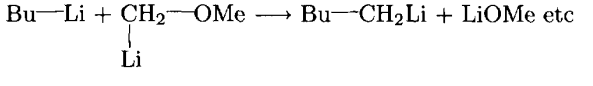
Introduction

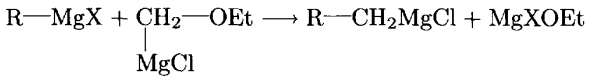
The conversion in living cells of squalene into steroids or of phenylalanine into tyrosine raised the question of an electrophilic hydroxylating agent [1a]. Many oxidizing systems have been proposed and investigated using dioxygen itself, hydrogen peroxide, alkyl hydroperoxides, etc. Most of the reactions thus performed involve free radicals or radicals associated with metallic ions [1b]. The simplest electrophilic hydroxylating agent would be HO^+ or HO-Z with Z being a (good) leaving group.

On the other hand, it is known that the electrophilic properties of carbon electrophiles are enhanced when the α-carbon atom is converted into a carbanion, in the so-called 'carbenoids' [2].

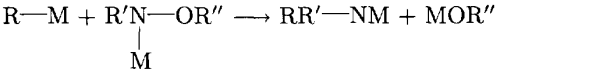


It is remarkable that in this type of compound even the methoxide ion becomes a relatively good leaving group as shown by its displacement by organometallic derivatives in metallated dimethyl ether [3].

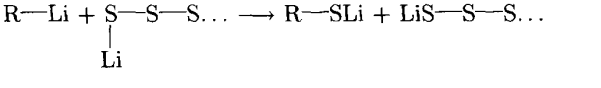




A similar reaction is known with analogous nitrogen compounds ('nitrenoids') [4]. Metallated hydroxylamine [4a] and *N*-methyl-*N*-lithiomethoxyamine [4b] undergo displacement of the methoxide ion and formation of an alkylated (metallated) amine. Other electrophilic nitrenoids have been developed more recently, and coupled with lithium or copper carbanions [4f-h].

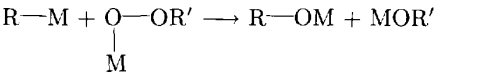


The well-known conversion of Grignard or organolithium compounds into thiolates by reaction with elemental sulfur is, at least formally, very similar [5, 14a].

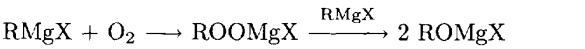


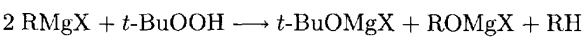
If it is then possible to transfer carbon-, nitrogen-, or sulfur-containing groups to organometallics, the question arose of a similar displacement reaction in which an oxygen atom would be the seat of the reaction, and would be transferred to an organometallic derivative. Several reagents have oxygen atoms attached to leaving groups. Considering the related results above a simple readily available example would be metallated hydroperoxides. The present work was undertaken in order to try and oxidize carbanions with these reagents. Preliminary results have been published [6a-c]. A similar approach has recently been discussed by Boche and his group [6d].

* Correspondence and reprints



This is reminiscent of another well-known reaction, namely the autoxidation of organometallics (Mg [7a-i] or Li [7j,k]) which has been shown to take place in two distinct steps. The organometallic first reacts with dioxygen to give a hydroperoxide salt, and, in a second step, another molecule of the organometallic is oxidized by this salt to give two molecules of the metal alkoxide.





The nature of this second step [7h] (overall redox reaction) was not clear. However, in the case of cyclopropyllithium [8] or vinyllithium [9] derivatives, it has been shown that the reaction involved retention of configuration. On the other hand, the autoxidation led to a mixture of stereoisomeric enolates. The conclusion was that the autoxidation would involve vinyl free radicals which are known to isomerize readily, whereas the reaction with lithium *tert*-butyl peroxide was of a different type.

Encouraged by what might very well have been an early example of the reaction under discussion, applied to alkyl carbanions, we started to investigate the oxidizing properties of hydroperoxide salts.

Aryl carbanions

These are known to autoxidize readily into phenoxides (for a review see [10]). The reaction with 2-*tert*-butylperoxy-1,3,2-dioxaborolane [11] has recently been described.

In view of the ready metallation of aromatic rings in the position *ortho* to so-called directing groups [12], the oxidation of such aryllithium derivatives was tried. This conversion is usually carried out through the boronate esters [13, 14].

Other oxidizing agents are capable of converting aryl anions into phenol derivatives, eg, bis(trimethylsilyl) peroxide [15], the molybdenum complex MoOPh [16], and nitrobenzene [17a-c].

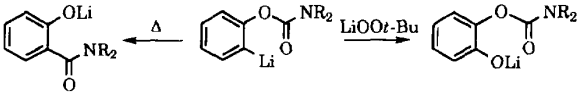
The reaction of polymethoxylated benzene rings with lithium *tert*-butyl peroxide itself has previously been performed in the synthesis of natural products with yields of 67 [18] and 17% [19].

Our first experiments were carried out with resorcinol dimethyl ether. It soon turned out that the conversion into pyrogallol 1,3-dimethyl ether indeed took place. *n*-BuLi (1 equiv) was used to convert the hydroperoxide into its salt, and the aromatic compound was metallated in another flask with the same base at the same temperature (−78 °C). A slight excess (1.2–1.5 equiv but no more) proved advantageous. Mixing the solutions via a cannula and raising the temperature to 0 °C led to the formation of the desired dimethoxyphenol in about 60% yield (see table I). The boronate technique gave 48% [20]. Conversely, the boronate technique was more efficient in the case of *tert*-butyl phenyl sulfone [12].

When *N*,*N*-diisopropylbenzamide was metallated with *n*-BuLi (1.2 equiv) and treated with a solution of LiOO*t*-Bu and 1 equiv *n*-BuLi for 2 h, the *ortho*-hydroxylated amide was obtained in 70% yield; this was raised to 80% when the metallation was performed with *sec*-BuLi and 1.2 equiv of LiOO*t*-Bu was used for 3.5 h. The autoxidation gave 37% [21], and the boronate route gave 56% [13b].

Similarly *N*,*N*-diethyl-2,4,5-trimethoxybenzamide was hydroxylated in 69% yield, whereas the autoxidation gave 52% [21].

It is known [22] that phenyl *N*,*N*-diethylcarbamate is easily metallated in the *ortho* position but the anion rearranges to *N*,*N*-diethylsalicylamide if the temperature is allowed to rise. Treatment of the carbamate with 1.1 equiv *sec*-BuLi and 1 equiv of LiOO*t*-Bu at 0 °C for 2 h gave the *ortho*-hydroxylated carbamate in 61% yield but also about 10% salicylamide and 30% starting carbamate. Lowering the temperature to −40 °C gave similar results; at −78 °C, the conversion was much smaller and the ratio desired/undesired reaction was only slightly improved.



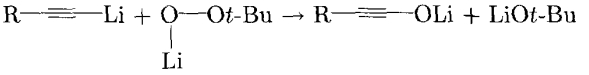
The corresponding *N*,*N*-diisopropylcarbamate, however, could be metallated in THF at 0 °C with *sec*-BuLi (preferably 1.9 equiv) without any rearrangement. Oxidation with LiOO*t*-Bu (1 equiv) gave the hydroxylated carbamate in 80% yield. In ether, however, a considerable amount of rearrangement was observed.

Acetylides

It is known that lithium acetylides do not react with dioxygen [7a] or 2-*tert*-butyl-1,3,2-dioxaborolane [11]. The reaction with bis(trimethylsilyl) peroxide takes place at the silicon atom and not at oxygen as do other organometallics [23].

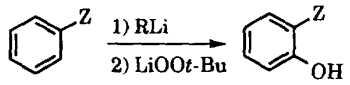
Alkynes are notoriously less readily oxidized than alkenes. They can, however, be converted by peroxomolybdenum or peroxotungsten complexes with mercuric cocatalysts into 1,2-dicarbonyl compounds or carboxylic acids (with cleavage of the triple bond) [24].

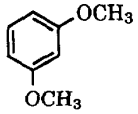
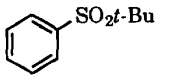
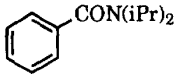
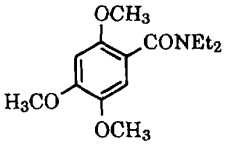
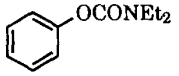
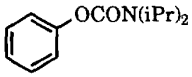
Terminal acetylenes have been converted into ynol carboxylates, sulfonates or phosphates by reaction with trivalent iodine derivatives [25]. The reaction under consideration with lithium *tert*-butyl peroxide would give lithium ynolates.



Although they have not been made in this way, ynolates are known. Ynols have been detected as transient intermediates [26] and calculations have been performed [27]. Ynolates salts were first prepared

Table I. Hydroxylation of aromatic compounds with LiOO*t*-Bu.



	Base[a]	*Equiv*	*Yield*	*Starting material*
	*n*-BuLi	1.2	61	38
	*n*-BuLi[b]	1.2	47	37
	*sec*-BuLi	1.1	80[c]	20
	*sec*-BuLi/ TMEDA	1.2	69	30
	*sec*-BuLi	1.1	60	30[d]
	*sec*-BuLi	1.9	80	14

[a] Type of base used for aromatic deprotonation. [b] Anion stirred at room temperature for 30 min before addition of lithiated peroxide. [c] 1.2 equiv of peroxide used, 3.5 h total reaction time. [d] *N*,*N*-Diethylsalicylamide isolated (10%).

by base-promoted opening of 3,4-diphenylisoxazoles [28]. A similar reaction of dihydrofuran has been described [29]. Ynol tosylates are formed in the oxidation of alkynes with higher valent iodine compounds; they can be converted by methyllithium into ynolates [30]. Trimethylsilylketene has been metallated to give lithium 2-(trimethylsilyl)ethyn-1-olate [31]. A convenient general way is the reaction of α-bromoketones with *tert*-BuLi [32], or reaction of esters with dibromomethyllithium and *n*-BuLi [33].

$$PhCOCH_2Br \rightarrow PhC(OLi)=CHBr \rightarrow PhC(OLi)=CLi-Br \rightarrow Ph-\equiv-OLi$$

$$PhCOOEt + LiCHBr_2 \rightarrow PhC(OLi)=CBr_2 \rightarrow PhC(OLi)=CBrLi \text{ etc}$$

Ynolates display anionic behavior with electrophiles through the oxygen or more frequently the carbon atom [28, 34].

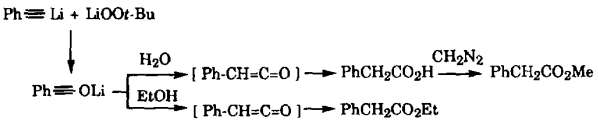
$$R-\equiv-O^- \longleftrightarrow R-C=C=O$$

Silylation takes place first at oxygen; the trimethylsilyl residue then migrates to the carbon atom [35]. Higher silyl residues give more stable compounds.

$$R-\equiv-OLi + RR'R''SiCl \rightarrow R-\equiv-OSiRR'R''$$

Silylynolethers [36], like alkoxyacetylenes, are valuable reagents; the [2+2] cycloaddition leads to cyclobutenones, and eventually to phenol derivatives [37] or to (*E*)-trisubstituted alkenes [38]. They would be readily available through the reaction under discussion between lithium acetylides and lithium *tert*-butyl peroxide. The hydrolysis is extremely easy, leading to the carboxylic acid derivatives.

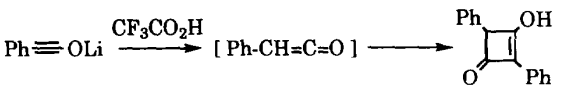
Phenylacetylene and *tert*-butyl hydroperoxide were metallated with *n*-BuLi (1 equiv each) and the solutions mixed at 0 °C. After 2 h, hydrolysis and treatment with diazomethane gave a mixture of methyl phenylacetate (6%), *tert*-butyl phenylacetate (21%) and *n*-butyl phenylacetate (17%) showing that the conversion into the ynolate had probably taken place. Hydrolysis would have given phenylketene, and this would react with the available alcohols.



The *n*-butyl ester results from some oxidation of butyllithium. When the hydrolysis was performed with ethanol, ethyl phenylacetate was the only ester isolated. Some unchanged phenylacetylene was recovered (16%). Another product was found in the aqueous phase after acidification and methylation with diazomethane. The mass (250) pointed to a dimer of phenylketene. Ketenes can dimerize to give enol β-lactones or cyclobutane-1,3-dione derivatives [39].

In fact, dehydrohalogenation of phenylacetyl chloride with triethylamine [40] gave, after treatment with diazomethane, an authentic sample of 3-methoxy-2,4-diphenyl-2-cyclobuten-1-one which proved to be identical to the byproduct of the above oxidation. Similarly, an analogous product formed in the oxidation of 1-octyne proved identical with an authentic sample of 2,4-dihexyl-3-methoxy-2-cyclobuten-1-one prepared by pyrolysis of 1-ethoxy-1-octyne according to the literature [41].

These dimers could be formed by dimerization of the ketenes produced in the hydrolysis but also perhaps by C-acylation of the ynolate by the ketene. When the oxidation mixture was quenched with trifluoroacetic acid at 0 °C, the diphenylhydroxycyclobutenone was obtained in 80% yield.

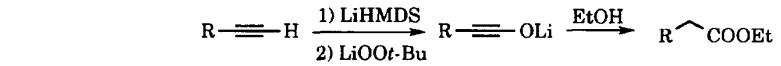


On the other hand, ethanolysis at −78 °C gave ethyl phenylacetate in 77% yield and ethyl octanoate in 86%

yield (see table II). It was found that the best results were obtained when lithium hexamethyldisilazamide (LiHMDS) (20% excess) was used for the metallations. Use of the corresponding sodium or potassium bases gave inferior results. *tert*-Butylacetylene could also be oxidized into ethyl *tert*-butylacetate in 85% yield with either lithium diisopropylamine (LDA) or LiHMDS as bases.

Thus, the conversion of alkynes into ynolates has been proved possible. These can then be converted into aldehydes (by semihydrogenation of the silyl ethers and hydrolysis) or carboxylic esters. It should be noted that this amounts to hydration of the triple bond in the anti-Markovnikov direction followed by oxidation.

Table II. Oxidation of 1-alkynes to ethyl carboxylates.



R	*Equivalents of base*[a]	*Ester yield (%)*
Ph	1.2	77
C_6H_{13}	1.2	84
*t*Bu	1.5	86

[a] Used for alkyne deprotonation.

Carboxylic acid dianions

The introduction of an oxygen atom in the α-position to a carbonyl or a carboxylic acid derivative is a very important step, and a variety of ways are known to achieve this conversion [42a]. Several solutions to this problem have been proposed, such as autoxidation by air or dioxygen [42b]. Activated carbon has also been recommended [43]. Titanium enolates have also been autoxidized [44]. Other reagents used include benzoyl peroxide [45a], dibenzyl peroxydicarbonate [45c], Mimoun's complex (MoOPh) [16, 46–48], sulfonyloxaziridines [49, 52], bis(trimethylsilyl) peroxide [15, 50, 51], ceric ammonium nitrate (CAN) [53], iodosylbenzoic acid [54], [bis(trifluoroacetoxy)iodo]benzene [55], thallium tosylate [56], and dioxirane [57]. Very recently, titanium enolates have been oxidized with lithium *tert*-butyl hydroperoxide [58]. Oxidation of silylenolethers or enamines, prepared from ketones, affords the corresponding keto-alcohols [59].

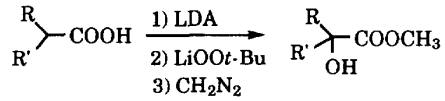
It was noted above that vinyllithium compounds could be oxidized to give enolate salts with lithium *tert*-butyl peroxide [9], and so these were not expected to be oxidized very readily under the same conditions. Our first attempts to oxidize enolate-type carbanions therefore used carboxylic acid dianions, which were expected to be more reactive [51].

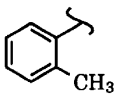
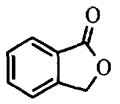
Phenylacetic acid dianion was generated with LDA [60] at 0 °C and treated with a solution of lithium *tert*-butyl hydroperoxide, prepared by means of butyllithium, LDA or LiHMDS in THF.

In these and other examples, it often proved advantageous to use the latter, apparently less prone to side reactions. After completion of the reaction, hydrolysis and treatment with diazomethane indeed gave methyl α-hydroxyesters which were analyzed by GLC. Methyl mandelate was obtained in a yield of 91%. Bis(trimethylsilyl) peroxide had given 53% [9b], whereas dioxygen oxidation had given 89% of a mixture of the α-hydroxy and α-hydroperoxy derivatives [61]. The other results reported in table III show that various carboxylic dianions can be hydroxylated in high yields, even if in some cases a slight excess of base was required. This method compares favorably with other oxidizing agents [9b, 61].

o-Toluic acid can also be metallated with LDA to give a dianion [62]. This was converted by LiOO*t*-Bu (1 equiv) for 2 h at 0 °C, acidic work-up, and action of diazomethane into phthalide (60%); 30% of methyl toluate was recovered. The yield could be increased to about 80% when a 20% excess of LDA was used. This reaction thus appears to be general for carboxylic acids of various types.

Table III. α-Hydroxylation of carboxylic acid dianions with LiOO*t*-Bu.



R	*R'*	*LDA*[a]	*Base*[b]	*Equiv*	*Yield (%)*	*SM*
Ph	H	2	LiHMDS	1	91	5
Ph	Ph	2	LiHMDS	1	88	12
Ph	Et	2.4	LiHMDS	1.2	80	10
C_6H_{13}	H	2	LiHMDS	1.2	77	16
$-(CH_2)_6-$		2.4	LDA	1.2	79	20
C_4H_9	C_2H_5	2.5[c]	LDA	1.2	82	10
		3 eq	LDA	1.5	81	11
						

[a] Equivalents used for acid deprotonation. [b] Base used for hydroperoxide deprotonation. [c] Anion stirred at 45 °C for 2 h before addition of the lithiated peroxide.

Carboxylic acid amides

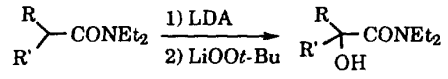
LDA (1.2 equiv) proved better than butyllithium for the metallation of *N*,*N*-diethylphenylacetamide. Treatment with LiOO*t*-Bu gave the α-hydroxyamide in 68% yield, 31% starting amide being recovered. A one-pot technique proved more convenient as illustrated in the oxidation of *N*,*N*-diethyloctanamide which was converted to the α-hydroxyamide in 70% yield.

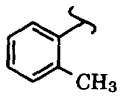
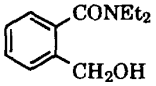
N,*N*-Diethyl-*o*-toluamide was treated with 1.1 equiv *sec*-BuLi followed by LiOO*t*-Bu prepared with excess *n*-BuLi (1.4 equiv), *N*,*N*-diethyl-2-(hydroxymethyl)-benzamide was obtained in 80% yield (in this case the autoxidation is reported to give 49% [21]).

Carboxylic esters

The esters were converted into their lithium enolates with LDA in the usual way [63], but did not at first

Table IV. α-Hydroxylation of carboxylic amide enolates with LiOO*t*-Bu.



R	*R'*	*Base*[a]	*Base*[b]	*Yield (%)*	*SM*
Ph	H	LDA 1.2	LDA	68[c]	31
C_6H_{13}	H	LDA 2.7[d]		70	24
		*sec*-BuLi/ TMEDA[e] 1.1	*n*-BuLi	80	13
					

[a] Type and equivalents of base used for amide deprotonation. [b] Base used to metallate the hydroperoxide in the two-pot procedure. [c] Prepared using the same technique as for acid dianions, amide deprotonation time: 40 min at 0 °C. [d] One-pot procedure for the oxidation of amides: 1.05 equiv of *t*-BuOOH; total equiv of base calculated as 1.3 times the total molar quantity of (moles amide + moles hydroperoxide). [e] Deprotonation at −78 °C for 45 min.

give good yields of α-hydroxyesters when treated under the conditions defined above. In the case of an ethyl or methyl ester, Claisen condensation of the starting material was the major product of the reaction in spite of the excess base used for deprotonation of both the ester and the *tert*-butyl hydroperoxide. In an attempt to minimize these problems, the *tert*-butyl ester derivatives were used in the reaction, providing the hydroxy esters in excellent to good yields.

The one-pot technique was also applied to the esters, and the best yields were obtained in the presence of a twofold excess of hydroperoxide (see table V). Hydroxylation at a secondary carbon center was shown to be possible in an aliphatic system in the case of *tert*-butyl octanoate, where the alcohol was synthesized in 80% yield. The oxidation of *tert*-butyl 10-undecenoate under the standard conditions gave the hydroxy ester in excellent yield without any evidence of epoxidation of the terminal double bond, even in the presence of excess peroxide.

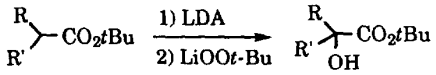
Hydroxylation of a tertiary center gave the tertiary alcohols in fair yields, the oxidation of the corresponding acids giving the hydroxylated product in better yield.

Experimental section

^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker AC 250; chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform (7.27 ppm). Coupling constants (J) are given in hertz (Hz). Multiplicities are recorded as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). ^{13}C NMR spectra were recorded on a Bruker AC 250 spectrometer. Mass spectra were recorded on a Nermag R10-10B spectrometer. The following abbreviations are used: CI and NH_3 for ammonia desorption chemical ionization. Microanalyses were performed by the Service de Microanalyses of Université Pierre-et-Marie-Curie. Thin-layer chromatography was performed on precoated plates of silica gel 60F 254 (Merck, Art 7735). Flash chromatography was performed on silica-gel Merck 60 230-400 mesh. Solvents were distilled as follows: tetrahydrofuran (THF) from sodium/benzophenone; dichloromethane from calcium hydride; and petroleum ether from phosphorus pentoxide.

Commercial products were purified or dried before use.

Table V. α-Hydroxylation of carboxylic ester enolates with LiOO*t*-Bu (2 equiv).



R	*R'*	*LDA*[a]	*Yield (%)*	*SM*
C_6H_{13}	H	3.4	80	Traces
$H_2C{=}CHC_7H_{14}$	H	3.4	87	Traces
$PhCH_2CH_2$	H	3.4	82	3%
Ph	C_2H_5	3.4	60	25
C_4H_9	C_2H_5	3.4	56	18

[a] Total equiv of base calculated as 1.13 times the total molar quantity of (moles ester + moles hydroperoxide).

*Aromatic compounds (table I)**

• tert-*Butyl phenyl sulfone: [4170-72-3].*
Prepared according to reference [64].

• N,N-*diisopropylbenzamide: [20383-28-2]*
Mp 69–70 °C; lit 69–71 °C [65].

• N,N-*diethyl-2,4,5-trimethoxybenzamide: [105518-12-5]*
Mp 73–74 °C; lit 74 °C [66].
^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.02 (t, J = 7.5 Hz, 3H), 1.21 (t, J = 7.5 Hz, 3H), 3.2 (q, J = 7.5 Hz, 2H), 3.55 (m, 2H), 3.8 (s, 3H), 3.84 (s, 3H), 3.9 (s, 3H), 6.5 (s, 1H), 6.76 (s, 1H).
^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.53, 13.69, 38.55, 42.52, 55.73, 56.13, 97.25, 110.93, 117.76, 142.81, 149.26, 149.72, 168.07.
MS (CI, NH_3): 268 (M + 1).

• *Phenyl* N,N-*diethylcarbamate: [65009-00-9]*
$Bp_{/15}$ 105–110 °C [67].
^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.12–1.35 (m, 6H), 3.32–3.51 (m, 4H), 6.71–7.40 (m, 5H).
^{13}C NMR ($CDCl_3$, 63 MHz): δ 13.41, 14.17, 42.02, 121.74, 125.01, 129.16, 151.52, 154.23.
MS (CI, NH_3): 211 (M + 18), 194 (M + 1).

• *Phenyl* N,N-*diisopropylcarbamate: [142075-48-7]*
$Bp_{/10}$ 120–125 °C.
^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.21–1.44 (m, 12H), 3.87–4.84 (m, 2H), 7.08–7.42 (m, 5H).
^{13}C NMR ($CDCl_3$, 63 MHz): δ 20–22.5, 45.5–47.5, 121.80, 124.89, 129.15, 151.37, 153.83.
MS (CI, NH_3): 238 (M + 18), 222 (M + 1).

* The numbers in brackets are *Chemical Abstract* registry numbers.

General procedure for the hydroxylation of aromatic compounds with LiOOt-Bu

To a stirred solution of 1,3-dimethoxybenzene (0.132 mL, 0.139 g, 1 mmol) in THF (2 mL) under argon at −78 °C, was added dropwise, a solution of *n*-BuLi (1.6 M in hexane, 0.754 mL, 1.2 mmol). In a separate round-bottomed flask, a solution of *n*-BuLi (1.6 M in hexane, 0.625 mL, 1 mmol) was added to a solution of *tert*-butyl hydroperoxide (3.7 M in toluene, 0.270 mL, 1 mmol) in THF (2 mL) at −78 °C under argon. After stirring for 30 min, the hydroperoxide anion solution was added by cannula to that of the aromatic anion, and stirring was continued for 2 h at 0 °C. The reaction was quenched by pouring into a cold 10% HCl solution. The aqueous layer was extracted with CH_2Cl_2, and the organic layer dried over $MgSO_4$. The crude reaction mixture was purified by flash chromatography.

• tert-*Butyl 2-hydroxyphenyl sulfone [2(*tert*-butylsulfonyl)phenol]: [29634-35-3]*

Mp 113°C; lit 112–113 °C [13c].

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.39 (s, 9H), 6.98–7.3 (m, 2H), 9.24 (s, 1H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 22.98, 61.79, 117.01, 118.76, 119.88, 131.33, 136.49, 157.66.

MS (CI, NH_3): 215 (M + 1).

• N,N-*Diisopropyl-2-hydroxybenzamide: [82860-53-5]*

^{1}H NMR and ^{13}C NMR spectra in agreement with those in reference [68].

• N,N-*Diethyl-2-hydroxy-3,4,6-trimethoxybenzamide: [106114-62-9]*

Mp 142 °C; lit 142 °C [69].

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.08–1.24 (m, 6H), 2.06 (s, 1H), 3.15–3.52 (m, 4H), 3.78 (s, 3H), 3.80 (s, 3H), 3.88 (s, 3H), 6.05 (s, 1H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 13.35, 55.86, 55.90, 61.04, 88.56, 106.46, 130.38, 147.60, 152.35, 153.14, 166.04.

MS (CI, NH_3): 284 (M + 1).

• *2-Hydroxyphenyl* N,N-*diethylcarbamate*

Mp 126 °C.

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.22 (t, J = 7.1 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H), 3.42 (q, J = 7.1 Hz, 2H), 3.48 (q, J = 7.1 Hz, 2H), 6.85–7.3 (m, 4H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 13.17, 14.03, 42.28, 42.53, 119.09, 120.54, 122.02, 126.47, 140.11, 147.96, 154.74.

MS (CI, NH_3): 227 (M + 18), 210 (M + 1).

• *2-Hydroxyphenyl* N,N-*diisopropylcarbamate*

Mp 154 °C.

^{1}H NMR ($CDCl_3$, 250 MHz), δ: 1.12–1.45 (m, 12H); 3.95–4.17 (m, 2H); 6.80–7.30 (m, 4H).

^{13}C NMR ($CDCl_3$, 63 MHz), δ: 20.30, 21.43, 46.61, 47.29, 119.48, 120.72, 121.90, 126.48, 140.29, 147.97, 154.26.

Anal calc for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07. Found: C, 65.78; H, 8.10.

Alkynes (table II)

• tert-*Butylacetylene (3,3-dimethyl-1-butyne) [917-92-0]*

Prepared according to reference [70].

Bp 37 °C; lit 36.4–37.8 °C [71].

• *Ethyl 3,3-dimethylbutanoate [5129-40-8]*

$Bp_{/10}$ 30–35 °C.

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.04 (s, 9H), 1.27 (t, J = 7.1 Hz, 3H), 2.20 (s, 2H), 4.12 (q, J = 7.1 Hz, 2H).

MS (CI, NH_3): 162 (M + 18), 145 (M + 1).

General procedure for the oxidation of 1-alkynes to ethyl carboxylates with LiOOt-Bu

To a stirred solution of lithium 1,1,1,3,3,3-hexamethyldisilazamide (1.0 M in THF, 1.2 mL, 1.2 mmol) in THF (2 mL) at −78 °C under argon was added phenylacetylene (0.111 mL, 0.102 g, 1 mmol) in THF (2 mL), and stirring was continued at room temperature for 30 min, followed by cooling to 0 °C.

In another round-bottomed flask at −78 °C under argon, *n*-BuLi (1.6 M in hexane, 0.625 mL, 1 mmol) was added to *tert*-butyl hydroperoxide (3.7 M in toluene, 0.270 mL, 1 mmol) in THF (2 mL). After stirring for 30 min, this solution was added by cannula to that of the anion, and stirring was continued for 2 h at 0 °C. The reaction mixture was quenched by addition of ethanol (2 mL) at 0 °C, followed by a saturated sodium hydrogen carbonate solution (10 mL). The aqueous layer was extracted with pentane, and the combined organic layers were dried over $MgSO_4$. The crude product was purified by flash chromatography.

• *Dimers: 2,4-diphenyl-3-methoxy-2-cyclobuten-1-one*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 4.0 (s, 3H), 4.87 (s, 1H), 7.2–7.4 (m, 10H).

MS (CI, NH_3): 268 (M + 18), 251 (M + 1).

Anal calc for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.57; H, 5.65.

• *2,4-Dihexyl-3-ethoxy-2-cyclobuten-1-one*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.90 (t, J = 6.7 Hz, 6H), 1.43 (t, J = 7.1 Hz, 3H), 1.2–1.7 (m, 18H), 2.07 (td, J_1 = 8.2 Hz, J_2 = 1.3 Hz, 2H), 3.37 (tt, J_1 = 5.6 Hz, J_2 = 1.3 Hz, 1H), 4.33 (qd, J_1 = 7.1 Hz, J_2 = 1.8 Hz, 2H).

MS (CI, NH_3): 298 (M + 18), 281 (M + 1).

• *2,4-Dihexyl-3-methoxy-2-cyclobuten-1-one*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.88 (t, J = 6.7 Hz, 6H), 1.20–1.39 (m, 14H), 1.4–1.5 (m, 2H), 1.52–1.65 (m, 2H), 2.15 (td, J_1 = 8.1 Hz, J_2 = 1.3 Hz, 2H), 3.80 (dt, J_1 = 5.8 Hz, J_2 = 1.5 Hz, 1H), 4.17 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.94, 22.35, 22.46, 22.48, 26.45, 28.52, 29.01, 29.29, 31.43, 31.56, 58.62, 59.16, 121.32, 179.87, 190.56.

Anal calc for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.65; H, 11.34.

Carboxylic acid dianions (table III)

General procedure for the α-hydroxylation of acid dianions with LiOOt-Bu

To a stirred solution of diisopropylamine (0.280 mL, 2 mmol) in THF (2 mL) at 0 °C under argon was added *n*-BuLi (1.6 M in hexane, 1.28 mL, 2 mmol). After 10 min at 0 °C, a solution of the acid (1 mmol) in THF (2 mL) was added, and stirring was continued for 30 min at 25 °C.

In another round-bottomed flask at 0 °C under argon, LDA (1 mmol) was prepared as above. After 10 min at

0 °C, the solution was cooled to −78 °C and *tert*-butyl hydroperoxide (3.7 M in toluene, 0.270 mL, 1 mmol) in THF (2 mL) was added. The reaction was stirred for 30 min at −78 °C. The metallated peroxide was then added to the dianion at 0 °C by cannula, and stirring was continued for 2 h at 0 °C. The reaction was quenched by pouring the mixture into a cold 10% HCl solution. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$. Treatment of the crude reaction mixture with diazomethane gave the methyl ester which was purified by flash chromatography.

• *Methyl 2-phenyl-2-hydroxybutanoate [76142-48-8]*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.94 (t, J = 7.4 Hz, 3H), 2–2.32 (m, 2H), 3.80 (s, 3H), 7.25–7.64 (m, 5H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 8.01, 32.60, 53.18, 78.74, 125.52, 127.63, 128.18, 141.67, 175.79.

MS (CI, NH_3): 212 (M + 18), 195 (M + 1).

• *Methyl 2-hydroxyoctanoate [73634-76-1]*

^{1}H and ^{13}C NMR in agreement with those of an authentic sample prepared by treatment of 2-hydroxyoctanoic acid with diazomethane.

• *Methyl 1-hydroxycyclohexanecarboxylate [6149-50-4]*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.2–1.4 (m, 2H), 1.55–1.87 (m, 8H), 2.84 (s, 1H), 3.78 (s, 3H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 21.07, 25.13, 34.63, 52.53, 73.58, 176.50.

MS (CI, NH_3): 176 (M + 18), 159 (M + 1).

• *Methyl 2-ethyl-2-hydroxyhexanoate*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.64 (t, J = 7.5 Hz, 3H), 0.68 (t, J = 7.1 Hz, 3H), 0.85 (m, 1H), 1.1 (m, 2H), 1.25 (m, 2H), 1.5 (m, 4H), 2.9 (s, 1H), 3.58 (s, 3H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 7.88, 13.96, 22.83, 25.81, 32.28, 38.86, 52.59, 78.04, 177.4.

MS (CI, NH_3): 192 (M + 18), 175 (M + 1).

Anal calc for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 61.96; H, 10.37.

Carboxylic amides (table IV)

• N,N-*Diethylphenylacetamide [2431-96-1]*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.10 (t, J = 7.2 Hz, 3H), 1.14 (t, J = 7.2 Hz, 3H), 3.10 (q, J = 7.2 Hz, 2H), 3.40 (q, J = 7.2 Hz, 2H), 3.71 (s, 2H), 7.2–7.37 (m, 5H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.68, 14.14, 40.07, 40.85, 42.29, 126.57, 128.54, 128.60, 135.48, 170.04.

MS (CI, NH_3): 209 (M + 18), 192 (M + 1).

• N,N-*Diethyloctanamide [996-97-4]*

This compound was prepared as described above for *N*,*N*-diethylphenylacetamide.

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.85 (t, J = 6.8 Hz, 3H), 1.0–1.2 (m, 6H), 1.25 (m, 8H), 1.61 (m, 2H), 2.26 (t, J = 7.3 Hz, 2H), 3.31 (m, 4H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 13.04, 14.0, 14.32, 22.55, 25.44, 29.08, 29.42, 31.66, 33.10, 39.92, 41.88, 172.25.

• N,N-*Diethyl-2-methylbenzamide [2728-04-3]*

This compound was prepared as described above for *N*,*N*-diethylphenylacetamide.

$Bp_{/1}$ 80–84 °C.

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.0 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H), 2.26 (s, 3H), 3.10 (q, J = 7.1 Hz, 2H), 3.3–3.85 (m, 2H), 7.1–7.28 (m, 4H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.80, 13.91, 18.71, 38.57, 42.5, 125.36, 125.72, 128.46, 130.23, 133.71, 137.08, 170.08.

MS (CI, NH_3): 209 (M + 18), 192 (M + 1).

General procedure for the α-hydroxylation of amides with LiOOt-Bu

To cooled THF (0 °C) under argon was added diisopropylamine (1.02 mL, 0.736 g, 7.27 mmol), followed by *n*-BuLi (2.5 M in hexane, 2.7 mL, 6.78 mmol). The reaction was stirred for 15 min at 0 °C. *N*,*N*-Diethyloctanamide (0.5 g, 2.5 mmol) in 1 mL of THF was then added. Stirring was continued at 0 °C for 20 min, then *tert*-butyl hydroperoxide (5.11 M in toluene, 0.515 mL, 2.6 mmol) was slowly added. After 2 h at 25 °C, the reaction was quenched by pouring into a cold saturated ammonium chloride solution. The aqueous layer was extracted with ethyl acetate, and the combined organic layers dried over $MgSO_4$, and concentrated to give a clear oil. The product was purified by flash chromatography (60% petroleum ether/30% diethyl ether/10% CH_2Cl_2).

• N,N-*Diethyl-2-(2-hydroxyphenyl)acetamide [65197-96-8]*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.79 (t, J = 7.1 Hz, 3H), 1.13 (t, J = 7.1 Hz, 3H), 2.97–3.2 (m, 2H), 3.27–3.59 (m, 2H), 4.86 (d, J = 6.3 Hz, 1H), 5.15 (d, J = 6.3 Hz, 1H), 7.23–7.4 (m, 5H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.52, 12.96, 40.65, 40.88, 71.48, 127.42, 128.36, 128.97, 139.79, 171.35.

MS (CI, NH_3): 225 (M + 18), 208 (M + 1).

• N,N-*Diethyl-2-hydroxyoctanamide*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.86 (m, 3H), 1.0–1.65 (m, 16H), 3.25 (m, 3H), 3.55 (m, 1H), 3.72 (d, J = 7.7 Hz, 1H), 4.25 (m, 1H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.77, 13.99, 14.04, 22.50, 24.86, 29.03, 31.65, 35.42, 40.13, 40.82, 67.94, 173.68.

MS (CI, NH_3): 216 (M + 1).

Anal calc for $C_{12}H_{25}NO_2$: C, 66.93; H, 11.70. Found: C, 66.94; H, 11.80.

• N,N-*Diethyl-2-(hydroxymethyl)benzamide [103258-38-4]*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.07 (t, J = 7.1 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H), 3.21 (q, J = 7.1 Hz, 2H), 3.57 (q, J = 7.1 Hz, 2H), 3.8 (s broad, 1H), 4.48 (s, 2H), 7.17–7.46 (m, 4H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.71, 13.99, 39.24, 43.33, 63.63, 125.69, 127.36, 129.44, 129.61, 135.97, 138.53, 171.27.

MS (CI, NH_3): 225 (M + 18), 208 (M + 1).

Carboxylic esters (table V)

• tert-*Butyl octanoate [5457-66-9]*

Prepared according to reference [72].

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.88 (t, J = 6.7 Hz, 3H), 1.28 (m, 10H), 1.44 (s, 9H), 2.2 (t, J = 7.4 Hz, 2H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 13.99, 22.54, 25.06, 28.04, 28.91, 28.99, 31.63, 35.56, 79.77, 173.27.

• tert-*Butyl 10-undecenoate [93757-41-6]*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.26 (s broad, 10H), 1.43 (s broad, 9H), 1.55 (m, 2H), 2.02 (m, 2H), 2.2 (t, J = 7 Hz, 2H), 4.82–5.5 (m, 2H), 5.8 (m, 1H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 25.04, 28.06, 28.84, 29.01, 29.19, 29.25, 33.75, 35.54, 79.78, 114.08, 139.09, 173.23.

MS (CI, NH_3): 258 (M + 18), 241 (M + 1).

• tert-*Butyl 4-phenylbutanoate [16537-11-4]*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.38 (s, 9H), 1.84 (m, 2H), 2.1 (t, J = 7.4 Hz, 2H), 2.3 (t, J = 7.4 Hz, 2H), 7.09 (m, 5H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 26.74, 28.08, 34.89, 35.10, 80, 125.86, 128.31, 128.46, 141.61, 172.86.

• tert-*Butyl 2-phenylbutanoate [41890-58-8]*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.91 (t, J = 7.5 Hz, 3H), 1.42 (s, 9H), 1.79 (m, 1H), 2.08 (m, 1H), 3.37 (t, J = 7.9 Hz, 1H), 7.3 (m, 5H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.14, 26.77, 27.92, 54.49, 80.34, 126.81, 127.81, 128.33, 139.71, 173.25.

• tert-*Butyl 2-ethylhexanoate [71648-27-6]*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.88 (m, 6H), 1.15–1.65 (m, 17H), 2.11 (m, 1H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 11.76, 13.93, 22.61, 25.65, 28.08, 29.54, 31.94, 48.14, 79.65, 175.82.

MS (CI, NH_3): 218 (M + 18), 201 (M + 1).

General procedure for the α-hydroxylation of esters with LiOOt-Bu

To cooled THF (0 °C) under argon was added diisopropylamine (0.984 mL, 0.710 g, 7.02 mmol), followed by *n*-BuLi (2.5 M in hexane, 2.65 mL, 6.6 mmol). The reaction was stirred for 10 min at 0 °C, then cooled to −78 °C. *tert*-Butyl 10-undecenoate (0.5 g, 1.95 mmol) in THF (1 mL) was then added. Stirring was continued at −78 °C for 40 min, then *tert*-butyl hydroperoxide (5.11 M in toluene, 0.763 mL, 3.9 mmol) was slowly added. After 2 h at 0 °C, the reaction was quenched by pouring into a cold saturated ammonium chloride solution. The aqueous layer was extracted with ethyl acetate, the organic layer dried over $MgSO_4$, and concentrated to give a yellow oil. The product was purified by column chromatography (95% petroleum ether/5% ethyl acetate).

• tert-*Butyl 2-hydroxyoctanoate*

Hydrolyzed into the hydroxyacid, ^{1}H NMR and ^{13}C NMR in agreement with a commercially available sample.

• tert-*Butyl 2-hydroxy-10-undecenoate*

Hydrolyzed into the hydroxyacid [34456-29-6].

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.1 (m, 10H), 1.6 (m, 2H), 1.85 (m, 2H), 4.1 (m, 1H), 4.78 (m, 2H), 5.62 (tdd, J_1 = 17 Hz, J_2 = 10.2 Hz, J_3 = 6.6 Hz, 1H), 6.62 (s large, 1H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 24.60, 28.70, 28.84, 29.02, 29.09, 33.59, 33.94, 70.13, 114.03, 138.96, 173.92.

MS (CI, NH_3): 218 (M + 18).

• tert-*Butyl 2-hydroxy-4-phenylbutanoate [138276-04-7]*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.51 (s, 9H), 1.8–2.2 (m, 2H), 2.78 (m, 2H), 2.95 (d, J = 5.2 Hz, 1H), 4.11 (m, 1H), 7.25 (m, 5H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 28.10, 31.17, 36.35, 70.02, 82.59, 126.03, 128.49, 128.57, 141.56, 174.55.

• tert-*Butyl 2-hydroxy-2-phenylbutanoate*

Hydrolyzed into the hydroxyacid [35468-69-0].

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.87 (t, J = 7.3 Hz, 3H), 1.95 (m, 1H), 2.2 (m, 1H), 7.26 (m, 3H), 7.62 (d, J = 7.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 8.44, 33.58, 79.20, 126.57, 128.17, 128.83, 144, 206.25.

MS (CI, NH_3): 198 (M + 18).

• tert-*Butyl 2-ethyl-2-hydroxyhexanoate*

^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.85 (q, J = 7.1 Hz, 6H), 1.00–1.81 (m, 15H), 3.29, (s, 1H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ 7.66, 13.92, 22.79, 25.58, 27.90, 32.25, 38.79, 77.46, 81.99, 176.05.

MS (CI, NH_3): 234 (M + 18), 217 (M + 1).

Anal calc for $C_{12}H_{24}O_3$: C, 66.63; H, 11.18. Found: C, 66.58; H, 11.16.

Acknowledgments

The support of the CNRS (URA 1686 and 1679) and the Université Pierre-et-Marie-Curie (Paris 6) is gratefully acknowledged. Thanks are also due to the Royal Chemical Society for a postdoctoral fellowship. The Alexander von Humboldt Foundation is to be specially thanked for providing the opportunity for one of us (MJ) to take sabbatical leave at the University of Freiburg.

References

1 a) Hamilton GA, *Prog Bioorg Chem* (1971) 1, 83
b) Sheldon RA, Kochi JK, *Metal-Catalyzed Oxidations of Organic Compounds*, Academic, New York, 1981.

2 a) Köbrich G, *Angew Chem Int Ed Engl* (1972) 11, 473 and references cited therein
b) Villieras J, Rambaud M, Kirschleger B,Tarhouni R, *Bull Soc Chim Fr* (1985) 837
c) Charreau P, Julia M,Verpeaux JN, *J Organomet Chem* (1989) 379, 201
d) Lima C de, Julia M, Verpeaux JN, *Synlett* (1992) 133.

3 a) Ziegler K, Gellert HG, *Liebigs Ann Chem* (1950) 567, 185
b) Normant H, Castro B, *C R Acad Sci Paris* (1964) 259, 830
c) Castro B, *Bull Soc Chim Fr* (1967) 1533.

4 a) Sheverdina NJ, Kosheschkow Z, *J Gen Chem USSR* (1938), 8, 1825
b) Beak P, Kokko BJ, *J Org Chem* (1982) 47, 2822
c) Beak P, Kokko BJ, Basha A, *J Am Chem Soc* (1984) 106, 511
d) Beak P, Meyers AI, *Acc Chem Res* (1986) 19, 356
e) Beak P, Selling GW, *J Org Chem* (1989) 54, 5574
f) Genêt JP, Mallart S, Greck C, Piveteau E, *Tetrahedron Lett* (1991) 32, 2359
g) Greck C, Bischoff L, Girard A, Majicek J, Genêt JP, *Bull Soc Chim Fr* (1994), 131, 429
h) Casarini A, Dembech P, Lazzari D, Marini E, Reginato G, Ricci A, Seconi G, *J Org Chem* (1993) 58, 5620.

5 Wakefield BJ, *The Chemistry of Organolithium Compounds*, Pergamon, Oxford, 1974, p 192.

6 a) Julia M, Pfeuty-Saint Jalmes V, Verpeaux JN, *Synlett* (1993) 233
b) Pfeuty-Saint Jalmes V, Thesis Paris (1993)

c) Chemla F, Julia M, Uguen D, *Bull Soc Chim Fr* (1994), 131, 639
d) Boche G, Bosold F, Lohrenz JCW, *Angew Chem Int Ed Engl* (1994) 1161.

7 a) Walling C, Buckler SA, *J Am Chem Soc* (1955) 77, 6032
b) Maher-Detweiler M, *Methoden der Organischen Chemie* (Houben-Weyl) 4th ed 1952-1988, Vol E13, part 1, p 176
c) Schöllkopf U, *ibid*, 1970, Vol 13/1, p 170
d) Nützel K, *ibid*, 1973, Vol 13/2a, p 234
e) Nützel K, *ibid*, 1973, Vol 13/2a, p 700
f) Nützel K, *ibid*, 1973, Vol 13/2a, p 908
g) Wedemeyer KF, *ibid*, 1976, Vol 6/1c, part 1, p 141
h) Lawesson SO, Yang NC, *J Am Chem Soc* (1959) 81, 4230
i) Wuyts H, *C R Acad Sci, Paris* (1909) 148, 930
j) Wakefield BJ in *Comprehensive Organometallic Chemistry*, Wilkinson G, Stone FGA, Abel EW Eds, Pergamon, Oxford, 1982, Vol 7, p 1 Wakefield BJ, *Organolithium Methods*, Academic, New York, 1988
k) Müller E, Töpel T, *Ber Dtsch Chem Ges* (1939) 72, 273.

8 Warner P, *J Org Chem* (1976) 41, 1459.

9 a) Panek EJ, Whitesides GM, *J Am Chem Soc* (1972), 94, 8768
b) Panek EJ, Kaiser LR, Whitesides GM, *J Am Chem Soc* (1977), 99, 3708
c) Neumann H, Seebach D, *Chem Ber* (1978) 111, 2782.

10 Dudfield PJ in *Comprehensive Organic Synthesis*, Vol 7 p 329, Trost BM, Fleming I, Ley SV Eds, Pergamon, Oxford, 1991.

11 Hoffmann RW, Ditrich K, *Synthesis* (1983) 107.

12 a) Snieckus V, *Chem Rev* (1990) 90, 879
b) Qesnelle C, Iihama T, Aubert T, Perrier H, Snieckus V, *Tetrahedron Lett* (1992) 33, 2625.

13 a) Hawthorne MF, *J Org Chem* (1957) 22, 1001
b) Beak P, Brown RA, *J Org Chem* (1982) 47, 34
c) Iwao M, Ihama T, Mahalanabis KK, Perrier H, Snieckus V, *J Org Chem* (1989) 54, 24.

14 a) Kharash MS, Reinmuth O, *Grignard Reactions of Non-Metallic Substances*, Prentice-Hall, New York, 1954, 1264
b) Parker KA, Koziski KA, *J Org Chem* (1987) 52, 674.

15 a) Taddei M, Ricci A, *Synthesis* (1986) 633
b) Camici L, Ricci A, Taddei M, *Tetrahedron Lett* (1986) 27, 5155.

16 Vedejs E, *J Am Chem Soc* (1974) 96, 5944.

17 a) Buck P, Köbrich G, *Tetrahedron Lett* (1967) 1563
b) Buck P, Köbrich G, *Chem Ber* (1970) 103, 1412
c) Wiriyachitra P, Cava MP, *J Org Chem* (1977) 42, 2274.

18 Nilsson M, Norin T, *Acta Chem Scand* (1963) 17, 1157.

19 a) Kemp MS, Burden RS, Loeffler RST, *J Chem Soc Perkin Trans I* (1983) 2267
b) Cambie RC, Hayward PC, Palmer BD, *Aust J Chem* (1982) 35, 1679.

20 Dang QQ, *Bull Soc Chim Fr* (1973) 767.

21 Parker KA, Koziski KA, *J Org Chem* (1987) 52, 674.

22 Sibi MP, Snieckus V, *J Org Chem* (1983) 48, 1935.

23 Canici L, Dembech P, Ricci A, Seconi G, Taddei M, *Tetrahedron* (1988) 44, 4197.

24 Ballistreri FP, Failla S, Tomaselli GA, *Tetrahedron* (1992) 48, 9999 and references cited therein.

25 a) Stang PJ, *Acc Chem Res* (1991) 24, 304
b) Stang PJ, *Angew Chem Int Ed Engl* (1992) 31, 274.

26 a) Chang Y, Kresge AJ, Hochstrasser R, Wirz J, *J Am Chem Soc* (1989) 111, 2355
b) Chang Y, Kresge AJ, Hochstrasser R, Wirz J, *Angew Chem Int Ed Engl* (1989) 28, 181
c) Von Baar B, Weiske T, TerlouwJK, Schwarz H, *Angew Chem Int Ed Engl* (1986) 25, 282.

27 a) Bouma WJ, Nobes RH, Radom L, Woodward CE, *J Org Chem* (1982) 47, 1869
b) Smith BJ, Radom L, Kresge AJ, *J Am Chem Soc* (1989) 111, 8297
c) Smith BJ, Radom L, *J Am Chem Soc* (1992) 114, 36
d) Wagner BD, Zgierski MZ, Lusztyk J, *J Am Chem Soc* (1994) 116, 6433.

28 Schöllkopf U, Hoppe I, *Liebigs Ann Chem* (1979) 219.

29 Groh BL, Magrum GR, Barton TJ, *J Am Chem Soc* (1987) 109, 7568.

30 Stang PJ, Roberts KA, *J Am Chem Soc* (1986) 108, 7125.

31 Rathke MW, *J Org Chem* (1978) 43, 376.

32 Kowalski CJ, Fields KW, *J Am Chem Soc* (1982) 104, 321.

33 a) Kowalski CJ, Serajul Haque M, Fields KW, *J Am Chem Soc* (1985) 107, 1429
b) Kowalski CJ, *J Org Chem* (1992) 57, 7194.

34 a) Barrett AGM, Quayle P, *J Chem Soc, Perkin Trans I* (1982) 2193
b) Stang PJ, Roberts KA, *J Am Chem Soc* (1986) 108, 7125
c) Zhdankin VV, Stang PJ, *Tetrahedron Lett* (1993) 34, 1461.

35 a) Kowalski CJ, Sankar Lal G, Serajul Haque M, *J Am Chem Soc* (1986) 108, 7127
b) Groh BL, Magrum GR, Barton TJ, *J Am Chem Soc* (1987) 109, 7568.

36 a) Pirrung MC, Hwu JR, *Tetrahedron Lett* (1983) 24, 565
b) Maas G, Brückmann R, *J Org Chem* (1985) 50, 2802.

37 a) Kowalski CJ, Sankar Lal G, *J Am Chem Soc* (1988) 110, 3693
b) Danheiser RL, Cha DD, *Tetrahedron Lett* (1990) 31, 1527
c) Danheiser RL, Brisbois RG, Kowalczyk JJ, Miller RF, *J Am Chem Soc* (1990) 112, 3093
d) Danheiser RL, Nishida A, Savariar S, *Tetrahedron Lett* (1988) 29, 4917.

38 Kowalski CJ, Sakdarat S, *J Org Chem* (1990) 55, 1977.

39 Patai S, *The Chemistry of Ketenes, Allenes, and Related Compounds*, Part I, Wiley, New York, 1980, p 279.

40 Farnum DG, Johnson JR, Hess RE, Marshall TB, Webster B, *J Am Chem Soc* (1965), 87, 5191.

41 Nieuwenhuis J, Arens JF, *Recl Trav Chim Pays Bas* (1958) 77, 761.

42 a) Jones AB in *Comprehensive Organic Synthesis*, Trost BM, Fleming I Eds, Pergamon, Oxford, 1991, Vol 7, p 151
b) Bailey EJ, Barton DHR, Elks J, Templeton, JF, *J Chem Soc* (1962) 1579
c) Baldwin JE, Barton DHR, Sutherland JK, *J Chem Soc* (1964) 3312.

43 Ananda GDS, Cremins PJ, Stoodley RJ, *J Chem Soc, Chem Commun* (1987) 882.

44 Adam W, Metz M, Prechtl, Renz M, *Synthesis* (1994) 563.

45 a) Larsen EH, Lawesson SO, *Organic Synthesis*, Coll Vol V (1973) 379
b) Maume GM, Horning EC, *Tetrahedron Lett* (1969) 343
c) Gore MP, Vederas JC, *J Org Chem* (1986) 51,3700 and references cited therein.

46 a) Mimoun H, Serée de Roch I, Sajus L, *Bull Soc Chim Fr* (1969) 1481

b) Mimoun H, Serée de Roch I, Sajus L, *Tetrahedron* (1970) 26, 37.

47 a) Vedejs E, Telshow JE, *J Org Chem* (1976) 41, 740
b) Vedejs E, Engler DA, Telschow JE, *J Org Chem* (1978) 43, 188
c) Gamboni R, Tamm C, *Tetrahedron Lett* (1986) 27, 3999
d) Vedejs E, Larsen S, *Organic Synthesis*, Coll Vol VII, p 277 (1990).

48 a) Gamboni R, Mohr P, Waespe-Sarcevic N, Tamm C, *Tetrahedron Lett* (1985) 203
b) Gamboni R, Tamm C, *Helv Chim Acta* (1986) 69, 615
c) Cohen N, Banner B, Laurenzano AJ, Carozza L, *Organic Synthesis* Coll Vol VII (1990) 297.

49 a) Davis FA, Vishwakarma LC, Billmers JM, Finn J, *J Org Chem* (1984) 49, 3241
b) Narasaka K, Ukaji Y, Watanabe K, *Bull Chem Soc Jpn* (1987) 60, 1457
c) Ohta T, Hosoi A, Nozoe S, *Tetrahedron Lett* (1988) 29, 329
d) Davis FA, Sheppard AC, *Tetrahedron* (1989) 45, 5703
e) Davis FA, Kumar A, *J Org Chem* (1992) 57, 3337.

50 Dembech P, Guerrini A, Ricci A, Seconi G, Taddei M, *Tetrahedron* (1990) 46, 2999.

51 Pohmakotr M, Winotai C, *Synth Commun* (1988) 18, 2141.

52 Davis FA, Chattopadhyay S, Towson JC, Lal S, Reddy T, *J Org Chem* (1988) 2087.

53 Baciocchi E, Ruzziconi R, *J Org Chem* (1986) 51, 1645.

54 Moriarty RH, Hou KC, Prakashi I, Arora SK, *Organic Synthesis*, Coll Vol VII (1990) 263.

55 Moriarty RM, Berglund BA, Penmasta R, *Tetrahedron Lett* (1992) 33, 6065.

56 Khanna MS, Garg CP, Kapoor RP, *Tetrahedron Lett* (1992) 33, 1495.

57 a) Adam W, Prechtl F, *Chem Ber* (1991) 124, 2369
b) Guertin KR, Chan TH, *Tetrahedron Lett* (1991) 32, 715
c) Adam W, Müller M, Prechtl F, *J Org Chem* (1994) 59, 2359.

58 Schultz M, Kluge R, Schüssler M, Hoffmann G, *Tetrahedron* (1995) 51, 3175.

59 Jones AB in Dudfield PJ in *Comprehensive Organic Synthesis*, Trost BM, Fleming I, Ley SV Eds, Pergamon, Oxford, 1991, Vol 7, p 151.

60 a) Petragani N, Yonashiro M, *Synthesis* (1982) 521
b) Wasserman HH, Lipshutz BH, *Tetrahedron Lett* (1975) 1731.

61 Konen DA, Silbert LS, Pfeffer PE, *J Org Chem* (1975) 40, 3253.

62 Hauser FM, Rhee R, *Synthesis* (1977) 245.

63 Ireland RE, Mueller RH, Willard AK, *J Am Chem Soc* (1976) 98, 2868.

64 Ipatieff VN, Pines H, Freidman BS, *J Am Chem Soc* (1938) 60, 2731.

65 Leister NA, Tarbell DS, *J Org Chem* (1958) 23, 1152.

66 Parker KA, Spero DM, Koziski KA, *J Org Chem* (1987) 52, 183.

67 Lustig E, Benson WR, Duy N, *J Org Chem* (1967) 32, 851.

68 Jennings WB, Randall D, Saket BM, *J Chem Soc, Chem Commun* (1982), 508.

69 Parker KA, Koziski KA, *J Org Chem* (1987) 52, 674.

70 Collier WL, Macomber RS, *J Org Chem* (1973) 38, 1367.

71 Ivitzky P, *Bull Soc Chim Fr* (1924) 35, 357.

72 Stadler PA, *Helv Chim Acta* (1982) 61, 1675.