

Ruthenium-Catalyzed Oxidation of Alkanes with *tert*-Butyl Hydroperoxide and Peracetic Acid

Shun-Ichi Murahashi,* Naruyoshi Komiya, Yoshiaki Oda,[†] Toshiyuki Kuwabara, and Takeshi Naota

Department of Chemistry, Graduate School of Engineering Science, Osaka University,
1-3, Machikaneyama, Toyonaka, Osaka 560-8531, Japan

mura@chem.es.osaka-u.ac.jp.

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The ruthenium-catalyzed oxidation of alkanes with *tert*-butyl hydroperoxide and peracetic acid gives the corresponding ketones and alcohols highly efficiently at room temperature. The former catalytic system, $\text{RuCl}_2(\text{PPh}_3)_3$ -*t*-BuOOH, is preferable to the oxidation of alkylated arenes to give aryl ketones. The latter system, $\text{Ru/C-CH}_3\text{CO}_3\text{H}$, is suitable especially for the synthesis of ketones and alcohols from alkanes. The ruthenium-catalyzed oxidation of cyclohexane with $\text{CH}_3\text{CO}_3\text{H}$ in trifluoroacetic acid/ CH_2Cl_2 at room temperature gave cyclohexyl trifluoroacetate and cyclohexanone with 90% conversion and 90% selectivity (85:15). The mechanistic study indicates that these catalytic oxidations of hydrocarbons involve oxo-ruthenium species as key intermediates.

Introduction

The catalytic oxidation of unactivated C–H bonds of alkanes under mild conditions is of importance in view of synthetic and industrial aspects.¹ In biological systems, harmful organic molecules including hydrocarbons are metabolized to give water-soluble compounds or biologically important materials. The existence of enzymatic systems that can catalyze the oxidation of alkanes has prompted the creation of their chemical analogues. Much effort has been devoted to understand the catalytic cycle of cytochrome P-450s, because of their strong ability for oxidation.² In 1979 Groves et al. first reported biomimetic oxidation of hydrocarbons with PhIO using $\text{Fe}(\text{TPP})\text{Cl}$ catalyst.³ Since then, the shunt process has been often used for the biomimetic oxidations of organic molecules, because oxo-metal species can be formed readily upon treatment with various oxygen donors such as iodosylbenzenes and hypochlorites.^{1,4} Among transition metals, ruthenium as well as iron has become increasingly important to be utilized for the catalytic oxidations.⁵

Generally, catalytic oxidation of alkanes under mild conditions is quite difficult, because of the lack of the reactivity of alkanes, which stems from their high C–H

bond energy. The ruthenium-catalyzed oxidations have been reported; however, the results reported are low conversions of alkanes.⁶ Hydroxylation of alkanes has been achieved with ruthenium porphyrin catalysts such as $\text{Ru}(\text{TMP})(\text{O})_2$ and $\text{Ru}(\text{TPFPP})(\text{CO})$ with 2,6-dichloropyridine *N*-oxide.^{7,8} Perfluorinated ruthenium phthalocyanine, which is encapsulated in zeolite, is an effective catalyst with *t*-BuOOH.⁹ Furthermore, a non-porphyrin *cis*-dioxo-ruthenium complex bearing the sterically bulky 2,9-dimethyl-1,10-phenanthroline ligand can be used for the oxidation of alkanes with H_2O_2 .¹⁰ Recently, ruthenium-substituted polyoxometalates were reported to be useful for oxidation of hydrocarbons, even with molecular oxygen.¹¹ These reactions are efficient for oxidation of tertiary C–H bonds of alkanes; however, secondary C–H bonds of alkanes such as cyclohexane are difficult to oxidize. Selective catalytic oxidation of cyclohexane with high conversion at room temperature still awaits to be explored. Catalytic oxidation of cyclohexane with *t*-BuOOH has been investigated extensively; however, the conversions obtained are still low.¹²

To generate oxo-ruthenium species, which may correspond to the oxo-iron(IV) species of cytochrome P-450, low-valent ruthenium complexes were treated with peroxides with the intention of generating middle-valent oxo-ruthenium species. Then, we found that alkanes can

* To whom correspondence should be addressed.

[†] On leave from Organic Synthesis Research Laboratory, Sumitomo Chemical Co., Ltd., Takatsuki, Osaka 569-1093, Japan.

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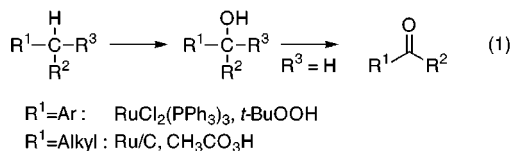
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be readily oxidized at room temperature by the two catalytic systems (i) $\text{RuCl}_2(\text{PPh}_3)_3$ – $t\text{-BuOOH}$ ¹³ and (ii) Ru/C (Ru on charcoal)– $\text{CH}_3\text{CO}_3\text{H}$ ¹⁴ to give the corresponding ketones and alcohols highly efficiently (eq 1).



The former catalytic system using $\text{RuCl}_2(\text{PPh}_3)_3$ and $t\text{-BuOOH}$ is particularly effective for the oxidation of alkylated arenes to the corresponding aryl ketones, while the latter Ru/C -catalyzed oxidation with peracetic acid is useful for the conversion of alkanes to the corresponding ketones. Catalytic oxidations using $t\text{-BuOOH}$ and $\text{CH}_3\text{CO}_3\text{H}$ are convenient because (i) $t\text{-BuOOH}$ and $\text{CH}_3\text{CO}_3\text{H}$ are readily obtained from aerobic oxidation of isobutane and acetaldehyde, respectively, and (ii) *tert*-butyl alcohol formed can be used for *tert*-butyl methyl ether as high octane fuel, and the acetic acid formed can be also used.

To raise the reactivity, a ruthenium-catalyzed oxidation was carried out in the presence of trifluoroacetic acid. Thus, the oxidation of cyclohexane with $\text{CH}_3\text{CO}_3\text{H}$ in the presence of $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ catalyst in trifluoroacetic acid– CH_2Cl_2 gave cyclohexyl trifluoroacetate and cyclohexanone with 90% conversion and 90% selectivity.

Full details of these novel oxidations of alkanes are described with respect to scope and reaction mechanism.¹⁵ These results are consistent with our previous results¹⁶ for the ruthenium-catalyzed cytochrome P-450

type oxidations of amines,¹⁷ amides,¹⁸ nitriles,¹⁹ alkenes,²⁰ alcohols,²¹ and phenols.²²

Results and Discussion

Ruthenium-Catalyzed Oxidation of Alkanes. To generate oxo-metal complexes, which may correspond to the oxo-iron(IV) species of cytochrome P-450, we wanted to generate middle-valent $\text{Ru}=\text{O}$ species,¹⁶ which may exhibit unique reactivity and be quite different from high-valent RuO_4 species, by the oxidation of low-valent ruthenium complexes.⁵ Then, we discovered that low-valent ruthenium species such as $\text{RuCl}_2(\text{PPh}_3)_3$ ¹³ and Ru/C ¹⁴ with peroxides are excellent catalytic systems for the oxidations of alkanes.

At first, the efficiency of these catalytic systems was examined for the oxidation of cyclohexane. To a stirred mixture of cyclohexane and ruthenium catalyst in benzene or ethyl acetate was added either a $t\text{-BuOOH}$ solution in benzene or a $\text{CH}_3\text{CO}_3\text{H}$ solution in ethyl acetate dropwise over a period of 30 min. Because the reaction is very rapid, it is completed immediately after the addition of the peroxide. The conversions of cyclohexane and the yields of cyclohexanone and cyclohexanol were determined by GC analysis using an internal standard after the addition of the peroxide. The $\text{RuCl}_2(\text{PPh}_3)_3$ -catalyzed oxidation of cyclohexane with 1 equiv of $t\text{-BuOOH}$ proceeds to give cyclohexanone and cyclohexanol (68:32) with 9.3% conversion and 82% selectivity. On the other hand, peracetic acid is more reactive. The Ru/C -catalyzed oxidation of cyclohexane with 0.7 equiv of $\text{CH}_3\text{CO}_3\text{H}$ proceeds with 9.1% conversion and 93% selectivity, where the ratio of cyclohexanone and cyclohexanol is 94:6. In view of the reactivity and selectivity, the Ru/C – $\text{CH}_3\text{CO}_3\text{H}$ system is more suitable for the oxidation of alkanes.

The rate of the addition of peracetic acid to the mixture of alkane and Ru/C catalyst in ethyl acetate must be controlled, because the reaction of ruthenium with peracetic acid is very fast and exothermic. The addition of peracetic acid solution dropwise over a period of 30 min

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Table 1. Ru/C-Catalyzed Oxidation of Cyclohexane with Peracetic Acid: Relation between Conversion of Cyclohexane and Selectivity of Cyclohexanone and Cyclohexanol^a

amt of CH ₃ CO ₃ H (equiv)	conv ^{b,c} (%)	yield ^b (selectivity ^d) (%)		total of selectivity ^e (%)
		cyclohexanone	cyclohexanol	
0	0	0	0	
0.7	9.1	7.9 (87)	0.5 (5)	92
1.2	20	16 (82)	0.9 (5)	87
1.7	29	22 (76)	1.1 (4)	80
2.2	38	28 (73)	1.1 (3)	76
2.7	45	32 (71)	0.9 (2)	73
3.0	51	35 (68)	0.9 (2)	70 ^f

^a To a stirred mixture of cyclohexane (2.00 mmol) and 5% Ru/C (0.020 mmol) in dry ethyl acetate (2.0 mL) was added dropwise a 30% solution of CH₃CO₃H in dry ethyl acetate at 20 °C under argon. ^b Determined by GLC analysis based on the starting substrate using an internal standard. ^c Conversion was controlled by the amount of peracetic acid. ^d Determined by GLC analysis based on the converted cyclohexane using an internal standard. ^e Cyclohexanone + cyclohexanol. ^f The overoxidation products, adipic acid, glutaric acid, and succinic acid (46:44:10), were formed in 25% yield.

for each 1 equiv of peracetic acid with respect to alkane is recommended.

To determine the optimized reaction conditions, the oxidation of cyclohexane was carried out with Ru/C catalyst by changing the amount of peracetic acid. The ketone/alcohol ratios of the present system are dependent on the conversions. The relation between the conversion of cyclohexane and the selectivity of products (cyclohexanol and cyclohexanone) was examined (Table 1). Although the conversion was increasing in proportion to the amount of peracetic acid, the selectivity for the sum of cyclohexanone and cyclohexanol was decreasing. Typically, the oxidation of cyclohexane with 0.7 equiv of CH₃CO₃H proceeds to give cyclohexanone and cyclohexanol (87:5) with 9.1% conversion and 92% selectivity, whereas the reaction with 3 equiv of CH₃CO₃H afforded cyclohexanone and cyclohexanol (68:2) with 51% conversion and 70% selectivity along with dicarboxylic acids (adipic acid:glutaric acid:succinic acid = 46:44:10) with 25% selectivity and trace amounts of diketones such as 1,4-cyclohexanedione. Control experiments showed that these dicarboxylic acids were formed by the oxidation of diketones such as 1,2- and 1,3-cyclohexanedione under the reaction conditions. Thus, the high selectivity (>90%) can be obtained using 0.7–1.0 equiv of peracetic acid with 10% conversion.

The representative results of the oxidation of various alkanes at 20 °C are shown in Table 2. It is noteworthy that all reactions proceed with high selectivity (>90%), when the conversion is controlled to around 10%. Cyclic alkanes such as cyclohexane and cyclooctane can be readily converted to the corresponding ketones and alcohols with 91–93% selectivities (entries 1–3). The product distribution of the oxidation of methylcyclohexane shows that the relative reactivity of the C–H bonds is in the order tertiary > secondary >> primary (entry 4). The tertiary/secondary selectivity on a per-bond basis for the oxidation of adamantane was calculated to be 20 (entry 5). Poorly reactive *n*-alkanes such as *n*-heptane and *n*-decane are also oxidized (entries 8 and 9). Because the reaction is heterogeneous, Ru/C catalyst can be recovered by the filtration and is reusable. Actually, the oxidation of cyclohexane with CH₃CO₃H can be repeated by using recovered Ru/C catalyst three times without loss

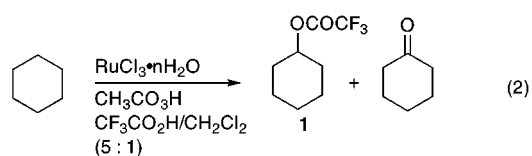
Table 2. Ru/C-Catalyzed Oxidation of Alkanes and Alkylated Arenes with CH₃CO₃H^a

entry	substrate	conv ^b (%)	product ^c	sel ^d (%)
1	cyclohexane	7.6	cyclohexanone cyclohexanol	93 4
2 ^e	cyclohexane	9.1	cyclohexanone cyclohexanol	87 5
3	cyclooctane	11	cyclooctanone cyclooctanol	87 4
4	methylcyclohexane	7.7	methylcyclohexanones ^h methylcyclohexanols ⁱ	59 35
5	adamantane	18	adamantanols ^j 2-adamantanone	87 13
6 ^f	adamantane	37	adamantanols ^k 2-adamantanone	85 12
7 ^g	adamantane	58	adamantanols ^l 2-adamantanone	84 12
8	<i>n</i> -heptane	8.4	heptanones ^m heptanols ⁿ	86 3
9	<i>n</i> -decane	7.2	decanones ^o decanols ^p	86 6

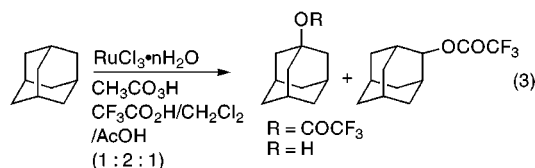
^a To a stirred mixture of substrate (2.00 mmol) and 5% Ru/C (0.020 mmol) in dry ethyl acetate (2.0 mL) was added dropwise a 30% solution of CH₃CO₃H (1.00 mmol) in dry ethyl acetate at 20 °C over a period of 15 min under argon. ^b Determined by GLC analysis based on the starting substrate using an internal standard. ^c Identified by GC-MS. ^d Determined by GLC analysis based on the converted substrate using an internal standard. ^e CH₃CO₃H (1.40 mmol) was used. ^f CH₃CO₃H (2.00 mmol) was used. ^g CH₃CO₃H (4.00 mmol) was used. ^h 2-one:3-one:4-one = 36:46:18. ⁱ 1-ol:2-ol:3-ol:4-ol = 94:2:3:1. ^j 1-ol:1,3-diol = 95:5. ^k 1-ol:2-ol:1,3-diol = 88:1:12. ^l 1-ol:2-ol:1,3-diol = 82:1:17. ^m 2-one:3-one:4-one = 36:42:22. ⁿ 2-ol:3-ol:4-ol = 40:40:20. ^o 2-one:3-one:(4 + 5)-ones = 18:24:58. ^p 2-ol:3-ol:(4 + 5)-ols = 25:25:50.

of reactivity and selectivity. It is noteworthy that the Ru/C–CH₃CO₃H system shows extremely high reactivity toward the oxidation of alkanes even at room temperature. The oxidation of cyclohexane can be carried out with >50% conversion, although such a high conversion cannot be achieved at room temperature in the other systems.^{6–11}

Next we aimed at both high conversion and high selectivity for the oxidation of alkanes. One can expect that active oxo–metal species bearing electron-withdrawing ligands would be more reactive species.²³ We found that trifluoroacetic acid is a suitable acid for such a purpose. Actually, we found that the RuCl₃·*n*H₂O-catalyzed oxidation of cyclohexane with CH₃CO₃H in a mixture of trifluoroacetic acid and dichloromethane (5:1) at 20 °C for 4 h gave cyclohexyl trifluoroacetate (**1**) and cyclohexanone in 90% selectivity (85:15) with 90% conversion (eq 2).¹⁴ It is particularly important that the



overoxidation is suppressed despite extremely high conversion. The oxidation is also successful for the oxidation of *t*-C–H bonds of alkanes. Thus, adamantane was converted to 1-adamantyl trifluoroacetate (89%), which was readily hydrolyzed to give 1-adamantanol during the workup, along with 2-adamantyl trifluoroacetate (9%) with 70% conversion (eq 3). Although trifluoroacetoxy-



lation of hydrocarbons has been reported to occur upon treatment with hydrogen peroxide in trifluoroacetic acid without metal catalyst,²⁴ the oxidation of alkanes does not take place under our reaction conditions. Thus, the reaction of cyclohexane with peracetic acid in a mixture of trifluoroacetic acid and CH_2Cl_2 (5:1) in the absence of $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ for 24 h gave **1** only in 3% yield, indicating that the present oxidation is based on the ruthenium-catalyzed reactions. Furthermore, the second-order rate constants for the ruthenium-catalyzed oxidation of cyclohexane with $\text{CH}_3\text{CO}_3\text{H}$ in trifluoroacetic acid and CH_2Cl_2 was determined to be $k = 5.4 \text{ M}^{-1} \text{ s}^{-1}$, where the rate law for the reaction is expressed by eq 4. The value

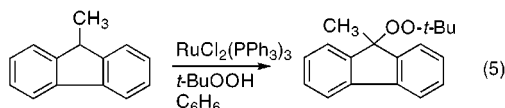
$$-\frac{[\text{cyclohexane}]}{dt} = k[\text{RuCl}_3 \cdot n\text{H}_2\text{O}][\text{CH}_3\text{CO}_3\text{H}] \quad (4)$$

is much larger than that ($k < 10^{-5} \text{ s}^{-1}$) for the oxidation without the catalyst. The present reaction is a general and efficient method for conversion of aliphatic C–H bonds of alkanes to the corresponding trifluoroacetates.

Ruthenium-Catalyzed Oxidation of Alkylated Arenes. In contrast to the Ru/C-catalyzed oxidation of alkanes with peracetic acid, the $\text{RuCl}_2(\text{PPh}_3)_3$ – $t\text{-BuOOH}$ system is highly useful for the oxidation of alkylated arenes. Thus, the $\text{RuCl}_2(\text{PPh}_3)_3$ -catalyzed oxidation of ethylbenzene with 4 equiv of $t\text{-BuOOH}$ proceeds with 98% selectivity to give acetophenone and α -phenethyl alcohol (93:7).

Various alkylated arenes can be oxidized to the corresponding aryl ketones, as listed in Table 3. Ethylbenzene and its derivatives are oxidized at the benzylic C–H bonds to give acetophenone and its derivatives selectively (entries 1–5). Diphenylmethane and fluorene can be readily converted into the corresponding ketones in high yields (entries 6 and 7). The reaction is convenient, because the product ketones can be readily isolated in high yields by short column (silica gel). Recently, benzylic oxidation with iodosylbenzene (3 equiv) in the presence of manganese salen catalyst (8–15 mol %) has been reported to give similar yields of ketones.²⁵

It is noteworthy that the oxidation of 9-methylfluorene gave 9-(*tert*-butyldioxy)-9-methylfluorene in 98% yield (eq 5). Furthermore, the ruthenium-catalyzed oxidation of

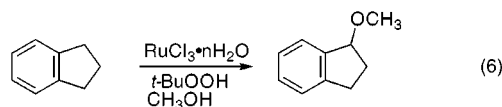


indane with $t\text{-BuOOH}$ in methanol gave 1-methoxyindane (20%) along with 1-indanone (12%) at 36% conversion of indane (eq 6). These results may indicate the intermediacy of carbocation species.

Table 3. $\text{RuCl}_2(\text{PPh}_3)_3$ -Catalyzed Oxidation of Alkylated Arenes with $t\text{-BuOOH}$ ^a

entry	alkylated arene	conv, ^b %	product	selectivity, ^c %
1		58		91 ^d
2		46		94
3		48		73
4		66		71
5		94		54
6		75		95
7		100		87 (86) ^e

^a To a stirred mixture of alkylated arene (2.00 mmol) and $\text{RuCl}_2(\text{PPh}_3)_3$ (0.020 mmol) in dry benzene (2.0 mL) was added dropwise a 3.59 M solution of $t\text{-BuOOH}$ in dry benzene (2.23 mL, 8.00 mmol) at 20 °C over a period of 2 h under argon. ^b Determined by GLC analysis based on the starting alkylated arene using an internal standard. ^c Determined by GLC analysis based on the converted alkylated arene. ^d α -Phenethyl alcohol is also produced in 7% yield. ^e Values in parentheses correspond to isolated yields.



Reaction Mechanism for the $\text{RuCl}_2(\text{PPh}_3)_3$ -Catalyzed Oxidation of Alkanes with $t\text{-BuOOH}$. Oxo–ruthenium complexes bearing bulky ligands such as porphyrins and bipyridines have been isolated and characterized.^{7,8,26} However, an oxo–ruthenium complex bearing simple ligands is unstable and has never been isolated. A reactive oxo–ruthenium complex may be formed in the $\text{RuCl}_2(\text{PPh}_3)_3/t\text{-BuOOH}$ system, and this is the reason the present system is highly efficient for the oxidation of secondary C–H bonds of alkanes at room temperature.

To clarify the mechanism, the relative reactivity of substituted toluenes ($\text{X}-\text{C}_6\text{H}_4\text{CH}_3$, $\text{X} = p\text{-CH}_3$, H, $p\text{-Cl}$, $m\text{-Cl}$) with $t\text{-BuOOH}$ in the presence of $\text{RuCl}_2(\text{PPh}_3)_3$ was determined. In the competitive reaction, a large excess of substrate was used to ensure that the rate is zero order in substrate. The relative rates can be determined by the conversions of toluenes when conversions are low (<5%).

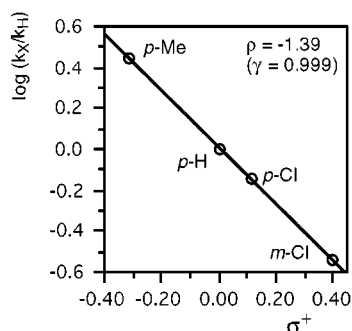
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Table 4. Relative Rate Constants for the Ruthenium-Catalyzed Oxidation of Substituted Toluenes with *t*-BuOOH^a

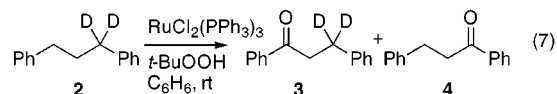
X in XC ₆ H ₄ CH ₃	σ^+	k_X/k_H	$\log(k_X/k_H)$
<i>p</i> -CH ₃	-0.311	2.77	0.443
H	0	1	0
<i>p</i> -Cl	0.114	0.722	-0.142
<i>m</i> -Cl	0.399	0.286	-0.543

^a Reaction conditions: toluene (1 mmol), substituted toluene (1 mmol), RuCl₂(PPh₃)₃ (0.01 mmol), *t*-BuOOH (0.2 mmol), benzene (2 mL), 20 °C.

**Figure 1.** Plot of $\log k_{\text{rel}}$ vs σ^+ values for the ruthenium-catalyzed oxidation of substituted toluenes with *t*-BuOOH.

Because the rate for oxidation of toluene to benzyl alcohol ($k_1 = 0.24 \text{ M}^{-1} \text{ s}^{-1}$) is slower than those for benzyl alcohol to benzaldehyde ($k_2 = 4.8 \text{ M}^{-1} \text{ s}^{-1}$) or benzaldehyde to benzoic acid ($k_3 = 1900 \text{ M}^{-1} \text{ s}^{-1}$),²⁷ the relative rates of oxidation of toluenes can be calculated by the sum of the yields of benzyl alcohols (X-C₆H₄CH₂OH), benzaldehydes (X-C₆H₄CHO), and benzoic acids (X-C₆H₄CO₂H) at low conversion (<5%) (Table 4). The rate data correlate well ($\gamma = 0.999$) with the Hammett linear free energy relationship with use of σ^+ values (Figure 1). Better correlation was obtained with a σ^+ value rather than σ , suggesting the existence of electrophilic high-valent metal species.²⁸ The ρ value is -1.39, which is similar to those obtained for the oxidation with cytochrome P-450 (-1.6)²⁹ and Fe(TPP)Cl-PhIO (-1.69).²⁸ The result indicates that substantial charge transfer from the substrate to the electrophilic oxo-metal complex is involved.²⁷ The observed ρ value (-1.39) is quite different from those obtained from the *t*-BuO• radical (-0.4)³⁰ and the *t*-BuOO• radical (-0.6)³¹ (Table 5). These kinetic data indicate the existence of a metal-dependent species such as oxo-ruthenium, which is similar to Fe=O of cytochrome P-450, rather than *t*-BuO• and *t*-BuOO• intermediates.

The intramolecular deuterium isotope effect (k_H/k_D) was examined for the oxidation of 1,1-dideuterio-1,3-diphenylpropane (**2**).³² The products were 3,3-dideuterio-1,3-diphenylpropan-1-one (**3**) and 1,3-diphenylpropan-1-one (**4**) (eq 7). The k_H/k_D value was determined to be 9.0

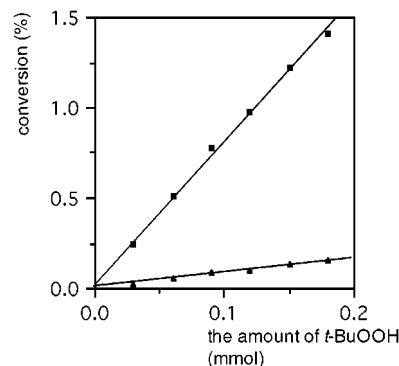


by means of GC-MS analyses of a mixture of the product ketones **3** and **4**. This large k_H/k_D value is similar to that

Table 5. Kinetics and Intra- and Intermolecular Deuterium Isotope Effects for the RuCl₂(PPh₃)₃-Catalyzed Oxidation of Hydrocarbons with *t*-BuOOH

syst	ρ^a	k_H/k_D^b	k_H/k_D^c
RuCl ₂ (PPh ₃) ₃ - <i>t</i> -BuOOH	-1.39	9.0	9.2
cytochrome P-450	-1.6 ^d	11 ^g	
<i>t</i> -BuO•	-0.4 ^e		4.2 ^h
<i>t</i> -BuOO•	-0.6 ^f		

^a Values from Hammett plots of $\log k_{\text{rel}}$ vs σ^+ for the competitive oxidation of substituted toluenes. ^b Intramolecular isotope effect for the oxidation of 1,1-dideuterio-1,3-diphenylpropane. ^c Intermolecular isotope effect for the oxidation of cyclohexane/cyclohexane-*d*₁₂. ^d Reference 29. ^e Reference 30. ^f Reference 31. ^g Reference 32. ^h Reference 33.

**Figure 2.** Relative rate of oxidation of cyclohexane (upper) and cyclohexane-*d*₁₂ (lower) by RuCl₂(PPh₃)₃ and *t*-BuOOH. Reaction conditions: cyclohexane (1.00 mmol), cyclohexane-*d*₁₂ (1.00 mmol), RuCl₂(PPh₃)₃ (0.01 mmol), *t*-BuOOH (0.03–0.18 mmol), benzene (2 mL), 20 °C.

obtained for the oxidation with cytochrome P-450 (11),³² indicating that the C-H bond breaking is the rate-determining step. Furthermore, the intermolecular isotope effect of the oxidation of cyclohexanes was determined to be 9.2 at low conversion (<2%) by GLC analysis of the competitive reactions of cyclohexane and cyclohexane-*d*₁₂ (Figure 2). This is in contrast to the smaller isotope effect (4.2) which was obtained from the reaction with *t*-BuO• (Table 5).³³

The oxidation can be rationalized by assuming the mechanism shown in Scheme 1. The ruthenium(II) complex **5** reacts with *t*-BuOOH to give the alkylperoxo-ruthenium(II) complex **6**,³⁴ which subsequently undergoes heterolytic cleavage of the O-O bond to give oxo-ruthenium(IV) species (**7**).³⁵ The reaction with *t*-BuO• or *t*-BuOO• is unlikely, because the oxidation of alkanes proceeds efficiently even in the presence of radical scavengers such as 2,6-di-*tert*-butyl-4-methylphenol. Abstraction of a hydrogen atom from an alkane by the intermediate **7** would form the caged complex **8**, bearing an alkyl radical and a hydroxo-ruthenium(III) interme-

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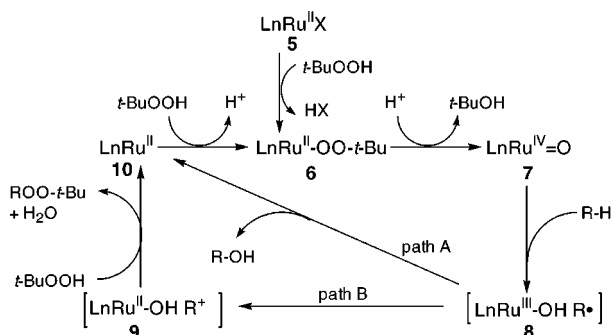
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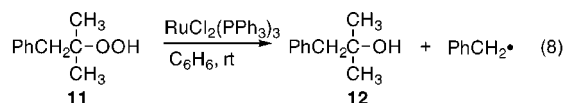
Scheme 1



diolate. Transfer of the hydroxy ligand to the caged alkyl radical (path A) would afford an alcohol and the Ru(II) species **10** to complete the catalytic cycle. The involvement of a Ru(III)–Ru(V) cycle to form an oxo–ruthenium(V) species cannot be excluded.⁸ Further oxidation of secondary alcohol thus formed gives the corresponding ketones under the reaction conditions. When the alkyl radical **8** has low oxidation potential, fast single-electron transfer would take place to give cation **9** (path B), which undergoes reaction with the second molecule of *t*-BuOOH to give the corresponding *tert*-butyldioxy product and water. The ratios of the *tert*-butyldioxy products to the total sums of ketones and alcohols for the RuCl₂(PPh₃)₃-catalyzed oxidation of hydrocarbon with *t*-BuOOH are in the order 9-methylfluorene (10:0) > cyclohexene (3:7) > cyclohexane (1:9). This tendency is in accordance with the stability of the corresponding cationic intermediate. Furthermore, the formation of 1-methoxyindane from the ruthenium-catalyzed oxidation of indane in methanol (eq 6) indicates the formation of the cationic intermediate **9**, which is trapped with the methanol under the reaction conditions.

To obtain further information about the reactive intermediate, Ingold's mechanistic probe of 2-methyl-1-phenyl-2-propyl hydroperoxide (MPPH; **11**)³⁶ was applied to the present oxidation. The peroxide **11** has been used to determine the mode of scission of the peroxidic O–O bond.³⁶ When MPPH is allowed to react with a metal catalyst, an oxo–metal or alkoxyl radical will be formed. In the case of formation of PhCH₂C(CH₃)₂O• radical, fast β-scission occurs to give benzyl radical, from which typical radical reaction products are formed. The product distributions derived from MPPH may enable the discrimination of the mechanism between Ru=O and *t*-BuO•.

The reaction of RuCl₂(PPh₃)₃ with MPPH (**11**) was carried out in benzene at room temperature (eq 8).



Dimethylbenzylcarbinol (**12**) was obtained as a major product (53%) along with the products derived from benzyl radical such as benzaldehyde (19%), benzoic acid (1%), benzyl benzoate (1%), phenyl benzoate (1%), diphenylmethane (2%), 1,2-diphenylethane (2%), and 2-methyl-1-phenyl-2-propyl benzyl ether (2%). The predominant

formation of **12** is remarkable. The product ratio of the alcohol **12** to the other products derived from benzyl radical is 53:28. The alcohol **12** would be formed by the heterolytic O–O bond cleavage of the PhCH₂C(CH₃)₂-OORuL_{*n*} complex (eq 8).³⁷ The corresponding ratio obtained from the Gif system (FeCl₃–picolinic acid–*t*-BuOOH in pyridine and AcOH) has been determined to be 16:59, where *t*-BuO• was determined to be a major reaction species.^{36b,38} The results for the Gif system is quite different from those for the present system. It seems reasonable to conclude that the reaction of MPPH with the ruthenium species would give an oxo–ruthenium species (Ru=O) as a major intermediate.

We next examined Minisci's test to distinguish the reactivities of *t*-BuO• and *t*-BuOO•. Minisci et al. determined the relative rates for Gif and Kharasch reactions, where *t*-BuO• and *t*-BuOO• radicals are key intermediates, respectively.^{38b} In these systems the solvent effect is remarkable; *t*-BuO• radical would be formed in polar solvents such as pyridine and acetic acid, whereas the *t*-BuOO• radical is formed in nonpolar solvents.^{38a} The relative reactivity of cyclohexane, toluene, cumene, cyclohexene, styrene, and THF in benzene toward the present RuCl₂(PPh₃)₃–*t*-BuOOH system was determined to be 1:0.26:1.5:13:3.2:2.0 at low conversions (0.5–5%), as shown in Table 6. The ratio is quite similar to that (1:0.27:1.2:7.2:3.5:3.3) obtained from the Fe(TPPFP)Cl–*t*-BuOOH system, where oxo–iron species are actually generated.³⁹ The relative reactivity obtained from the present system are different from those obtained from *t*-BuOO• reactions (1:65:>100:>100:>100:>100)^{38a} (Table 6). The difference between the present system and the *t*-BuO• system is rather small to distinguish; however, a remarkable difference in reactivity was observed for the oxidation of cumene. The ratio of reactivity between cyclohexane and cumene is 1.5 for RuCl₂(PPh₃)₃/–*t*-BuOOH, while the ratio for the *t*-BuO• system is 0.5. Furthermore, the relative reactivity of the oxidation of tertiary and secondary hydrogen in adamantane is 9.2 for the RuCl₂(PPh₃)₃–*t*-BuOOH system, while that for the *t*-BuO• system is 2.7.^{38b} These results also show that the active species of the RuCl₂(PPh₃)₃–*t*-BuOOH system is neither *t*-BuO• nor *t*-BuOO• radical.

All data such as ρ values, k_H/k_D ratios, and relative oxidation rates in the various substrates described above revealed that the active species of the RuCl₂(PPh₃)₃–*t*-BuOOH system is the oxo–ruthenium species.

Reaction Mechanism for the Ruthenium-Catalyzed Oxidation of Alkanes with Peracetic Acid. An intermolecular deuterium isotope effect (k_H/k_D) was examined for the Ru/C-catalyzed oxidation of cyclohexane and cyclohexane-*d*₁₂ with peracetic acid. The k_H/k_D value was determined to be 6.8 by GC analysis at 0.05–2.1% conversion. The isotope effect ($k_H/k_D = 6.8$) is smaller than those (9.2) obtained for the RuCl₂(PPh₃)₃-catalyzed oxidation with *t*-BuOOH, indicating that a more reactive

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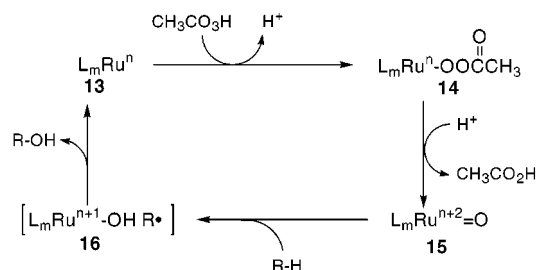
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Table 6. Relative Reactivities of Hydrocarbons for the Oxidation of Cyclohexane, Toluene, Cumene, Cyclohexene, Styrene, and THF by $\text{RuCl}_2(\text{PPh}_3)_3-t\text{-BuOOH}$, $\text{Fe}(\text{TPFP})\text{Cl}-t\text{-BuOOH}$, Gif , $t\text{-BuO}^\bullet$, Kharasch, and $t\text{-BuOO}^\bullet$ Systems

substrate	$\text{RuCl}_2(\text{PPh}_3)_3-t\text{-BuOOH}^a$	$\text{Fe}(\text{TPFP})\text{Cl}-t\text{-BuOOH}^a$	$\text{Fe}^{\text{III}}-t\text{-BuOOH}$ AcOH (Gif) ^b	$t\text{-BuO}^\bullet$ ^b	$\text{Cu}^{\text{II}}-t\text{-BuOOH}$ (Kharasch) ^b	$t\text{-BuOO}^\bullet$ ^b
cyclohexane	1	1	1	1	1	1
toluene	0.26 ± 0.02	0.27 ± 0.02	0.21	0.14	70	65
cumene	1.5 ± 0.1	1.2 ± 0.1	0.61	0.54	>100	>100
cyclohexene	13 ± 1	7.2 ± 0.8	3.66	3.56	>100	>100
styrene	3.2 ± 0.3	3.5 ± 0.2	1.42	1.63	>100	>100
THF	2.0 ± 0.1	3.3 ± 0.3	2.77	5.13	>100	>100

^a The competitive reaction was carried out with cyclohexane (1.00 mmol), substrate (1.00 mmol), catalyst (0.010 mmol), and $t\text{-BuOOH}$ (0.05–0.20 mmol) in dry benzene (2.0 mL) at 20 °C. The values have been determined at five different conversions (0.5–5%). ^b Reference 38a.

Scheme 2

species is present in the present system. Actually, the oxidation of secondary C–H bonds of aliphatic hydrocarbons with the present system gave higher conversions than those with $\text{RuCl}_2(\text{PPh}_3)_3-t\text{-BuOOH}$.

The oxidation can be rationalized by assuming a reaction pathway similar to that shown in Scheme 2. The low-valent ruthenium complex L_mRu^n (**13**) reacts with peracetic acid to give the acetylperoxo–ruthenium complex **14**, which undergoes heterolytic cleavage of the O–O bond to give the oxo–ruthenium species **15**²⁶ and acetic acid. Bruce et al. showed that the acylperoxo–metalloporphyrins undergo heterolytic cleavage more cleanly than alkylperoxo–metal complexes.⁴⁰ Abstraction of a hydrogen atom from an alkane by **15** would form the caged complex **16**, in which transfer of hydroxy ligand to the caged alkyl radical would afford an alcohol and the ruthenium species L_mRu^n (**13**) to complete the catalytic cycle. The presence of freely diffusing alkyl radicals is unlikely, because Russell-type termination of alkylperoxyl radicals forms equal amounts of alcohols and ketones,⁴¹ but the present reaction gives ketones predominantly. In the presence of trifluoroacetic acid, the secondary alcohols thus formed can be trapped with trifluoroacetic acid to give the corresponding ester faster than the sequential oxidation to ketones.

Conclusions

The two catalytic systems $\text{RuCl}_2(\text{PPh}_3)_3-t\text{-BuOOH}$ and $\text{Ru/C}-\text{CH}_3\text{CO}_3\text{H}$ have been found to oxidize alkanes at room temperature. The former is suitable for synthesis of aryl ketones from alkylated arenes, and the latter is suitable for catalytic oxidation of alkanes. Both reactions need only simple ruthenium catalysts and peroxides such as $t\text{-BuOOH}$ and peracetic acid. The intermediacy of oxo–ruthenium species has been demonstrated in both catalytic systems by means of kinetic study, isotope effects,

and product analyses. Highly efficient and selective oxidation of hydrocarbons can be also performed by the ruthenium-catalyzed oxidation of alkanes with peracetic acid in the presence of trifluoroacetic acid.

Experimental Section

General Procedure for the Ruthenium-Catalyzed Oxidation of Alkanes with $\text{CH}_3\text{CO}_3\text{H}$. In a 10 mL round-bottomed flask equipped with a Teflon-coated magnetic stirring bar and a 10 mL pressure-equalizing dropping funnel to a three-way stopcock were placed alkane (2.00 mmol), 5% Ru/C (40 mg, 0.020 mmol for Ru), and dry EtOAc (2.0 mL). A 30% solution of $\text{CH}_3\text{CO}_3\text{H}$ in EtOAc (253 mg, 1.00 mmol) was placed in the dropping funnel and added dropwise to the stirred mixture at 20 °C over a period of 15 min. The reaction mixture was then poured into a 10% aqueous Na_2SO_3 solution (10 mL) slowly and extracted with ether (5 mL \times 2). The combined organic layer was washed with a saturated aqueous NaHCO_3 solution and dried over Na_2SO_4 . The conversion of starting alkane and the yields of products were determined by GLC analysis using an internal standard (acetophenone). The identities of the products were verified by co-injection with authentic samples and in some cases by GC-MS. These results are listed in Table 2.

Ruthenium-Catalyzed Oxidation of Cyclohexane with $\text{CH}_3\text{CO}_3\text{H}$ in the Presence of Trifluoroacetic Acid. The reaction was performed using a 50 mL round-bottomed flask, in which cyclohexane (210 mg, 2.50 mmol), $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ (6.5 mg, 0.025 mmol), trifluoroacetic acid (5 mL), and CH_2Cl_2 (1 mL) were placed. A 30% solution of $\text{CH}_3\text{CO}_3\text{H}$ in EtOAc (1.27 g, 5.00 mmol) was added dropwise to the stirred mixture at 20 °C over a period of 2 h. After the mixture was stirred for a further 2 h, the reaction mixture was poured into a 5% aqueous Na_2SO_3 solution (5 mL) slowly and extracted with CH_2Cl_2 (5 mL \times 2). The combined organic layer was washed with a saturated aqueous NaHCO_3 solution and water (5 mL) and dried over Na_2SO_4 . The conversion of cyclohexane (90%) and the selectivities of products (77% (cyclohexyl trifluoroacetate); 13% (cyclohexanone)) were determined by GLC analysis using an internal standard (acetophenone). The identities of the products were verified by co-injection with authentic samples and by GC-MS.

Oxidation of Cyclohexane with $\text{CH}_3\text{CO}_3\text{H}$ in Trifluoroacetic Acid in the Absence of $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ Catalyst (Control Experiment). The same reaction as above was carried out in the absence of $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$. After the mixture was stirred for a further 15 h, the reaction mixture was poured into a 5% aqueous Na_2SO_3 solution (5 mL) slowly and extracted with CH_2Cl_2 (5 mL \times 2). The combined organic layer was washed with a saturated aqueous NaHCO_3 solution and water (5 mL) and dried over Na_2SO_4 . GLC analysis shows that the yield of cyclohexyl trifluoroacetate is 3%, and trace amounts of cyclohexanone and cyclohexanol can be detected.

General Procedure for the Ruthenium-Catalyzed Oxidation of Alkylated Arenes with $t\text{-BuOOH}$. To a stirred solution of alkylated arene (2.00 mmol), $\text{RuCl}_2(\text{PPh}_3)_3$ (19 mg, 0.020 mmol), and dry benzene (2.0 mL) was added dropwise a 3.59 M solution of $t\text{-BuOOH}$ in dry benzene (2.23 mL, 8.00

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mmol) at 20 °C over a period of 2 h. The reaction mixture was then poured into a 10% aqueous Na₂SO₃ solution (10 mL) slowly and extracted with ether (5 mL × 2). The conversion of alkylated arene and the yields of products were determined by GLC analysis using an internal standard (acetophenone). The results of the oxidation of alkylated arenes are listed in Table 3. The product was isolated by column chromatography on silica gel (eluent hexanes–ethyl acetate).

Competitive Reactions of Substituted Toluenes for the Ruthenium-Catalyzed Oxidation with *t*-BuOOH. To a mixture of toluene (92 mg, 1.00 mmol), substituted toluene (1.00 mmol), and RuCl₂(PPh₃)₃ (10 mg, 0.01 mmol) in dry benzene (2.0 mL) was added dropwise a 4.32 M solution of *t*-BuOOH in dry benzene (0.05 mL, 0.20 mmol) at 20 °C over a period of 10 min. After complete addition of the peroxide, the mixture was quenched as described above and analyzed by GC (TC–WAX column) using an internal standard, and the ratios of conversions were determined. As products, benzyl alcohols (X–C₆H₄CH₂OH), benzaldehydes (X–C₆H₄CHO), and benzoic acids (X–C₆H₄CO₂H) were formed. Under these conditions, the conversions of toluene and substituted toluene were <5% with a mass balance of >95%. The ratios obtained are as follows: X = *p*-CH₃ ($k_X/k_H = 2.77$), *p*-Cl (0.722), *m*-Cl (0.286) (Table 4). Correlation of the relative rate data using a single-parameter Hammett equation gave fair linear correlations against σ^+ . The ρ value for the reaction is –1.39 with $\gamma = 0.999$ (Figure 1).

Relative Reactivities for the Ruthenium-Catalyzed Oxidation of Cyclohexane, Toluene, Cumene, Cyclohexene, Styrene, and THF with *tert*-Butyl Hydroperoxide. The reaction was performed by using equal amounts of cyclohexane (84 mg, 1.00 mmol) and a substrate (1.00 mmol) in the presence of RuCl₂(PPh₃)₃ (0.0096 g, 0.010 mmol) in benzene (2 mL), to which a 4.32 M solution of *t*-BuOOH in benzene (0.05–0.20 mmol) was added over a period of 10 min. After complete addition of the peroxide, the mixture was quenched as described above and analyzed by GC (TC–WAX column) using an internal standard. The reaction was repeated five times, and the values of the relative reactivities of six substrates were determined by the conversion of substrates at five different conversions (0.5–5%). The results are shown in Table 6.

Ruthenium-Catalyzed Oxidation of 1,1-Dideuterio-1,3-diphenylpropane (2**) with *t*-BuOOH (Intramolecular Deuterium Isotope Effect).** To a mixture of **2** (20 mg, 0.100 mmol) and RuCl₂(PPh₃)₃ (1.0 mg, 0.0010 mmol) in dry benzene (0.1 mL) was added a 3.59 M solution of *t*-BuOOH in dry benzene (0.028 mL, 0.10 mmol) all at once, and the mixture was stirred at 20 °C for 10 min. Under these conditions, the conversion of **2** was <5%. The k_H/k_D value was determined to be 9.0 by mass chromatography analysis of the mixture of 3,3-dideuterio-1,3-diphenyl-1-propanone (**3**) ($M^+ 212$) and 1,3-diphenyl-1-propanone (**4**) ($M^+ 210$).

Competitive Reaction of Cyclohexane and Cyclohexane-*d*₁₂ for the Ruthenium-Catalyzed Oxidation with *t*-BuOOH (Intermolecular Deuterium Isotope Effect).

The reaction was performed by using equal amounts of cyclohexane (84 mg, 1.00 mmol) and cyclohexane-*d*₁₂ (96 mg, 1.00 mmol) in the presence of RuCl₂(PPh₃)₃ (19 mg, 0.020 mmol) in dry benzene (2.0 mL), to which a 2.94 M solution of *t*-BuOOH (0.03–0.18 mmol) in dry benzene was added dropwise at 20 °C. After complete addition of the peroxide for 1–10 min, the mixture was quenched as described above and analyzed by GC (TC–WAX column) using an internal standard (diethyl carbonate). Under these conditions, the conversions of cyclohexanes were <2% with a mass balance of >95%. The conversions were determined from the yields of products such as cyclohexanol, cyclohexanone, cyclohexanol-*d*₁₁, and cyclohexanone-*d*₁₀, and the ratio of the conversion of cyclohexane/cyclohexane-*d*₁₂ (k_H/k_D) was determined to be 9.2 ± 0.1 at six different conversions between 0.02% and 1.4% (Figure 2).

Competitive Reactions of Cyclohexane and Cyclohexane-*d*₁₂ for the Ruthenium-Catalyzed Oxidation with CH₃CO₃H (Intermolecular Deuterium Isotope Effect). To a mixture of cyclohexane (0.0842 g, 1.00 mmol), cyclohexane-*d*₁₂ (0.0962 g, 1.00 mmol), and 5% Ru/C (0.040 g, 0.020 mmol for Ru) in dry EtOAc (2.0 mL) was added a 30% solution of CH₃CO₃H (0.04–0.20 mmol) in EtOAc at 20 °C. After complete addition of the peroxide for 1–10 min, the mixture was quenched as described above and analyzed by GC (TC–WAX column) using an internal standard. Under these conditions, the conversions of cyclohexanes were <2% with a mass balance of >95%. The conversions were determined from the yields of products such as cyclohexanol, cyclohexanone, cyclohexanol-*d*₁₁, and cyclohexanone-*d*₁₀, and the ratio of the conversion of cyclohexane/cyclohexane-*d*₁₂ (k_H/k_D) was determined to be 6.8 ± 0.3 at five different conversions between 0.05% and 2.1%.

Reaction of 2-Methyl-1-phenyl-2-propyl Hydroperoxide (11**) with RuCl₂(PPh₃)₃.** To a stirred solution of RuCl₂(PPh₃)₃ (0.9 mg, 0.0009 mmol) in dry benzene (0.5 mL) was added dropwise a solution of **11**^{36a} (30 mg, 0.18 mmol) in benzene over a period of 15 min at 20 °C. After 2 h, the yields of dimethylbenzylcarbinol (**12**; 53%), benzaldehyde (19%), benzoic acid (1%), benzyl benzoate (1%), phenyl benzoate (1%), diphenylmethane (2%), 1,2-diphenylethane (2%), and 2-methyl-1-phenyl-2-propyl benzyl ether (2%) were determined by GLC analysis (TC–WAX). The product ratio of the alcohol **12** to the other species, which are derived from benzyl radical, was determined to be 53:28.

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Supporting Information Available: Text giving detailed experimental procedures, including analytical and spectroscopic data (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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