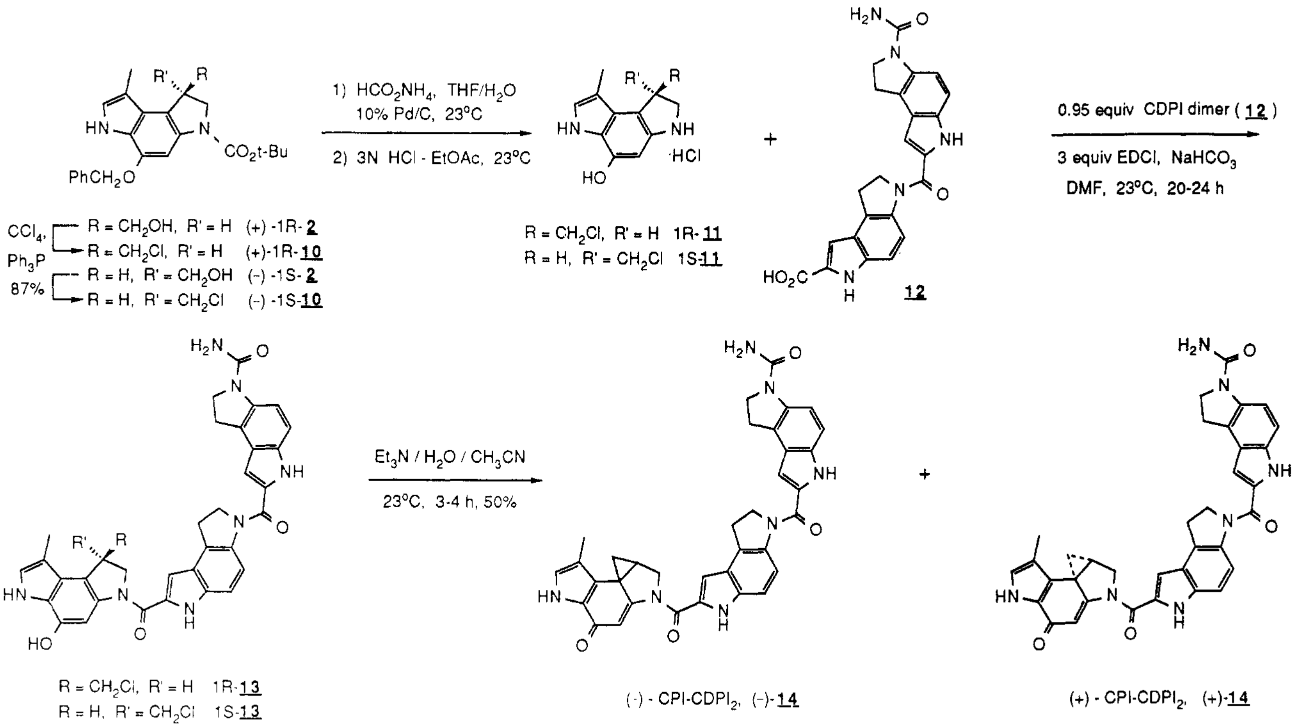
Scheme I



Preparative HPLC Separation of (1*R*,2′*R*)-4 and (1*S*,2′*R*)-4. A solution of (1*RS*,2′*R*)-4 (95 mg in 0.5 mL of CH_2Cl_2) was subjected to chromatography on an Altech 10 mm × 25 cm column packed with 10 μm SiO_2 using 2% EtOAc–98% CH_2Cl_2 eluant at a flow rate of 3.5 mL/min. The effluant was monitored at 280 nm and the diastereomeric esters (1*R*,2′*R*)-4 and (1*S*,2′*R*)-4 eluted with retention times of 15.3 min and 17.2 min, respectively. The separated diastereomers were collected and the solvent was removed in vacuo to afford (1*R*,2′*R*)-4 and (1*S*,2′*R*)-4 (90% recovery). HPLC analysis of the separated diastereomers showed that the faster eluting diastereomer ((1*R*,2′*R*)-4) was ≥99% pure and the slower eluting diastereomer ((1*S*,2′*R*)-4) was 93% diastereomerically pure. This procedure routinely afforded (1*R*,2′*S*)-4 of ≥99% diastereomeric purity and (1*S*,2′*S*)-4 of 93–98% diastereomeric purity.

(1*R*,2′*R*)-4: $[\alpha]^{23}_{D}$ −22.8° (*c* 1.29, CH_2Cl_2); $[\alpha]^{23}_{578}$ −24.3° (*c* 1.29, CH_2Cl_2).

(1*S*,2′*R*)-4: $[\alpha]^{23}_{D}$ −43.8° (*c* 1.17, CH_2Cl_2, 95% optically pure), calcd $[\alpha]^{23}_{D}$ −46.1° (*c* 1.17, CH_2Cl_2); $[\alpha]^{23}_{578}$ −45.4° (*c* 1.17, CH_2Cl_2, 95% optically pure), calcd $[\alpha]^{23}_{578}$ −47.8° (*c* 1.17, CH_2Cl_2).

5-(Benzyloxy)-3-((*tert*-butyloxy)carbonyl)-1-(hydroxymethyl)-8-methyl-1,2-dihydro-3*H*-pyrrolo[3,2-*e*]indole (2). The diastereomeric esters (1*R*,2′*R*)-4 (≥99% diastereomerically pure) and (1*S*,2′*R*)-4 (98% diastereomerically pure) were independently subjected to lithium hydroxide promoted ester hydrolysis by treatment of a solution of the ester in 0.5 mL of THF/CH_3OH (3:2) with a solution of aqueous lithium hydroxide (0.1 mL of 4.0 N, 0.4 mmol, 5 equiv). The reaction mixtures were stirred 3 h at 20 °C. The solvents were removed in vacuo and the residues were chromatographed (0.5 × 10 cm SiO_2, 0–10% EtOAc–CH_2Cl_2 gradient elution) to afford (+)-(1*R*)-2 (25.8 mg, 76% from (±)-2) and (−)-(1*S*)-2 (27.9 mg, 83% from (±)-2) as colorless oils. ^1H NMR ($CDCl_3$, 300 MHz) δ 8.10 (br s, 1 H, NH), 7.72 (br s, 1 H, C4-H), 7.5–7.35 (m, 5 H, $PhCH_2O$), 6.92 (s, 1 H, C7-H), 5.21 (s, 2 H, $PhCH_2O$), 4.3–3.65 (m, 6 H, C1-H, C2-H, CH_2OH and CH_2OH), 2.41 (s, 3 H, CH_3), 1.59 (s, 9 H, CO_2-*t*-Bu); IR (neat) ν_{max} 3428, 3334, 2928, 1684, 1588, 1503, 1453, 1419, 1405, 1367, 1345, 1320, 1242, 1171, 1141, 1029, 896 cm^{-1}; EIMS, *m/e* (relative intensity) 408 (M^+, 24), 352 (28), 321 (75), 231 (44), 187 (20), 186 (15), 91 (base), 57 (58); CIMS (isobutane), *m/e* (relative intensity) 409 (37), 308 (31), 391 (6), 353 (base), 309 (11); HRMS, *m/e* 408.2052 ($C_{24}H_{28}N_2O_4$ requires 408.2049).

(+)-(1*R*)-2: $[\alpha]^{23}_{D}$ +7.0° (*c* 0.63, CH_2Cl_2).

(−)-(1*S*)-2: $[\alpha]^{23}_{D}$ −7.1° (*c* 0.74, CH_2Cl_2).

Acknowledgment. We gratefully acknowledge the financial support of the National Institues of Health (CA 41986), the Alfred P. Sloan Foundation, and Purdue University (David Ross Fellowship to R.S.C.). We thank Dr. Robert C. Kelly and Dr. Martha A. Warpehoski (The Upjohn Company) for providing preprints of their work (ref 8 and 9), for comparative rotations of (+)- and (−)-14, and for many helpful discussions.

Supplementary Material Available: Spectroscopic characterization of 3, 10, and 13 (2 pages). Ordering information is given on any current masthead page.

Formation of 9,10-Diphenylanthracene Radical Cation from Friedel–Crafts Alkylation Reactions. Absence of the Triphenylsilyl Radical

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In our continued interest in ESR studies of triphenylmethyl radicals,[1] we noticed that although the triphenylmetal radicals of group IV elements (M = C, Si, Ge, Sn)[2] have been well studied, the ESR spectrum of $Ph_3Si^{\bullet}$ in solution has not been reported.[3] We demonstrate that well-resolved ESR spectra recorded from mixtures of

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[1] (a) Trapp, C.; Wang, C. S.; Filler, R. *J. Chem. Phys.* **1966**, *45*, 4372. (b) Kulkarni, S. V.; Trapp, C. *J. Am. Chem. Soc.* **1969**, *91*, 191. (c) Kulkarni, S. V.; Trapp, C. *J. Am. Chem. Soc.* **1970**, *92*, 4801. (d) Trapp, C.; Kulkarni, S. V. *J. Phys. Chem.* **1984**, *88*, 2704. (e) Kulkarni, S. V.; Trapp, C. *Magn. Reson. Chem.* **1986**, *24*, 5.

[2] Hudson, A.; Jackson, R. A.; Rhodes, C. J.; del Vecchio, J. *J. Organomet. Chem.* **1985**, *280*, 173 and references therein.

[3] Only a poorly resolved spectrum attributed to unsubstituted $Ph_3Si^{\bullet}$ has been reported in X-ray-irradiated single crystals of Ph_3SiH, see: Geoffroy, M.; Luchen, E. A. C. *Helv. Chim. Acta* **1970**, *53*, 813.

0022-3263/88/1953-0698$01.50/0

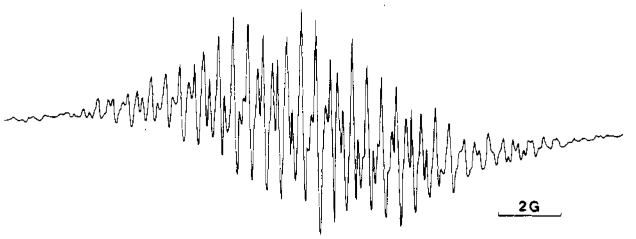


Figure 1. ESR spectrum from the Ph_3SiH–$CHCl_3$–$AlCl_3$ system.

Table I. ESR Spectral Data

mixture	data
Ph_3SiH–$CHCl_3$–$AlCl_3$	$g = 2.0027$
	$a(1) = 2.63$G (4 H)
	$a(2) = 1.23$G (4 H)
	$a(3) = 0.45$G (10 H)
C_6H_6–$CHCl_3$–$AlCl_3$	$g = 2.0027$
	$a(1) = 2.62$G (4 H)
	$a(2) = 1.25$G (4 H)
	$a(3) = 0.45$G (10 H)
C_6H_6–CCl_4–$AlCl_3$	$a = 2.0026$
	$a(1) = 2.607$G (4 H)
	$a(2) = 1.244$G (4 H)
	$a(3) = 0.474$G (10 H)

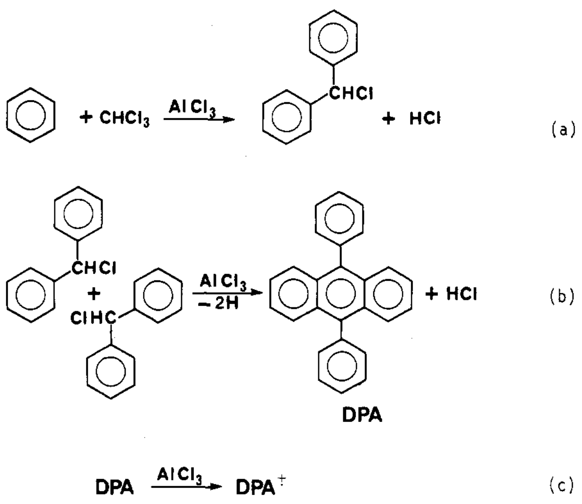
Ph_3SiX (X = H, OH) and $AlCl_3$ in chloroform, which have been attributed to the triphenylsilyl radical,[4] are in fact due to the 9,10-diphenylanthracene radical cation.

The ESR spectrum of the Ph_3SiH–$CHCl_3$–$AlCl_3$ system is shown in Figure 1. Essentially identical spectra were obtained from the C_6H_6–$CHCl_3$–$AlCl_3$ system and from the C_6H_6–CCl_4–$AlCl_3$ system as shown in the supplementary material.[5] All the radicals are identified as the 9,10-diphenylanthracene (DPA) radical cation $DPA^{\bullet+}$ by computer simulation[5] and by comparison with the reported spectra.[6] The pertinent ESR spectral parameters are summarized in Table I. Hyperfine splittings $a(1)$ are assigned to the 1, 4, 5, and 8 protons;[7] $a(2)$ to the 2, 3, 6, and 7 protons; and $a(3)$ to the 10 protons in the two phenyl rings in $DPA^{\bullet+}$. This assignment for $DPA^{\bullet+}$ has been confirmed by an ENDOR study.[6d]

We have not observed the satellites[2] due to ^{29}Si in the Ph_3SiX (X = H, OH)–$CHCl_3$–$AlCl_3$ system. This, in itself, is a good indication that the radicals from these systems are not the silicon-centered radical $Ph_3Si^{\bullet}$, which might have been expected. The preparation of the unsubstituted triphenylsilyl radical in solution may be difficult.[2]

Friedel–Crafts alkylation reaction systems consist of an aromatic compound, an alkyl halide, and a Lewis acid as the three essential components.[8] Aromatic rings are contained in triphenylsilyl compounds, and both the Lewis acid $AlCl_3$ and the alkyl halide $CHCl_3$ or CCl_4 have been used. Thus, the present radical production processes are similar to Friedel–Crafts reactions.

Scheme I



In Ph_3SiH–$CHCl_3$–$AlCl_3$ and Ph_3SiH–CCl_4–$AlCl_3$ systems, the color changes and evolution of hydrogen chloride gas are quite similar to the reaction involving benzene. Furthermore, the fact that the radical generation processes are not influenced by the variation of X (X = H, OH) in the systems containing Ph_3SiX[4] nor by the substitution of benzene for Ph_3SiH is a further indication that the relevant reactions are determined by their common properties. All these systems contain aromatic phenyl rings, which are substrates for the Friedel–Crafts reactions. Moreover, certain Friedel–Crafts reactions are known to generate radicals.[9]

The proposed mechanism of these reactions can be represented by Scheme I using the system involving benzene and chloroform as an example. Step a is the usual Friedel–Crafts type alkylation process with the evolution of HCl gas.[8] In the Ph_3SiH–$CHCl_3$–$AlCl_3$ system, chloroform reacts with triphenylsilane to give benzyl chloride. The condensation step (b) produces DPA. This kind of ring-closure reaction involving the elimination of two HCl molecules and two hydrogen atoms has been previously noticed in some systems.[9b,10,11] The single-electron transfer from hydrocarbons to $AlCl_3$ (step c) has been used to generate radical cations from their parent compounds.[6b,10,12]

The yellow triphenyl carbonium cation is formed from C_6H_6–$CHCl_3$–$AlCl_3$ and C_6H_6–CCl_4–$AlCl_3$ reaction systems.[8] The yellow color in the Ph_3SiH–$CHCl_3$–$AlCl_3$ system indicates the presence of the triphenylcarbonium cation in this system also, but the triphenylsilyl radical is absent. The radical cations generated are quite persistent and accumulate so as to deeply color the mixture.[13]

Moreover, we can obtain high-quality spectra in the originally air-saturated systems. The vigorous evolution of gaseous HCl from the Friedel–Crafts type reactions efficiently removes the dissolved oxygen in the solutions and protects the reaction systems from the influence of atmospheric oxygen. Additional degassing is not necessary.

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(5) See the paragraph at the end of the paper about the supplementary material.

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(7) The numbering system is the same as that usually adopted.[6]

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(10) Rooney, J. J.; Pink, R. C. *Proc. Chem. Soc., London* **1961**, 142.

(11) Balaban, A. T.; Nenitzescu, C. D. *Friedel-Crafts and Related Reactions*; Olah, G. A., Ed.; Wiley-Interscience: New York, 1964; Vol. II, Part 2, p 979 (especially p 1025).

(12) Courtneidge, J. L.; Davies, A. G. *Acc. Chem. Res.* **1987**, *20*, 90.

(13) It is then questionable that the appearance of a yellow color in these systems can be used as a qualitative test for the presence of phenyl compounds as described in many organic chemistry texts, for example, see ref 8.

Usually, radical cations are much more difficult to prepare and, hence, are less frequently reported than radical anions.[12] The present reactions are a simple preparation, which is quite different from the method of chemical oxidation[6a-d] and anode electrolysis[6e] usually used to obtain the radical cation. Using the Friedel–Crafts reaction, we are able to observe several new aromatic radicals, which will be described in detail subsequently.

Experimental Section

All reagents were Aldrich products with the highest possible purities (usually with "Golden" labels) without further purification.

ESR spectra were recorded from a Varian E-109 X band sepctrometer at room temperature. A phenyl compound triphenylsilane (0.05 g) or benzene (10 drops), a polychloromethane (10 drops), and aluminum chloride (0.05 g) were mixed in a standard 4-mm o.d. quartz ESR tube. Immediately, a bright yellow color appeared in the originally colorless liquid phase, accompanied by the evolution of hydrogen chloride gas. ESR signals appeared when a dark color developed.

Registry No. DPA, 1499-10-1; $DPA^{\bullet+}$, 34480-04-1; Ph_3SiH, 789-25-3; $CHCl_3$, 67-66-3; $AlCl_3$, 7446-70-0; C_6H_6, 71-43-2; CCl_4, 56-23-5; Ph_2CHCl, 90-99-3.

Supplementary Material Available: ESR spectra from the systems C_6H_6–$CHCl_3$–$AlCl_3$ and C_6H_6–CCl_4–$AlCl_3$ and a computer-simulated spectrum (3 pages). Ordering information is given on any current masthead page.

Concerning Enhanced Reactivities of α-Keto Hydroperoxides

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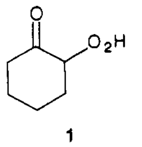
Attempts to kinetically model the $Co(OAc)_2$/NaBr-catalyzed O_2 oxidation of cyclohexanone, an oscillating reaction,[1] suggested the presence of an oxidizing species for Co^{2+} more powerful than an ordinary hydroperoxidde. Hydroperoxides that can form internal hydrogen bonds seem to be more active than ordinary hydroperoxides. Peracids, 2-hydroperoxy-1,1,1,3,3,3-hexafluoro-2-propanol,[2] and a variety of carbonyl-containing hydroperoxides,[3] for example, are useful olefin epoxidizing agents, whereas simple hydroperoxides are not.[4] One logical candidate as the species responsible for the enhanced oxidation of Co^{2+} in the oscillating cyclohexanone oxidation reaction therefore is 2-hydroperoxycyclohexanone (1), an intermediate claimed to be obtainable in the oxidation of cyclohexanone under a variety of conditions.[6] Attempts to prepare 1 using a variety of literature methods[6-8] afforded impure materials with low hydroperoxide content when assayed by NaI titration. Liquid chromatographic separation of peroxide compounds produced by radical-initiated (*t*-BuOOCO-*t*-Bu) O_2 oxidation of neat cyclohexanone at 80 °C afforded no compounds with NMR signals appropriate for 1. α-Keto hydroperoxide 1 therefore appears to be quite unstable, and its oxidation chemistry could not be studied directly. In order to test the effectiveness of 1 as an oxidant for Co^{2+}, α-keto hydroperoxides 2–4[7,8] were prepared by low-temperature O_2 oxidation of ketone potassium enolates. Di-isopropyl ketone hydroperoxide 2 was chosen for detailed study because it could be obtained in highest purity. The relative reactivities of 2 and simple hydroperoxides with Co^{2+} were studied. The surprising results of the study led us to examine the relative reactivities of the hydroperoxides with triphenylphosphine, iodide ion, and olefins in both basic and inert solvents.



1

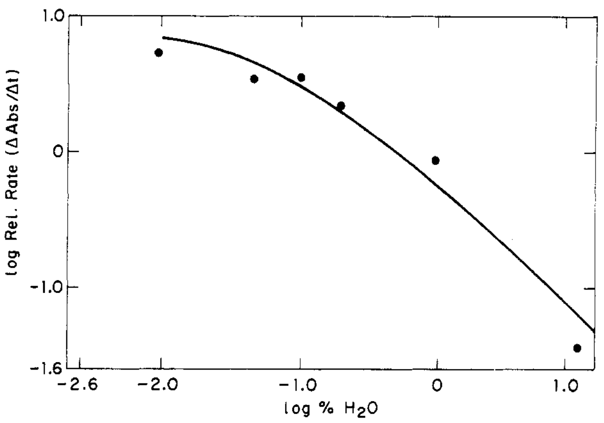
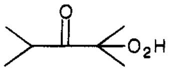


Figure 1. Dependence of relative rates of reactions, between Co^{2+} and diisopropyl ketone hydroperoxide (2), in dry HOAc at 40 °C, on concentration of added H_2O.



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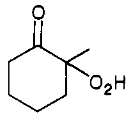

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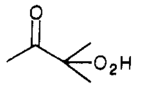

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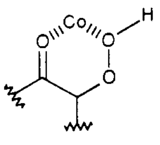
Results and Discussion

In dry HOAc at 40 °C, 2 rapidly converts $Co(OAc)_2$ to Co^{3+}, whereas unsubstituted primary, secondary, or tertiary alkyl hydroperoxides react at least 500 times slower (Table I). Conversely, under the same conditions, 2 does not reduce Co^{3+} to Co^{2+}, while the same unsubstituted alkyl hydroperoxides rapidly convert Co^{3+} to Co^{2+}. The presence of H_2O in HOAc decreases the reactivity of 2 with Co^{2+} (Figure 1). Similarly, H_2O is known to decrease the reactivity of peracids with Co^{2+} in HOAc.[9] The enhanced rate of oxidation of Co^{2+} in acetic acid by 2 might be explained by a chelate such as 5. The diminished reactivity observed upon addition of water, a more basic solvent, is consistent with this hypothesis. In decalin at



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[1] To be published elsewhere.

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[4] With one exception,[5] involving t-$C_4H_9O_2H$, significant amounts of olefin epoxidation by unsubstituted alkyl hydroperoxides without metal catalysis have not been reported.

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