Mechanism of the Reduction of Ketones by Trialkylsilane. Hydride Transfer, SET-Hydrogen Atom Abstraction, or Free Radical Addition[1]

D. Yang[2] and D. D. Tanner*

Department of Chemistry, University of Alberta, Edmonton, Alberta T6G 2G2, Canada

Received December 3, 1985

The mechanism for the fluoride ion catalyzed reduction of ketones with phenyldimethylsilane was investigated. With reactive substrates (i.e., α,α,α-trifluoroacetophenone) the silane can act as a reducing agent to give, upon hydrolysis, moderate yields of the corresponding alcohol. The pentavalent anion formed from the silane and fluoride anion is, as had been previously reported, an excellent hydride reducing agent and even with moderate acceptors (i.e., α-fluoroacetophenone and cyclopropyl phenyl ketone) the anion acts as a SET reagent to give minor amounts of radical derived reduction products.

The reduction of aldehydes and ketones with trialkylsilanes has been recognized as a useful synthetic method for a number of years.[3] The reduction is catalyzed by trifluoroacetic acid and gives excellent yields of the corresponding alcohol. A heterolytic hydride transfer process has been proposed as the mechanism leading to reduction. Quite recently the reduction was shown to be catalyzed by fluoride ion under neutral conditions.[4] Again, the mechanism for the reduction was reported as proceeding by a hydride transfer process, this time catalyzed by the formation of pentavalent silicon (see Scheme I). Presumably the pentavalent anion acts as an excellent hydride transfer agent. The substrates reported by these workers consisted of a series of α-substituted ketones substituted by a variety of electron-withdrawing groups. The corresponding alcohols were obtained in excellent yields without the complication of the reduction of the substituents.

Recently we reported the results of an attempt to differentiate between two processes for reduction: single electron transfer (SET)–hydrogen atom abstraction, and hydride transfer.[5,6] Three aromatic aliphatic ketones, α,α,α-trifluoroacetophenone (I), α-fluoroacetophenone (II), and cyclopropyl phenyl ketone (III), have been used as model compounds to study the mode of carbonyl reduction by trialkyltin hydrides. With triphenyltin hydride the substrates underwent an uninitiated homolytic reaction. The uninitiated reduction of the fluorinated ketone showed both homolytic and heterolytic reactivity. The homolytic reactions were initiated by SET, and the propagation sequence, likewise, contained an electron transfer step.

Since trialkysilanes show both homolytic[7,8] and hetrolytic[9,10] reactivity, as do their congeners, the stannanes, it was not unreasonable to investigate the reactivity of the silanes with the mechanistic probes previously used to establish the mechanism for the tin hydride reductions.

Results and Discussion

The reduction of α,α,α-trifluoroacetophenone (I) was carried out with phenyldimethylsilane in solvent Me_2SO (62 °C 35 h) and upon hydrolysis it was found that 22% of the ketone had been converted to its corresponding alcohol IV. When tetra-*n*-butylammonium fluoride (5%) was added the reaction was indeed catalyzed, as 86% of alcohol IV was realized. The uncatalyzed reaction was not initiated by the addition of AIBN. Neither the fluoride ion catalyzed reaction nor the uncatalyzed reduction was inhibited by *p*-dinitrobenzene (DNB). The reaction mixture with added DNB turned green, and although the yield of alcohol IV (80%) was not greatly affected, a diluted aliquot solution of this mixture showed an EPR spectrum which was identified as the 25-line spectrum (g = 2.0050) of the radical anion of DNB.[11]

The same spectrum was obtained when the ketone I was omitted; however, when TBAF was omitted, no EPR signal could be obtained.

The observation that the trifluoro ketone underwent reduction without catalysis was consistent with either a homolytic or heterolytic pathway. Although a silylenium ion, the intermediate inferred from a hydride transfer process, has not been demonstrated to be implicated in the reactions of silanes,[12] the catalysis of the reduction of ketone by trifluoroacetic acid implies such a species, see Scheme II. However, the uncatalyzed reaction of trimethylsilane and hexafluoroacetone has also been ration-

Scheme I

$$R_3SiH + F^- \rightleftharpoons R_3SiH(F)^- \quad (1)$$

$$R_3SiH(F)^- + R'_2C{=}O \longrightarrow R_3SiF + R'_2\overset{O^-}{\underset{|}{C}}H \quad (2)$$

$$R'_2\overset{O^-}{\underset{|}{C}}H + R_3SiF \rightleftharpoons R'_2CHOSiF(R)_3^- \quad (3)$$

$$R'_2CHOSi(R)_3F^- \longrightarrow R'_2CHOSi(R)_3 + F^- \quad (4)$$

Scheme II

$$R\overset{O}{\overset{\|}{C}}R + CF_3CO_2H \rightleftharpoons R\overset{OH^+}{\overset{\|}{C}}R + CF_3CO_2^- \quad (5)$$

$$Ph(CH_3)_2SiH + R\overset{OH^+}{\overset{\|}{C}}R \longrightarrow Ph(CH_3)_2Si^+ + R\overset{OH}{\overset{|}{C}}HR \quad (6)$$

Scheme III

$$R_3SiH + CF_3CO_2^- \longrightarrow R_3SiH(OCOCF_3)^- \quad (7)$$

$$R_3SiH(OCOCF_3)^- + R_2C{=}OH^+ \longrightarrow R_2CHOH + R_3SiOCOCH_3 \quad (8)$$

(1) Presented in part at the "Special International Symposium on Free Radicals", Lanzhou, The People's Republic of China, September 6–10, 1985.

(2) Visiting Scientist, Department of Chemistry, Lanzhou University, Lanzhou, The People's Republic of China.

(3) Kursanov, D. N.; Parnes, Z. N.; Loin, N. M. *Synthesis* **1974**, 633.

(4) Fujita, M.; Hiryama, T. *J. Am. Chem. Soc.* **1984**, *106*, 4629.

(5) Tanner, D. D.; Diaz, G. E.; Potter, A. *J. Org. Chem.* **1985**, *50*, 2149.

(6) Presented in part at "The 1984 International Chemical Congress", Honolulu, Hawaii, December 1984, Abstract 10G02.

(7) Jackson, R. A. *Adv. Free-Radical Chem.* **1969**, *3*, 231.

(8) Jackson, R. A. *Essays in Free-Radical Chemistry, Chem. Soc. Spec. Publ. No. 24*, **1970**, 295.

(9) Washburne, S. S. In *Silicon Compounds, Register and Review*; Petrarch Systems; Levittown, PA, 1982.

(10) Flemins, I. *Organic Silicon Chemistry* in Comprehensive Organic Chemistry, Pergamon Press: New York, 1979; Vol. 2, Chapter 13.

(11) Freed, J. H.; Fraenkel, G. K. *J. Chem. Phys.* **1964**, *40*, 1815.

(12) To date only one report of a silylenium ion intermediate in a solution-phase reaction has been reported, see: Lambert, J. B.; Schulz, W. J., Jr. *J. Am. Chem. Soc.* **1983**, *105*, 1671.

0022-3263/86/1951-2267$01.50/0

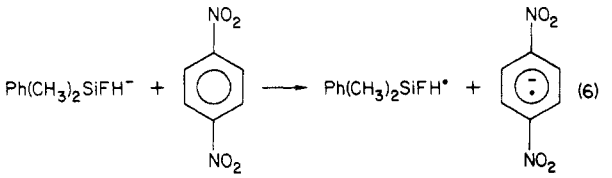
alized as proceeding by an intermediate complex zwitterion, V, which formed the addition product by an in-

$$Me_3SiHOC(CF_3)_2$$

V

tramolecular or intramolecular hydride transfer. Similarly, the acid-catalyzed reduction could conceivably proceed via a pentavalent intermediate, see Scheme III.

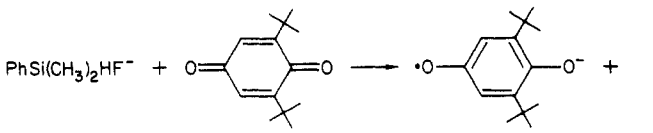
Since the silane fluoride ion complex showed an EPR signal with DNB, a homolytic pathway was considered for the ketone reduction. However, the uncatalyzed reduction was not initiated by AIBN nor inhibited by either oxygen or DNB. There appeared to be no evidence for the intermediacy of a silyl radical. As the reduction was catalyzed by fluoride ion, as previously reported,[4] and the catalyzed reaction was again apparently not inhibited by DNB, the only evidence for a radical process was the EPR signal obtained. The EPR spectrum of the given solution clearly showed the 25-line spectrum of the radical anion of DNB. Since the silane itself did not produce the radical ion when treated with DNB, it was apparent that the electron transfer was due to the interaction of the pentavalent silyl anion with DNB, eq 9.



(6)

Radicals Produced from $PhSi(CH_3)_2H$ and TBAF. Since the pentacovalent anion can transfer an electron to DNB, the mixture of the silane and TBAF (5%) was added to another acceptor, 2,6-di-*tert*-butylbenzoquinone (DTBQ), which also acts as an efficient silyl radical trap.[13] A green stable radical product (VI) was formed. The radical showed a three-line (1:2:1) EPR spectrum (a^H = 1.95 G, g = 2.00496 G), see Figure 1. The spectrum was that of the semiquinone of DTBQ (VII). The structure of the radical was assigned to VII since an identical spectrum (g = 2.00496 G, a^H_m = 1.95 G) was obtained from the electrolysis of a Me_2SO solution of DTBQ containing tetra-*n*-butylammonium perchlorate as the electrolyte.

As expected a mixture of the silane and DTBQ did not give an EPR signal in the absence of TBAF, confirming the suggestion that the pentavalent anion was the SET reagent (eq 10). Furthermore, since no evidence had been



VII

$$[PhSi(CH_3)_2\dot{H}F] \quad (10)$$

obtained for a silyl radical intermediate, the fact that the spin–trap addition product, VI, was not formed during the reaction was additional evidence for its absence.[14]

Reduction of α-Haloacetophenones. The reduction of these substrates have been used as a diagnostic probe to differentiate between the two mechanisms leading to reduction;[5,15] SET–hydrogen atom abstraction (A) and hydride transfer (B), see Scheme IV.

The reduction of α-fluoroacetophenone (II) with the silane–TBAF reagent (40 °C, 12 h) yielded two products,

(13) Chen, K. S.; Foster, T.; Wan, J. K. S. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1288.

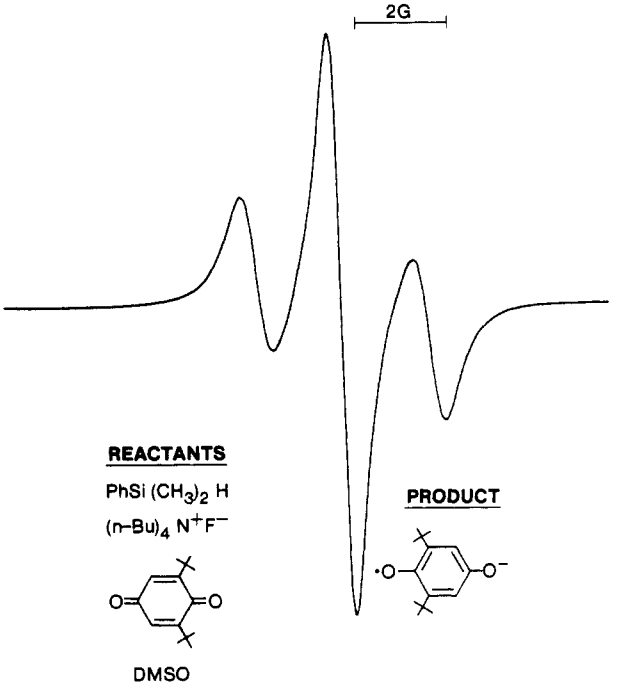
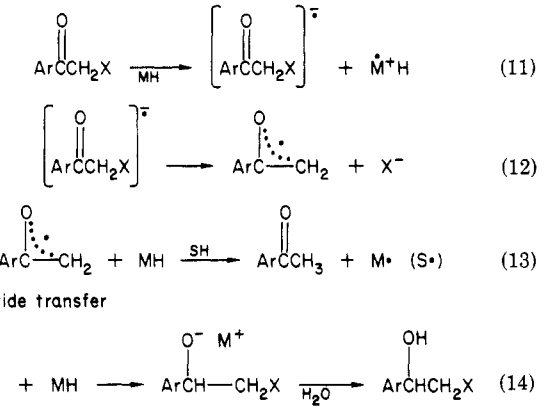


Figure 1. EPR spectra of 2,6-di-*tert*-butylbenzosemiquinone generated from the SET reaction of DTBQ with phenyldimethylsilane–TBAF in Me_2SO.

Scheme IV

(A) SET-hydrogen abstraction

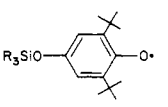


(B) hydride transfer

1-phenyl-2-fluoroethanol (VIII) (73–89%) and acetophenone (0.6–3.5%). The formation of acetophenone could be eliminated by the addition of small amounts of dinitrobenzene.

The observation that acetophenone was formed during the reduction was an indication that a SET–hydrogen atom abstraction sequence had taken place, since the reduction of this substrate by a hydride transfer process yields only

(14) The spin adducts of a number of silyl radicals with DTBQ have been reported, see ref 13. The coupling constants, a_n^H, reported for the adducts were found to be considerably smaller than those reported for the semiquinone itself, e.g.,



VI

R = CH_3 a_n^H = 1.12 g
R_2 = Ph a_n^H = 1.18 g

(15) (a) Tanner, D. D.; Diaz, G. E.; Wong, K.; Lane, P.; Urasaki, I. Abstracts, The 1984 International Chemical Congress of Pacific Bases Societies, Honolulu, Hawaii, December, 1984, No. 10G02. (b) Wong, K. C. O. M.Sc. Dissertation; University of Alberta, 1985.

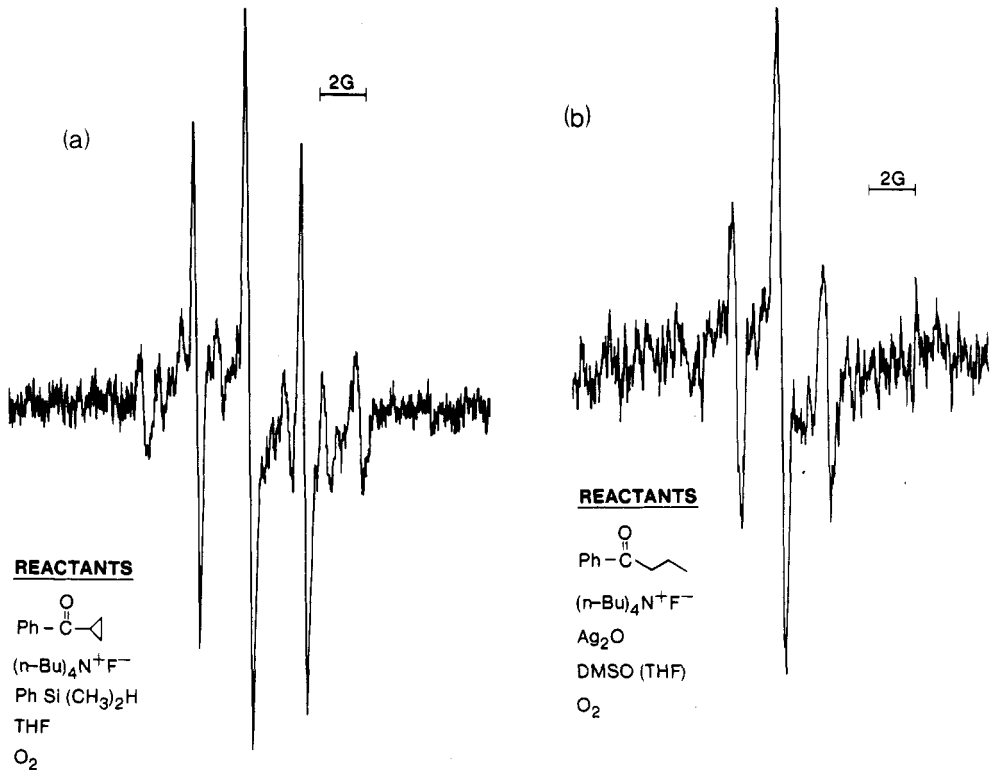


Figure 2. EPR spectra (a) generated from phenyl cyclopropyl ketone and (b) generated from butyrophenone.

fluoro alcohol VIII, whereas the two-step process yields acetophenone directly. Apparently the hydrogen atom transfer with silane does not compete favorably with the hydride transfer from the pentavalent silyl anion since only a small amount of defluorination was found. Acetophenone is most likely formed in a very short chain process. Nevertheless, small amounts of DNB efficiently interfere with the electron transfer and eliminate even this small amount of radical product.

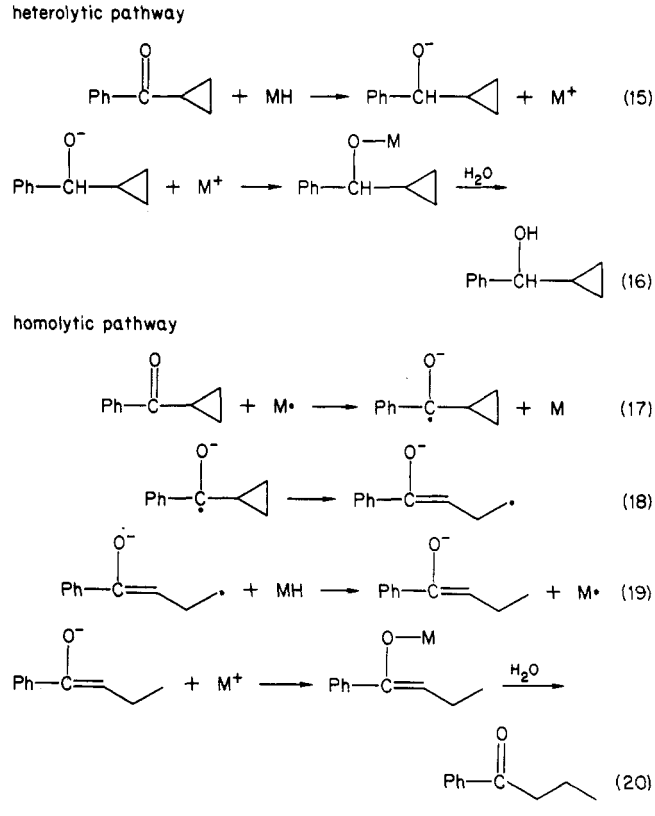
Reduction of Phenyl Cyclopropyl Ketone (III). Another ketone, which has been used as a mechanistic probe to examine the possibility of differentiating between heterolytic and homolytic pathways for reduction, is cyclopropyl phenyl ketone. If reduced by the hydride transfer mechanism it yields phenylcyclopropylcarbonol, while the homolytic pathway, proceding by a ketyl intermediate, yields open chain phenyl propyl ketone,[5,15,16] see Scheme V.

The substrate III was allowed to react with the silane–TBAF reagent. The reaction (40 °C, 12 h) turned from light yellow to straw colored and, upon isolation, three products were detected in 52% yield. The products were identified by comparison of their GC–IR and GC–MS spectra as cyclopropylphenylcarbinol (IX), 4-chloro-1-phenyl-1-butene (X), and butyrophenone (XI). It was shown that X was formed during the hydrolysis of the alkoxysilane of IX with 1 M HCl. Butyrophenone was only formed in trace amounts (<1%). When the reaction was carried out in an EPR tube that had been degassed, no sign of an EPR signal could be detected; however, when the reaction vessel was not degassed, a very well defined spectra was observed.

The structural assignment for the radical responsible for the EPR spectra could not be made; however, a similar spectra could be obtained from the treatment of butyrophenone with TBAF and Ag_2O in the presence of atmospheric oxygen, see Figure 2.

Again, although only a minor part of the reaction proceeds by the ketyl pathway, SET from the petavalent silyl anion was observed.

Scheme V



Conclusions. With very good acceptors (i.e., α,α,α-trifluoroacetophenone) the silane can act as a reducing agent to give, upon hydrolysis, moderate yields of the corresponding alcohol. The pentavalent complex is, as had been previously reported, an excellent hydride reducing agent and even with moderate acceptors (i.e., α-fluoroacetophenone and cyclopropyl phenyl ketone) the anion acts as a SET reagent to give minor amounts of radical-derived reduction products.

Experimental Section

Materials. All of the volatile materials were checked for purity before use by GLPC (50-m SE-30 or 25-m FFAP glass capillary column) and were found to be of the purity quoted.

The standard, *p*-di-*tert*-butylbenzene (Aldrich Chemical Co.), was recrystallized from dichloromethane (>99.9%).

p-Dinitrobenzene (mp 122–124 °C), 2,6-di-*tert*-butyl-1,4-benzoquinone (>98% pure), mp 65.6–66.5 °C, and tetrabutylammonium fluoride (1 M in THF) were used as received (Aldrich Chemical Co.).

Phenyldimethylsilane (Petrarch Systems Inc.) (>99.8%) was used as supplied.

Dimethyl sulfoxide, Me_2SO (British Drug Houses), was purified by being passed through a column (80 cm) of neutral alumina (Camag 507-C). The Me_2SO was treated with potassium hydroxide for 3 h at 90 °C and distilled at reduced pressure.

α,α,α-Trifluoroacetophenone was prepared by treating trifluoroacetic acid with an ether solution of phenylmagnesium bromide.[17] Fractional distillation (69–70 °C (30 mm)) (lit.[18] bp 75 °C (37 mm)) gave the product in 58% yield: IR (neat) 5.78 (CO) μm; MS, *m/e* 174, 105 (>99.6%).

α-Fluoroacetophenone was prepared by treating fluoroacetyl chloride with benzene in the presence of aluminum trichloride.[19] Fractional distillation, bp 70–72 °C (1.5 mm) (lit.[19] bp 65–70 °C (1 mm)) gave the product in 81% yield: mp 26–27 °C (lit.[19] mp 27–28 °C); NMR ($CDCl_3$) δ 5.57 (d, 2 H, J = 47.5 Hz), 7.36–8.10 (m, 5 H); IR (neat) 5.86 (CO) μm; MS, *m/e* 183, 105.

Cyclopropyl phenyl ketone (Aldrich Chemical Co.) was redistilled, bp 90 °C (2.8 mm) (lit.[20] bp 121–123 °C (15 mm)) (>99.6%).

Instrumental Methods. GLPC Analysis. All quantitative values were determined by using standard calibration curves constructed using known mixtures of the authentic materials. The areas were determined by using a HP5840A GLPC terminal interfaced to a HP 5840A gas chromatograph fitted with a FID and a capillary injector. A 50-m SE-30 or a 25-m FFAP glass capillary column was used for the analytical separations.

GLPC/IR data were obtained on a Nicolet 7199 FT/IR spectrometer interfaced to a Varian 3700 gas chromatograph.

GLPC/MS data were obtained on a VG 7070E mass spectrometer fitted with a Visa 6000 gas chromatograph using a 30-m OV-351 glass capillary column. The spectrometer was interfaced to a VG11-250 data system.

EPR spectra were obtained on a BRUKER CR 400 spectrometer with a 100-KHz modulation and a VARIAN 12 in. magnet system with a fieldial regulator. The magnetic field and microwave frequency were monitored by a ALPHA 3009 NMR gaussmeter and a HPX532B microwave frequency meter.

Reduction of Ketones with Phenyldimethylsilane. In one branch of an H-tube was placed a Me_2SO solution of the ketone (0.17 M, 0.5 mmol) and phenyldimethylsilane (0.17 M, 10.5 mmol) and in the other branch was placed 0.5 mL of a 0.5 M THF solution of tetra-*n*-butylammonium fluoride, if the fluoride was to be added. The reaction vessel was degassed, by the freeze–thaw method, sealed, and thermostated at either 40 °C or 62 °C. After equilibration the solutions were mixed and allowed to react for the times indicated. The reaction mixture was treated with 10 mL of 1 N hydrochloric acid, and the organic material was extracted with dichloromethane. The organic solution was washed 3 times with water, dried over anhydrous sodium sulfate, and analyzed by GLPC, GLPC/MS, and GLPC/IR.

Control experiments showed that the organic material was not lost during the isolation procedure.

In the case of the reduction reactions of cyclopropyl phenyl ketone, the first-formed alkoxydimethylphenylsilane, upon hydrolysis, forms α-cyclopropylbenzyl alcohol. When this alcohol was treated with 1 N hydrochloric acid under the conditions of hydrolysis it could be converted to 1-phenyl-4-chloro-1-butene.

EPR of Reaction Mixtures with the Phenyldimethylsilane–TBAF Reagent. An H-tube constructed such that one branch of the tube was a quartz EPR tube was used as a reaction vessel. In one branch of the tube was placed a Me_2SO solution of *p*-dinitrobenzene (0.03 M, 0.05 mmol) and phenyldimethylsilane (0.13 M, 0.2 mmol), and in the other branch was placed a Me_2SO solution of TBAF in THF (0.03 M, 0.05 mmol). The reaction mixtures were degassed, sealed, and mixed at 23 °C. The ESR were carried out as quickly as possible. The procedure was used not only for DNB but for the spectrum obtained from silane and DTBQ. The spectrum obtained from the reaction of cyclopropyl phenyl ketone was obtained in the same manner, except that when no signal was observed the tube was opened to the atmosphere and subsequently the spectrum appeared almost immediately.

Registry No. I, 434-45-7; II, 450-95-3; III, 3481-02-5; IV, 340-04-5; VIII, 450-94-2; IX, 1007-03-0; X, 1794-47-4; trifluoroacetic acid, 76-05-1; phenyl bromide, 108-86-1; fluoroacetyl chloride, 359-06-8; benzene, 71-43-2; phenyldimethylsilane, 766-77-8; acetophenone, 98-86-2.

(16) Unpublished work from this laboratory.
(17) Dishart, K. T.; Levine, R. *J. Am. Chem. Soc.* **1956**, *78*, 2268.
(18) Simmons, J. H.; Ramler, E. O. *J. Am. Chem. Soc.* **1943**, *65*, 389.
(19) Bergmann, F.; Kalmus, A. *J. Am. Chem. Soc.* **1954**, *76*, 4137.
(20) Aldrich Catalog Handbook of Fine Chemicals, 1984–85.

Chemical Modification of Polystyrene Resins. Approaches to the Binding of Reactive Functionalities to Polystyrene Resins through a Dimethylene Spacer

Graham D. Darling and Jean M. J. Fréchet*

Department of Chemistry, University of Ottawa, Ottawa, Ontario, Canada K1N 9B4

Received November 21, 1985

By an appropriate sequence of simple and often quantitative chemical steps, reticulated bromopolystyrene or (chloromethyl)polystyrene can be modified to support any of hydroxy, halo, acyloxy, sulfonoxy, amino, sulfonamido, thio, phosphino, or other chemical groups on a two-carbon spacer extending from the insoluble matrix. This structural feature can enhance stability, reactivity, and/or selectivity in many applications of functionalized polystyrenes as reagents or catalysts. For example, *p*-lithiated polystyrene reacts with ethylene oxide to afford *p*-(2-hydroxyethyl)polystyrene free from grafted oligoethylene glycol. (2-Hydroxyethyl)polystyrene is tosylated rapidly and quantitatively by treatment with diisopropylamine and tosyl chloride in refluxing carbon tetrachloride while a similar reaction of the supported alcohol with tosyl chloride in a tertiary amine leads directly and quantitatively to the quaternary ammonium salt resin. Other simple procedures have been devised to transform the tosylated polymer into primary, secondary, or tertiary amines without overalkylation.

For three decades now,[1,2] cross-linked polystyrene resins carrying chemically reactive groups have proliferated in form and application, variously as photochemical, acylation, phase-transfer or other catalysts,[3] chemical reagents,[3]

0022-3263/86/1951-2270$01.50/0