REACTION OF SUBSTITUTED ACETOPHENONES WITH PENTAFLUOROPHENYLTRIMETHYLSILANE AND RELATED COMPOUNDS UNDER CONDITIONS OF NUCLEOPHILIC CATALYSIS

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In continuing the investigation of the study of reactions catalyzed by cyano anions, we found [1] that pentafluorophenyltrimethylsilane (I) undergoes addition at the carbonyl group (CG) of aldehydes, ketenes, and nonenolized ketones, in the presence of catalytic admixture of the complex KCN•18-crown-6 (II), with the formation of the corresponding adducts of 1:1 composition. In the case of the enolized acetophenone, the trimethylsilyl ether of the enol was obtained with a good yield. It seemed of interest, taking the substituted acetophenones as an example, to study the influence of steric and electronic factors on the course of the catalytic reactions under consideration. With this aim, the reactions of the silane (I) with substituted acetophenones, initiated by cyanide anions, were performed under comparable standard conditions. We showed that the reaction of the enolized 2,3,4,5,6-pentafluoroacetophenone (III) with an equimolar amount of the silane (I) leads to the formation of 1-pentafluorophenvl-1-(trimethylsiloxy)ethane (IV). The reaction of the ketone (III) proceeds slowly (6 months at $\sim 20^{\circ}$ C) in comparison with the nonfluorinated analog [1]. This can be explained by the marked decrease in the basicity of the CG owing to the electron-acceptor character of the polyfluoro aromatic ring [2]. In contrast, the reaction of the nonenolized α, α, α -trifluoroacetophenone (V) with the silane (I) under comparable conditions is completed in 10 min with the formation of l-phenyl-l-pentafluorophenyl-l-trimethylsiloxy-2,2,2-trifluoroethane (VI). This reaction is probably initiated by the cyanide anions which interact with the silane (I); the pentafluorophenyl anions are thereby generated. After this, the stages of the nucleophilic addition of the C_6F_5 anions at the CG of the ketone (V) and the regeneration of the C_6F_5 carbanions follow.

An attempt to carry out the reaction of the silane (I) with the very sterically hindered tertbutyl phenylketone (VII) was unsuccessful. Trimethylcyanosilane proved to be more reactive. Its reaction with the ketone (VII) leads to the O-trimethylsilylated cyanohydrin (VIII) [3]. It is known that the reaction of Me₃SiCN with carbonyl compounds is initiated both by electrophilic ZnI₂ and nucleophilic (cyanide anions) catalysts [4]. We observed the analogous situation in the reactions of α, α, α -trifluoro-2,4,6-trimethylacetophenone (IX) with the silane (I) and trimethylcyanosilane. The silane (I) does not react with the ketone (IX) (10 days at ~20°C), whereas the adduct (X) is formed in high yield in the reaction with Me₃SiCN under comparable conditions:



(2)

The sterically hindered 2,4,6-trimethylacetophenone (XI) appeared to be an interesting object of investigation. Its reaction with the silane (I), initiated by the complex (II) in ether at

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~20°C, proceeds with the formation of the silyl ether (XII) of the enol. The ketone (XI) reacts analogously with Me₃SiCH₂CN and Me₃SiCN, e.g.,



The mechanism of the formation of the silyl ethers of enols in the reactions of ketones with the silane (I) and Me₃SiCH₂CN was previously considered [1]. In regard to the reaction (3), it is unusual. It is known that trimethylcyanosilane is widely employed for the selective protection of the CG. Its reaction with ketones under the conditions of nucleophilic catalysis usually leads to 0-silylated cyanohydrins [4, 5]. The reaction (3) is the first example of the reaction of Me₃SiCN with a carbonyl compound, initiated by anions, proceeding with the formation of the silyl ether of an enol. Reactions including a stage of enolization are characteristic of the ketone (XI). Thus, the corresponding lithium enolate is formed in high yield by the reaction of the ketone (XI) with lithium diisopropylamide. The subsequent reaction of this enolate with Me₃SiCl leads to the formation of compound (XII) [6]. Moreover, it was noted several years ago in [7] that the ketone (XI) and other alkyl mesityl ketones react unusually with Grignard reagents with the formation of halomagnesium enolates. The study of their reactivity and the reaction mechanism continues [8-10]. We showed by the method of PMR that the silyl ether (XII) of the enol gives an equilibrium system with the equilibrium const K = 0.533 [cf. Eq. (4)], in THF at ~20°C after 8 h, in the reaction with acetophenone initiated by a catalytic amount of the complex (II).

$$-\underbrace{\begin{pmatrix} OSiMe_3 & O \\ -C=CH_2 + & -C-CH_3 & \stackrel{CN-}{\longleftarrow} & -\underbrace{\begin{pmatrix} O & OSiMe_3 \\ \parallel & -C-CH_3 + & -C-CH_2 \\ (XIII) & -C=CH_2 \end{pmatrix}}_{(XIII)} (4)$$

It was established that the equilibrium state of the system does not change in the temperature range of 20-60°C. A similar migration of the trimethylsiloxy fragment was previously postulated in the aldol condensation reactions of the silyl ethers of enols with carbonyl compounds. These reactions were initiated by fluoride anions [11]. The NH₂ fragment, besides the CG, was also subjected to attack in the reaction of p-aminoacetophenone (XIV) with the silane (I). The resulting p-trimethylsilylaminoacetophenone (XV) was isolated in 85% yield. The structure of the product (XV) was confirmed by the 29 Si NMR spectrum. Thus, the chemical shift of 1.30 ppm is characteristic of the SiN bond [12]

$$\begin{array}{c} O & OSiMe_{8} \\ H_{2}N - \swarrow - \overset{\parallel}{C}CH_{3} + 2Me_{3}SiC_{6}F_{5} \xrightarrow{CN-} Me_{3}SiNH - \swarrow - \overset{\parallel}{C} = CH_{2}. \end{array}$$

$$(5)$$

The reaction proceeds analogously in the case of m-aminoacetophenone. The fact that compound (XIV) and its m analog have readily silylated amino groups was confirmed by the reaction of diphenylamine with the silane (I) initiated by cyanide anions. The yield of diphenyl(trimethylsilyl)amine (XVII) was ~100%. The silane (I) reacts sufficiently readily with p- and mnitroacetophenones with the formation of 1-(4-nitrophenyl)-1-trimethylsiloxyethane (XVIII) and 1-(3-nitrophenyl)-1-trimethylsiloxyethane (XIX). It is known that the rate of the exchange of deuterium, initiated by bases in a series of p-substituted acetophenones, increases in the presence of acceptor substituents and decreases in the presence of donor substituents [13].

EXPERIMENTAL

The ¹H and ^{2°}Si NMR spectra were obtained on a Tesla BS-487C (80 MHz) instrument for solutions in CCl₄. The measurements of the chemical shifts of ^{2°}Si were carried out by the method of heteronuclear INDOR. The IR spectra were taken on a UR-20 instrument in a thin layer. The GLC analysis was performed on a Khrom-4 instrument with a katharometer. All the reactions were carried out in evacuated glass ampuls at 20°C. <u>1-Pentafluorophenyl-1-trimethylsiloxyethene (IV)</u>. A mixture of 3 g of 2,3,4,5,6-pentafluoroacetophenone (III), 2.70 g of the silane (I), 0.14 g of the complex KCN*18-crown-6 (II), and 35 ml of ether was stirred with a magnetic stirrer for 6 months. After distillation, 2.64 g (66%) of (IV) were isolated; the product had bp 86-88°C (10 mm) and $n_D^{2^\circ}$ 1.4367. Found: C 46.72; H 3.29; F 33.90; Si 4.87%. C₁₁H₁₁F₅OSi. Calculated: C 46.80; H 3.29; F 33.65; Si 4.95%. IR spectrum (ν , cm⁻¹): 847, 1250 (Me₃Si), and 1622 (C=C). PMR spectrum (δ , ppm): 0.27 singlet (9H, SiMe₃), 4.53 multiplet, and 4.78 doublet (2H, =CH₂, J = 1.85 Hz). δ^{2^9} Si 21.13 ppm.

<u>1-Pentafluorophenyl-1-phenyl-1-trimethylsiloxy-2,2,2-trifluoroethane (VI)</u>. A mixture of 3.00 g of (V), 4.14 g of (I), 0.13 g of (II), and 30 ml of MeCN was stirred for 10 min. We isolated 6.05 g (85%) of (VI) by distillation; the product had bp 83°C (0.5 mm) and n_D^{20} 1.4637. Found: C 49.67; H 3.66; F 36.02; Si 6.34%. C₁₇H₁₄F₈OSi. Calculated: C 49.28; H 3.41; F 36.68; Si 6.78%. IR spectrum (v, cm⁻¹): 840, 1250 (SiMe₃), and 1130-1200 (=CF, CF₃). PMR spectrum (δ , ppm): 0.003 singlet (9H, SiMe₃) and 7.34 singlet (5H, C₆H₅).

 $\frac{2-\text{Phenyl-}2-\text{trimethylsiloxy-}3,3-\text{dimethylbutyronitrile (VIII).} A \text{ mixture of } 3.00 \text{ g of}}{(\text{VII}), 1.83 \text{ g of Me}_3\text{SiCN}, 0.12 \text{ g of (II}), and 30 \text{ ml of THF was stirred for } 2 \text{ h. We isolated}} 4.57 \text{ g (95\%) of (VIII) by distillation; the product had bp 64°C (0.5 mm) and <math>n_D^{2^\circ}$ 1.4795. Found: C 68.98; H 8.93; N 5.20; Si 10.62%. C₁₅H₂₃NOSi. Calculated: C 68.91; H 8.87; N 5.36; Si 10.74%. IR spectrum (ν , cm⁻¹): 850, 890 (Me}_3Si), 1135 (SiOC), and 2230 (C \equiv N). PMR spectrum (δ , ppm): 0.13 singlet (9H, SiMe}_3), 0.98 singlet (9H, CMe}_3), and 7.33 multiplet (5H, C_6-H_5), δ^{2° Si 20.64 ppm.

Reaction of 2,4,6-Trimethyl- α, α, α -trifluoroacetophenone (IX) with the Silane (I). A mixtue of 3.00 g of (IX), 3.33 g of (I), 0.13 g of (II), and 25 ml of THF was stirred for 10 days. We isolated 2.0 g (98%) of tetrafluoropolyphenylene by filtration [14, 15], and the initial acetophenone (IX) recurred unchanged.

2-(2,4,6-Trimethylphenyl)-2-trimethylsiloxy-3,3,3-trifluoropropionitrile (X). The quantitative formation of (X), which was controlled by PMR spectroscopy, proceeds as a result of the reaction (THF, 20°C, 48 h) of 2.50 g of (IX) with 1.15 g of Me₃SiCN in the presence of 0.12 g of (II). However, distillation in vacuo (0.5 mm, bath temperature of 76-86°C) only succeeds in the isolation of 2.05 g of the mixture, containing 85% of (IX) and 15% of (X), having the bp 60-63°C (0.5 mm). The ratio of (IX) to (X) in the mixture was determined by the method of GLC. IR spectrum (ν , cm⁻¹): 840, 1250 (SiMe₃), and 1200 (CF₃). PMR spectrum (δ , ppm): 0.33 singlet, (9H, SiMe₃), 2.27 singlet (3H, p-CH₃), 2.58 singlet (6H, o-CH₃), and 5.39 singlet (2H, C₆H₂). Mass spectrum (m/z): 315 M⁺, 246 [M - CF₃]⁺, 225 [M - Me₃SiOH]⁺, and 147 [M - F₃CC(OSiMe₃)CN]⁺.

<u>Reaction of 2,4,6-Trimethylacetophenone (XI) with Me₃SiCN.</u> A mixture of 2.00 g of (XI), 1.22 g of Me₃SiCN, 0.12 g of (II), and 30 ml of THF was stirred with a magnetic stirrer for 6.5 months. We isolated 2.01 g (70%) of 1-(2,4,6-trimethylphenyl)-1-trimethylsiloxyethene (XII) by distillation; the product had bp 56°C (0.5 mm) and $n_D^{2°}$ 1.4935. Found: C 72.17; H 9.24; Si 10.26%. C₁₄H₂₂OSi. Calculated: C 71.73; H 9.46; Si 10.26%. IR spectrum (v, cm⁻¹): 850, 1250 (SiMe₃), 1011 (SiOC), and 1632 (C=C). PMR spectrum (δ , ppm): 0.15 singlet (9H, SiMe₃), 2.21 singlet (3H, p-CH₃), 2.25 singlet (6H, o-CH₃), 4.05 doublet, 4.49 doublet (2H, =CH₂, J = 0.5 Hz), and 6.01 singlet (2H, C₆H₂). $\delta^{2°}$ Si 15.5 ppm.

By analogy, 2.22 g (77%) of (XII) were isolated from 2.00 g of (IX), 2.96 g of (I), and 0.13 g of (II) (ether, 51 h).

 $\frac{4-N-Trimethylsilylaminoacetophenone (XV).}{g of (II), and 30 ml of MeCN was stirred for 7 h. We isolated 3.93 g (85%) of (XV) by distillation the product had bp 121°C (0.5 mm) and n_D^{2°} 1.5858. Found: C 63.52; H 8.24; N 6.81; Si 13.48%. C₁₁H₁₇NOSi. Calculated: C 63.72; H 8.27; N 6.76; Si 13.55%. PMR spectrum (<math>\delta$, ppm): 0.26 singlet (9H, SiMe₃), 2.40 singlet (3H, CH₃), 4.69 singlet (1H, NH), 6.64 doublet, and 7.71 doublet (4H, C₅H₄, J = 8.06 Hz). $\delta^{2°}$ Si 1.30 ppm.

 $\frac{1-(4-N-Trimethylsilylaminophenyl)-1-trimethylsiloxyethene (XVI).}{(XIV), 10.70 g of (I), 0.12 g of (II), and 30 ml of MeCN was stirred for 30 h. We isolated 5.24 g (85%) of (XVI) by distillation; the product had bp 102-103°C (0.5 mm) and <math>n_D^{20}$ 1.5238. Found: C 60.36; H 8.86; N 4.99; Si 19.62%. $C_{14}H_{25}NOSi_2$. Calculated: C 60.15; H 9.02; N 5.01; Si 20.10%. IR spectrum (ν , cm⁻¹): 830, 1250 (SiMe₃), 1020 (SiOC), 1602 (C=C), and 3390 (NH). PMR spectrum (δ , ppm): 0.24 singlet (18H, SiMe₃), 3.34 singlet (1H, NH), 4.13 doublet, 4.60 doublet (2H, =CH₂, J = 1.35 Hz), and 6.45-7.27 multiplet (4H, C₆H₄). δ^{29} SI was 16.8 (SiO) and 2.35 ppm (SiN).

Diphenylaminotrimethylsilane (XVII). A mixture of 2.00 g of diphenylamine, 3.44 g of (I), 0.10 g of (II), and 20 ml of THF was stirred for 2 h. After the recrystallization from hexane, we obtained 2.00 g (70%) of (XVII) with mp 44-45°C. The PMR spectrum (δ , ppm): 0.25 singlet, (9H, SiMe₃) and 6.84-7.33 multiplet (10 H, C₆H₅). δ^{29} Si 6.1 ppm.

 $\frac{1-(4-\text{Nitrophenyl})-1-\text{trimethylsiloxyethene (XVIII).}}{\text{g of (I), 0.12 g of (II), and 30 ml of MeCN was stirred for 24 h. We isolated 3.60 g (84%) of (XVIII) by distillation the product had bp 96-97°C (0.5 mm) and n²⁰ 1.5421. Found: C 55.62; H 6.51; N 6.16; Si 11.84%. C₁₁H₁₅NO₃Si. Calculated: C 55.69; H 6.37; N 5.90; Si 11.84%. IR spectrum (<math>\nu$, cm⁻¹): 860, 1250 (SiMe₃), 1025 (SiOC), and 1620 (C=C). PMR spectrum (δ , ppm): 0.33 singlet (9H, SiMe₃), 4.56 doublet, 5.07 doublet (2H, =CH₂, J = 2.25 Hz), and 7.77-8.05 multiplet (4H, C₆H₄), δ^{29} Si 20.13 ppm.

 $\frac{1-(3-\text{Nitrophenyl})-1-\text{trimethylsiloxyethene (XIX).}{\text{g of (I), 0.13 g of (II), and 30 ml of MeCN was stirred for 3 h. We isolated 3.30 g (82%) of (XIX) by distillation; the product had bp 82-83°C (0.5 mm) and n₀^{2°} 1.5254. Found: C 55.48; H 6.81; N 6.33; Si 11.61%. C₁₂H₁₅NO₃Si. Calculated: C 55.69; H 6.37; N 5.90; Si 11.84%. IR spectrum (<math>\nu$, cm⁻¹): 850, 1250 (SiMe₃), 1016 (SiOC), and 1622 (C=C). PMR spectrum (δ , ppm): 0.33 singlet (9H, SiMe₃), 4.52 doublet, 5.00 doublet (2H, =CH₂, J = 2.20 Hz), and 7.46-8.31 multiplet (4H, C₆H₄), δ^{29} Si 20.3 ppm.

CONCLUSIONS

1. The reactions of pentafluorophenyltrimethylsilane with substituted acetophenones, initiated by cyanide anions, can be significantly retarded or rendered as unrealizable under the influence of electronic (e.g., 2,3,4,5,6-pentafluoroacetophenone) and/or steric (α,α,α -tri-fluoro-2,4,6-trimethylacetophenone) factors.

2. A high yield of the respective silyl ether of the enol is formed instead of the expected O-trimethylsilylated cyanohydrin in the catalytic reaction of the sterically hindered 2,4,6-trimethylacetophenone with trimethylcyanosilane.

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