REACTIONS OF POLYFLUOROCARBONYL COMPOUNDS WITH PHENOLATES*

V. I. Dyachenko, A. F. Kolomets,
and A. V. Fokin

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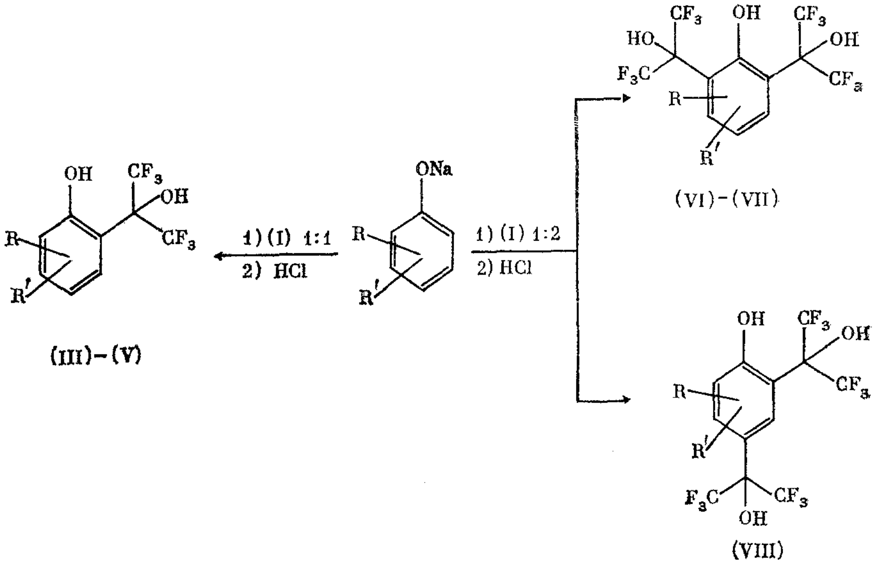
A characteristic feature of the uncatalyzed reactions of C-alkylated phenols with hexafluoroacetone (I) and methyl trifluoropyruvate (II) is that, depending on the total and local π-electron density of the aromatic ring, these reactions occur at about 20°C or upon heating above 120°C [2, 3]. Such strong C-nucleophiles as trihydroxybenzenes, resorcin, its ethers, and m-aminophenol derivatives are highly active in these conversions while pyrocatechol, hydroquinone, its ethers, alkylphenols, dialkylphenols, and unsubstituted phenol have low activity in this reaction.

In the present work, we studied the reactions of (I) and (II) with the sodium phenolates of phenols with low activity.

The reaction of anhydrous sodium m-cresolate with (I) in Freon 113 commences even at −30°C and is complete in 1 h with a quantitative yield of adduct (III). The reaction of (I) with sodium p-cresolate and sodium 2,3-xylenolate occur under the same conditions or at 80°C over 0.5 h to give exclusively the ortho-alkylation products (IV) and (V) in yields not below 90%.

The double C-alkylation of the phenolates occurs with excess (I). In this case, the phenolates of p-methoxyphenol and p-cresol give the ortho,ortho-dialkylation products (VI) and (VII) in yields above 80%. Sodium m-cresolate, in contrast to sodium p-cresolate, reacts with (I) to give the ortho,para-dialkylation product (VIII). In this case, the second C-alkylation is achieved with greater difficulty and the yield of (VIII) after heating at 100°C for 2 h does not exceed 50%.



(III)-(V)

(VI)-(VII)

(VIII)

R = H, R' = m-CH_3(III); R = H, R' = p-CH_3(IV); R = o-CH_3, R' = m-CH_3(V); R = H, R' = p-OCH_3(VI); R = H, R' = p-CH_3(VIII); R = H, R = m-CH_3(VIII).

In the case of sodium 2,3-xylenolate, the double C-alkylation by the action of (I) does not proceed at 100°C. Not only the ortho,ortho-dialkylation product (IX) but also

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*For previous communication, see ref. [1].

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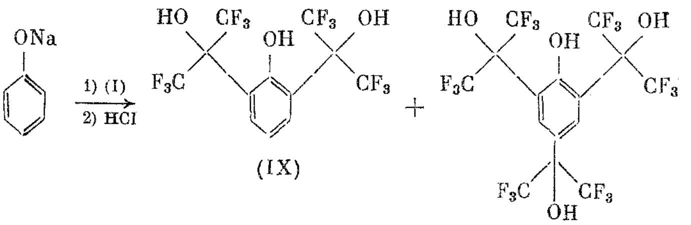
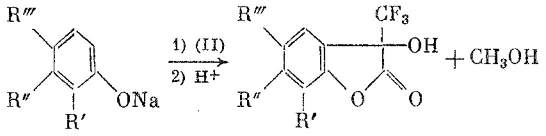
the triple C-alkylation product (X) is formed from sodium phenolate at 80-90°C over 2 h.



(IX)

(X)

Ketone (II) also C-alkylates sodium phenolates under mild conditions. In the absence of solvents, its reaction with phenolates is extremely exothermal. However, sodium p-cresolate and sodium 2,3-xylenolate unequivocally undergo ortho-alkylation by ketone (II) in benzene, in which homogeneous conditions are established after mixing of the reagents. These reactions are complete in 0.5 h at 80°C and the products after acid work-up were isolated as benzofuranones (XI) and (XII) in 80 and 95% yield, respectively.



(XI), (XII)

$R' = R'' = H$, $R''' = CH_3$ (XI); $R' = R'' = CH_3$, $R''' = H$ (XII).

The structures of the previously undescribed compounds, (V)-(X) and (XII) were confirmed by ^1H, ^{13}C, and ^{19}F NMR spectroscopy and elemental analysis. Products (III), (IV), and (XI) were identical to the samples described in previous work [3, 4].

EXPERIMENTAL

The NMR spectra were obtained at 20°C on a Bruker R-200SY spectrometer at 200.12 MHz for the ^1H NMR spectra, 50.31 MHz for the ^{13}C NMR spectra and 188.30 MHz for the ^{19}F NMR spectra relative to TMS as the internal standard for the ^1H and ^{13}C NMR spectra and CF_3CO_2H as the external standard for the ^{19}F NMR spectra. The R_f values were given for Kavalier Silufol UV-254 plates with elution by 1:3 acetone:CCl_4 and detection by UV light. Products (IV) and (VII) were described in our previous work [1].

2-(α-Hydroxyhexafluoroisopropyl)-5-methylphenol (III). A sample of 8.3 g (I) was condensed into a glass ampul containing 5.2 g anhydrous m-cresolate and 25 ml Freon 113 cooled to −78°C. The ampul was sealed, warmed to 25°C, and maintained at this temperature for 1 h. The ampul was cooled to −78°C and opened. The reaction mass after warming was treated with 30 ml 10% hydrochloric acid. The organic layer was separated and the aqueous layer was extracted with two 15-ml portions of CCl_4. The organic layer and the extract were dried over $CaCl_2$ and passed through a layer of 40 × 100 silica gel. The solvent was evaporated to give 10.5 g (95.8%) (III), mp 81-82°C (from hexane) [3].

2-(α-Hydroxyhexafluoroisopropyl)-5,6-dimethylphenol (V) was obtained from 4.32 g sodium 2,3-xylenolate and 4.98 g ketone (I) under the conditions for the synthesis of (III) with completion of the reaction in 0.5 h at 80°C. The yield of (V) was 8.20 g (94.9%), mp 110-112°C (from hexane), $R_f = 0.50$. ^{13}C NMR spectrum (δ, ppm, J, Hz, in acetone): 153.72 (C^1), 139.22 (C^3), 124.95 (C^2), 123.33 (C^5), 122.08 (CF_3, $^1J_{C-F}$ 287.50), 110.07 (C^6), 79.08 (C^7, $^2J_{C-F}$ 31.02), 18.05 and 9.96 ($2CH_3$). Found, %: C 48.80, H 3.13, F 39.88. $C_{11}H_{10}F_6O_2$. Calculated, %: C 45.83, H 3.47, F 39.58.

2,6-Di(α-hydroxyhexafluoroisopropyl)-4-methoxyphenol (VI) was obtained from 4.38 g sodium p-methoxyphenolate and 11.62 g (I) under the conditions for the synthesis of (III). The reaction was completed in 1.5 h at 80-90°C. The yield of (VI) was 10.94 g (80%), mp 92-94°C, $R_f = 0.52$. PMR spectrum (α, ppm, in deuteroacetone): 9.13 br. s (3H, 3OH), 7.25 s (2H, H^3, H^5), 3.80 s (3H, CH_3), ^{19}F NMR spectrum (δ, ppm, in deuteroacetone): −3.9 s. Found, %: C 34.21, H 1.75, F 50.00. $C_{13}H_8F_{12}O_4$. Calculated, %: C 34.01, H 1.58, F 50.37.

2,4-Di-(α-hydroxyhexafluoroisopropyl)-5-methylphenol (VIII) and 2-(α-hydroxyhexafluoroisopropyl)-5-methylphenol (III). A mixture of 3.9 g sodium m-cresolate and 11.62 g (I) in 25 ml Freon 113 was heated in a sealed glass ampul at 100°C for 2 h. The ampul was cooled to −78°C and opened. The contents were treated with 30 ml 10% hydrochloric acid. The crystals formed were filtered off and dried over to P_2O_5 to give 5.5 g (41.7%) (VIII) mp 120°C, R_f 0.38. PMR spectrum (δ, ppm, deuteroacetone): 7.70 s (1H, H^3), 6.90 s (1H, H^6), 2.50 s (3H, CH_3). ^{19}F NMR spectrum (δ, ppm, in deuteroacetone): −4.00 s and −2.50 s (1:1). Found, %: C 35.40, H 1.69, F 52.29. $C_{13}H_8F_{12}O_3$. Calculated, %: C 35.46, H 1.82, F 51.82. The organic layer obtained by treatment of the reaction mass by the ordinary method gave 4.5 g (54.7%) (III), mp 81-82°C.

2,6-Di(α-hydroxyhexafluoroisopropyl)phenol (IX) and 2,4,6-tri(α-hydroxyhexafluoroisopropyl)phenol (X). A mixture of 2.34 g sodium phenolate and 11.62 g (I) in 30 ml Freon 113 was heated in a sealed glass ampul for 2 h at 80-90°C. The ampul was cooled at −78°C and opened. The contents after warming were treated with 30 ml 10% hydrochloric acid. The precipitate of (X) was filtered off and dried over P_2O_5. The organic layer of the filtrate was separated and cooled at −25°C to precipitate (IX). The yield of (IX) was 5.04 g (58.7%), mp 138-140°C (from benzene), R_f 0.51. ^{13}C NMR spectrum (δ, ppm, acetone): 156.08 (C^1), 129.69 (C^3, C^5), 121.86 (CF_3, $^1J_{C-F}$ 280.00 Hz), 119.06 (C^4), 115.11 (C^2, C^6), 79.07 (C^7, $^2J_{C-F}$ 31.01 Hz). Found, %: C 33.98, H 1.41, F 53.60. $C_{12}H_6F_{12}O_3$. Calculated, %: C 33.80, H 1.41, F 53.52.

The yield of (X) was 4.05 g (33.8%), mp 175-177°C (from benzene), R_f 0.45. PMR spectrum (δ, ppm, deuteroacetone): 9.10 br. s (3H, 3OH), 8.23 s (2H, H^3, H^5), 8.00 s (1H, OH). ^{19}F NMR spectrum (δ, ppm, in deuteroacetone): −3.4 br. s and −2.5 s (2:1). Found, %: C 30.37, H 1.03, F 57.98. $C_{15}H_6F_{18}O_4$. Calculated, %: C 30.41, H 1.01, F 57.77.

3-Hydroxy-5-methyl-3-trifluoromethyl-2(3H)benzo[b]furanone (XI). A mixture of 3.9 g finely ground sodium p-cresolate, 4.68 g (II), and 20 ml benzene was heated for 0.5 h at 80°C, cooled, and treated with 15 ml 10% hydrochloric acid. The organic layer was separated and the solvent was distilled off. The residue was heated at reflux for 1 h in 20 ml glacial acetic acid. The acid was eavporated in vacuum. The residue gave 5.57 g (80%) (XI), mp 95-97°C [3].

3-Hydroxy-6,7-dimethyl-3-trifluoromethyl-2(3H)benzo[b]furanone (XII) was obtained from 2.88 g sodium 2,3-xylenolate and 3.12 g (II) under the conditions for the synthesis of (XI). The yield of (XII) was 5.11 g (95%), mp 94-95°C (from hexane), R_f 0.48. ^{13}C NMR spectrum (δ, ppm, in acetone): 168.59 (C^2), 151.40 (C_a^7), 141.49 (C^6), 125.07 (C^4), 121.81 (CF_3, $^1J_{C-F}$ 282.5 Hz), 121.64 (C^5), 119.16 (C^7), 118.27 (C_a^3), 74.22 (C^2, $^2J_{C-F}$ 30.9 Hz), 17.81 and 9.64 ($2CH_3$). Found, %: C 53.28, H 3.10, F 23.30. $C_{11}H_9F_3O_3$. C 53.66, H 3.66, F 23.17.

CONCLUSIONS

Hexafluoroacetone and methyl trifluoropyruvate react under mild conditions with sodium phenolate, sodium alkoxyphenolates, sodium alkylphenolates, and sodium dialkylphenolates to give the ortho-alkylation and ortho,ortho-dialkylation products. In the case of sodium phenolate, the tri-C-alkylation product is also obtained.

The second C-alkylation of meta-substituted sodium phenolates was found to be difficult.

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