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SHORT COMMUNICATIONS

Convenient Synthesis of 1-Aryl-1-chloro-2,2,2-trifluoroethyl Isocyanates

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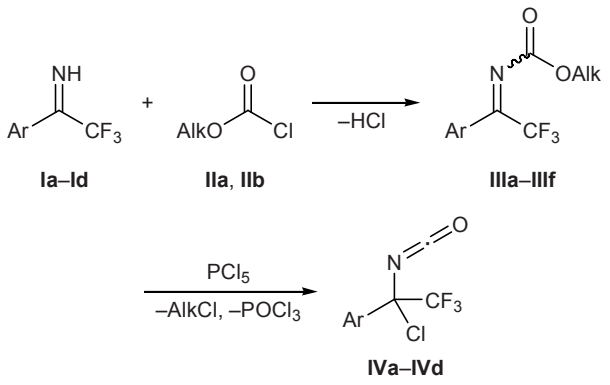
1-Aryl-1-chloro-2,2,2-trifluoroethyl isocyanates and their derivatives are convenient models for studying anionotropy [1] and effective electrophilic agents ensuring regioselective preparation of various trifluoromethyl-substituted heterocyclic systems [2, 3]. Fetyukhin et al. [4] described a procedure for the synthesis of 1-aryl-1-chloro-2,2,2-trifluoroethyl isocyanates via reaction of aryl trifluoromethyl ketone imines with trichloromethyl isocyanate, followed by thermal decomposition of *N*-(1-aryl-2,2,2-trifluoroethylidene)-*N*′-dichloromethylideneureas thus formed by the action of hydrogen chloride. During the last 30 years, this procedure was the only one providing preparation of 1-aryl-1-chloro-2,2,2-trifluoroethyl isocyanates; however, its considerable disadvantage is the necessity of using highly toxic and difficultly accessible trichloromethyl isocyanate which is obtained by thermolysis of trichloroacetyl azide [5].

We now propose a more convenient (from the preparative viewpoint) approach to 1-aryl-1-chloro-2,2,2-trifluoroethyl isocyanates. Acylation of aryl trifluoromethyl ketone imines **Ia**–**Id** with alkyl chloroformate **IIa** or **IIb** on heating in xylene at 140°C gives the corresponding alkyl 1-aryl-2,2,2-trifluoroethylidenecarbamates **IIIa**–**IIIf**. According to the ^{19}F NMR data, the reaction mixtures also contain up to 10–15% of adducts of **III** with hydrogen chloride, which can be decomposed by the action of triethylamine. The subsequent reaction of ethylidenecarbamates **IIIa**–**IIIf** with phosphorus pentachloride in boiling phosphoryl chloride leads to the formation of target isocyanates **IVa**–**IVd** in 65–86% yield.



Ia–Id **IIa**, **IIb** **IIIa–IIIf** **IVa–IVd**

I, **IV**, Ar = Ph (**a**), 4-FC_6H_4 (**b**), 4-MeC_6H_4 (**c**), 4-$MeOC_6H_4$ (**d**); **II**, Alk = Me (**a**), Et (**b**); **III**, Alk = Me, Ar = Ph (**a**), 4-FC_6H_4 (**b**); Alk = Et, Ar = Ph (**c**), 4-FC_6H_4 (**d**), 4-MeC_6H_4 (**e**), 4-$MeOC_6H_4$ (**f**).

It was formerly believed that aryl trifluoromethyl ketone imines can be acylated only with such strong electrophilic reagents as trichloromethyl isocyanate [4] or 1-chloroalkyl isocyanates [6] because of reduced nucleophilicity of the nitrogen atom. The proposed procedure for the acylation of aryl trifluoromethyl ketone imines at elevated temperature with less electrophilic alkyl chloroformates considerably extends the synthetic potential of this reaction and ensures relatively easy preparation of ethylidenecarbamates like **III**. The only previously known representative of such carbamates was synthesized by reaction of difficultly accessible 1-(4-bromobenzoyloxy)-2,2,2-trifluoro-1-phenylethyl isocyanate with methanol [7].

Alkyl 1-Aryl-2,2,2-trifluoroethylidenecarbamates IIIa–IIIf (*general procedure***).** A mixture of 0.02 mol of ketone imine **Ia**–**Id** and 0.025 mol of alkyl chloroformate **IIa** or **IIb** in 60 ml of xylene (isomer mixture) was heated for 15 h under reflux. The mixture was cooled, 0.55 ml (0.004 mol) of triethylamine was added, the mixture was stirred for 0.5 h, the precipitate was filtered off, the filtrate was evaporated, and the residue was purified by vacuum distillation.

Methyl 2,2,2-trifluoro-1-phenylethylidenecarbamate (IIIa). Yield 68%, bp 60–62°C (0.2 mm), n_D^{20} = 1.4775; published data [7]: bp 105–107°C (12 mm), n_D^{20} = 1.4785.

Methyl 2,2,2-trifluoro-1-(4-fluorophenyl)ethylidenecarbamate (IIIb). Yield 73%, bp 63–64°C (0.035 mm), n_D^{20} = 1.4636. IR spectrum, ν, cm^{-1}: 1760 (C=O), 1700 (C=N). ^1H NMR spectrum, δ, ppm: 3.78 s (3H, CH_3), 7.19–7.24 m (2H, H_{arom}), 7.70–7.75 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: –70.69 (CF_3), –105.84 (FC_6H_4). Found, %: F 30.74; N 5.88. $C_{10}H_7F_4NO_2$. Calculated, %: F 30.50; N 5.62.

Ethyl 2,2,2-trifluoro-1-phenylethylidenecarbamate (IIIc). Yield 68% , bp 89–92°C (0.09 mm), n_D^{20} = 1.4675. IR spectrum, ν, cm^{-1}: 1765 (C=O), 1695 (C=N). ^1H NMR spectrum, δ, ppm: 1.22 t (3H, CH_3), 4.25 q (2H, CH_2), 7.47–7.63 m (5H, H_{arom}). ^{19}F NMR spectrum: δ_F –70.44 ppm (CF_3). Found, %: F 22.95; N 5.83. $C_{11}H_{10}F_3NO_2$. Calculated, %: F 23.24; N 5.71.

Ethyl 2,2,2-trifluoro-1-(4-fluorophenyl)ethylidenecarbamate (IIId). Yield 72%, bp 56–58°C (0.035 mm), n_D^{20} = 1.4603. IR spectrum, ν, cm^{-1}: 1760 (C=O), 1700 (C=N). ^1H NMR spectrum, δ, ppm: 1.26 t (3H, CH_3), 4.26 q (2H, CH_2), 7.13–7.17 m (2H, H_{arom}), 7.74–7.19 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: –70.81 (CF_3), –106.23 (FC_6H_4). Found, %: F 28.64; N 5.13. $C_{11}H_9F_4NO_2$. Calculated, %: F 28.87; N 5.32.

Ethyl 2,2,2-trifluoro-1-(4-methylphenyl)ethylidenecarbamate (IIIe). Yield 77%, bp 70–72°C (0.035 mm), n_D^{20} = 1.4771. IR spectrum, ν, cm^{-1}: 1760 (C=O), 1705 (C=N). ^1H NMR spectrum, δ, ppm: 1.25 t (3H, CH_3), 2.35 s (3H, CH_3), 4.26 q (2H, CH_2), 7.26 d (2H, H_{arom}), 7.54 d (2H, H_{arom}). ^{19}F NMR spectrum: δ_F –69.45 ppm (CF_3). Found, %: F 22.22; N 5.56. $C_{12}H_{12}F_3NO_2$. Calculated, %: F 21.99; N 5.40.

Ethyl 2,2,2-trifluoro-1-(4-methoxyphenyl)ethylidenecarbamate (IIIf). Yield 71%, bp 95°C (0.035 mm), n_D^{20} = 1.4985. IR spectrum, ν, cm^{-1}: 1755 (C=O), 1690 (C=N). ^1H NMR spectrum, δ, ppm: 1.28 t (3H, CH_3), 3.78 s (3H, CH_3O), 4.20 q (2H, CH_2), 6.97 d (2H, H_{arom}), 7.62 d (2H, H_{arom}). ^{19}F NMR spectrum: δ_F –70.08 ppm (CF_3). Found, %: F 20.90; N 5.31. $C_{12}H_{12}F_3NO_3$. Calculated, %: F 20.71; N 5.09.

1-Aryl-1-chloro-2,2,2-trifluoroethyl isocyanates IVa–IVd (*general procedure*). A mixture of 0.01 mol of carbamate **IIIa**–**IIIf** and 2.5 g (0.012 mol) of phosphorus pentachloride in 5 ml of phosphoryl chloride was heated for 4 h under reflux. The mixture was cooled, and a stream of dry sulfur dioxide was passed through the mixture until it no longer warmed up. Phosphoryl chloride was distilled off, and the residue was purified by vacuum distillation.

1-Chloro-2,2,2-trifluoro-1-(4-fluorophenyl)ethyl isocyanate (IVb). Yield 79% (from **IIIc**), 75% (from **IIId**), bp 72°C (10 mm), n_D^{20} = 1.4560. IR spectrum: ν 2260 cm^{-1} (N=C=O). ^1H NMR spectrum, δ, ppm: 7.13–7.18 m (2H, H_{arom}), 7.69–7.74 m (2H, H_{arom}). ^{19}F NMR spectrum, δ_F, ppm: –81.43 (CF_3), –110.85 (FC_6H_4). Found, %: F 30.17; N 5.72. $C_9H_4F_4ClNO$. Calculated, %: F 29.94; N 5.53.

The physical constants of isocyanates **IVa**, **IVc**, and **IVd** coincided with those reported in [4]. Compound **IVa**: yield 86% (from **IIIa**), 74% (from **IIIb**). Compound **IVc**: yield 76%. Compound **IVd**: yield 65%.

The IR spectra were recorded on a UR-20 spectrometer from solutions in methylene chloride. The ^1H and ^{19}F NMR spectra were measured in $CDCl_3$ on a Varian VXR-300 instrument (299.95 and 75.4 MHz, respectively) relative to tetramethylsilane (^1H) or trichlorofluoromethane (^{19}F).

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