Two-step phosphorus-mediated substitution of hydroxy groups in selected primary alcohols for fluorinated alkyl or aryl substituents: the molecular structure of 1,1-bis(fluorosulfonyl)-1-fluoro-2-phenylethane

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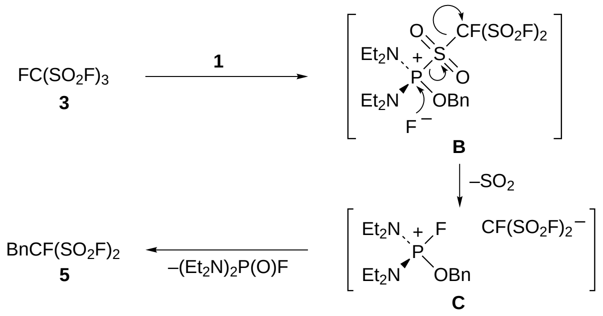
In an Arbuzov type reaction, amido phosphites $(Et_2N)_2POR^1$ and a broad range of halofluoro organic halides (X = Cl, Br) formed the corresponding alkylated derivatives R^1–R^2 [R^1 = Bn, R^2 = $C(SO_2F)_3$, CCl_2F, CCl_2CF_3, CBr_2F, $C(CF_3)_3$, C_6F_5; R^1 = Et, CH_2CF_3, Me, R^2 = CCl_2CF_3], whereas with $FC(SO_2F)_3$ and loss of SO_2, $BnCF(SO_2F)_2$ was obtained, as shown by X-ray crystallography.

Owing to the chemical and biological properties of organofluorine compounds,[1] considerable efforts have been made to find new reagents and methods for the fluorination of alcohols, oxy acids and glucosides. Nucleophilic fluoroalkylation is one of the most attractive routes for introducing fluorinated moieties.[2] However, to the best of our knowledge, there are no methods for substituting oxy groups in alcohols (directly or using their corresponding tosylates or triflates) for fluorinated carbon-centered anions. Phosphorus-containing reagents, *e.g.* the three component system $CF_3Br/P(NEt)_3$/electrophile or trifluoromethyl tris(dialkylamino)phosphonium salts,[3] have proven to be versatile reactants for trifluoromethylation of a variety of organic and organoelement compounds, *e.g.* Me_3SiCF_3, in its turn a powerful CF_3 transfer agent, too.[3,4] As we have recently shown, the phosphitylation of alcohols and oxy acid esters with $(Et_2N)_2PCl$, followed by the low temperature reaction of $(CF_3S)_2$ with the diamido phosphites formed, is an effective route for addition of the lipophilic SCF_3 moiety to sp^3-hybridized carbon atoms under mild reaction conditions;[5] in the case of CCl_4 and some Cl_3C group-containing species, trichloromethylated alkanes, 1,1-dichloromethyl esters and 1,1-dichloroethyl substituted phosphines were obtained.[6–8] Our preliminary results show that the reaction of $(Et_2N)_2POR^1$ (R^1 = Bn) with $XC(SO_2F)_3$ (X = F, Cl), X_3CF (X = Cl, Br), Cl_3CCF_3 and $BrC(CF_3)_3$, BrC_6F_5, and of $(Et_2N)_2POR^1$ (R^1 = Et, CH_2CF_3, Me) with Cl_3CCF_3 is a novel, convenient and generally applicable method for a two step substitution of hydroxy groups in primary alcohols for wide range of different fluorinated species; respective literature syntheses give fairly different and preparatively demanding approaches with low yields, *e.g.* $MeC(SO_2F)_3$ has been synthesized from MeI and $AgC(SO_2F)_3$,[9] $BnCCl_2CF_3$ by electrochemical cross-coupling,[10] $MeCCl_2CF_3$ from 2,2-dichloropropionic acid and SF_4,[11] $EtCCl_2CF_3$ and $CF_3CH_2CCl_2CF_3$ have been prepared photolytically,[12,13] and $BnC(CF_3)_3$ has been prepared from 1,1,3,3,3-pentafluoro-2-trifluoromethylpropene, CsF and $PhCHCl_2$.[14] For BnC_6F_5, BnCl and pentafluorobenzoyl chloride were required.[15]

In a superior general alternative to the already known methods, mentioned above, bis(diethylamido) phosphites, $(Et_2N)_2POR^1$, **1** (R^1 = Bn)[5] and the fluoro species $ClC(SO_2F)_3$ **2a**,[9] CCl_3F **2b**, CCl_3CF_3 **2c**, CBr_3F **2d**, $BrC(CF_3)_3$ **2e** and BrC_6F_5 **2f** underwent an Arbuzov type reaction to give in good yields R^1–R^2 **4a–f** [R^1 = Bn, R^2 = $C(SO_2F)_3$ (**4a**), CCl_2F (**4b**) CCl_2CF_3 (**4c**), CBr_2F (**4d**), $C(CF_3)_3$ (**4e**), C_6F_5 (**4f**)] and the corresponding halogeno amidates, $(Et_2N)_2P(O)X$ (X = Cl, Br),‡ (see Table 1). Gaseous SO_2 was formed when $FC(SO_2F)_3$ **3** was allowed to interact with **1** yielding $BnCF(SO_2F)_2$ **5**§ and $(Et_2N)_2P(O)F$. (Scheme 1) Reacting $(Et_2N)_2POR^1$ (R^1 = Et (**6**), CH_2CF_3 (**8**),[16] Me (**10**)] with **2c** gave the corresponding alkanes R^1–CCl_2CF_3 [R^1 = Et (**7c**),[12] CH_2CF_3 (**9c**),[13] Me (**11c**)[11]]. The products, either colorless liquids or low melting point solids, were easily separated from the phosphorus-containing substances by distillation or column chromatography on silica. The fluoro species R^1–$C(SO_2F)_3$ **4a**, R^1–CCl_2F **4b**, R^1–CBr_2F **4d** and R^1–$CF(SO_2F)_2$ **5** (R^1 = Bn) have not been described previously.¶ THF or triglyme were required as solvent; however, in the case of $XC(SO_2F)_3$ (X = F, Cl)[9] the reaction exclusively proceeds in aprotic, non-polar media, such as pentane. If *no* solvent is used, either no reaction occurs or products with P–C bond formation were obtained.[17]



Scheme 1

It is possible that, in a two step Arbuzov reaction *via* halogenophilic attack of phosphorus at R^2—X (X = Cl, Br),

Table 1 Preparation of R^1–R^2

Reactants $R^1OP(NEt_2)_2/R^2$–X[a]	Product R^1–R^2	Yield (%)
1/2a	**4a**[b,c]	80
1/2b	**4b**[b,d]	40
1/2c	**4c**[b,d]	90
1/2d	**4d**[b,d]	40
1/2e	**4e**[b,e]	81
1/2f	**4f**[d,f]	80
1/3	**5**[b,d]	86
6/2c	**7c**[b,d]	80
8/2c	**9c**[b,d]	70
10/2c	**11c**[b,e]	85

[a] $R^1OP(NEt_2)_2$ (10 mmol) in 10 ml solvent was added to a 10 ml solution of R^2–X (10 mmol), cooled to −50 to −78 °C within 5 min. [b] Reaction time: 15–30 min at −50 to −78 °C. [c] In pentane. [d] In THF. [e] In triglyme. [f] Reaction time: 90 min at −50 to −78 °C.

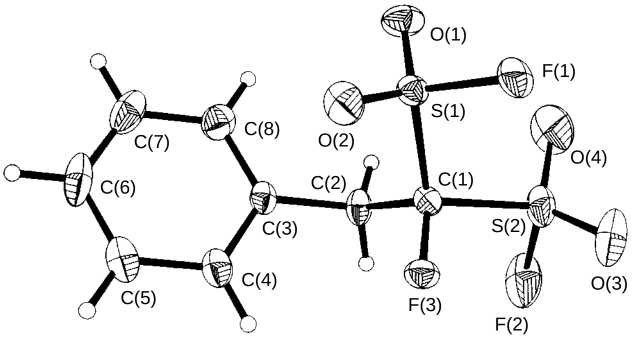


Fig. 1 Crystal structure of **5** with thermal ellipsoids. Selected bond distances (pm) and angles (°): C(1)–S(1) 183.8(3), C(1)–S(2) 183.3(3), C(1)–C(2) 151.5(4), C(2)–C(3) 151.7(4), C(3)–C(4) 138.3(4), S(1)–O(1) 140.5(1), S(2)–O(3) 141.8(2), S(1)–F(1) 154.7(2), S(2)–F(2) 152.0(2), C(1)–F(3) 137.3(3); C(2)–C(1)–S(1) 110.7(2), C(2)–C(1)–S(2) 111.8(2), F(3)–C(1)–C(2) 112.1(2), C(1)–C(2)–C(3) 114.3(2), F(3)–C(1)–S(1) 105.7(2), F(3)–C(1)–S(2) 106.2(2), S(2)–C(1)–S(1) 110.1(2), O(1)–S(1)–F(1) 107.02(12), O(3)–S(2)–F(2) 106.9(2), O(1)–S(1)–O(2) 122.36(14), O(4)–S(2)–O(3) 121.0(2), F(1)–S(1)–C(1) 100.51(12), F(2)–S(2)–C(1) 98.49(12).

unstable quasi-phosphonium intermediates $[(Et_2N)_2P(OR^1)X]^+ [R^2]^-$ **A** are formed, which in turn yield R^1–R^2 and $(Et_2N)_2P(=O)X$. For the reaction of **3** with **1**, a halogenophilic pathway seemed unlikely. However, the λ^3,σ^3 phosphorus nucleophile might attack sulfur (intermediate **B**) displacing a fluoride anion, which induced loss of SO_2 (intermediate **C**) and the proposed formation of $[CF(SO_2F)_2]^-$ (Scheme 1). Despite being the conjugated base of super acid (pK_a −12),[18] the tris(fluorosulfonyl)methanide anion[19] was able to be alkylated under mild conditions in pentane. Attempts to react this anion, as tetrabutylammonium tris(fluorosulfonyl)methanide, with alkyl tosylates and BnBr failed, even at elevated temperature.[18] The intermediate **A** probably exists as a tight ion pair, which facilitates the trapping of the incipient $[C(SO_2F)_3]^-$ anion *via* an intramolecular Arbuzov rearrangement. In THF or triglyme no methanide alkylation could be observed. In the case of $BrC(CF_3)_3$ **2e**, no perfluorobutene or its reaction products were found. No substitution of fluorine in the C_6F_5 moiety occurred. With C_6F_5Br **2f** the reaction was slower and accompanied by C_6F_5H formation, originating from the interaction of the corresponding anion with the solvent.[17] A concerted mechanism with λ^5,σ^5 phosphorane intermediates or a radical pathway could not be ruled out.[20]

The single crystal X-ray structure determination§ of **5** (Fig. 1), the first carried out on an alkyl derivative of $HCF(SO_2F)_2$, showed a slightly distorted tetrahedral geometry at C(1) bearing the SO_2F groups and C(2). The bond length of C(1)–S(1) corresponds to a single bond,[9] and the bond lengths C(1)–F(3), C(1)–C(2), C(2)–C(3), C(3)–C(4), S(1)–O(1) and S(1)–F(1) are all in the expected ranges.[21]

The outlined synthetic approach for introducing carbon-centered anions with a broad range of nucleophilicity to the sp^3-hybridized carbon of BnOH can be considered a simple alternative, superior to already known procedures. Preliminary positive results for EtOH, CF_3CH_2OH and MeOH promise extension of the procedure to various alkanes $R^FCCl_2(Br_2)CH_2R$, which, when successively dehydrohalogenated, offer an easy access to fluoroalkylated alkenes $R^FCCl(Br)$=CHR and alkynes $R^FC{\equiv}CR$, which are in turn building blocks for fluoro heterocycles and other versatile precursors.[22]

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Notes and References

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‡ All new compounds gave satisfactory elemental analyses and mass spectra.

§ *Crystal data* for **5**: $C_8H_7F_3O_4S_2$, M = 288.3, orthorhombic, space group *Pbca*, a = 1010.7(3), b = 1100.5(2), c = 1984.7(3) pm, V = 2.2075(8) nm^3, Z = 8, D_c = 1.735 Mg m^{-3}, λ(Mo-Kα) = 71.073 pm, Siemens P4 m/v diffractometer, θ region $2.88 \leqslant \theta \leqslant 27.51°$, T = 173(2) K; 3323 reflections collected, 2536 independent (R_{int} = 0.0485), full-matrix least-squares refinement at F^2 (SHELXL 93); goodness of fit on F^2 0.857, final R-values [$I > 2\sigma(I)$] $R1$ = 0.0461, wR_2 = 0.0978; R-values (all data) $R1$ = 0.0847, wR_2 = 0.1065, extinction coefficient 0.0065(7), difference electron density 422 and −494 e nm^{-3}. CCDC 182/767.

¶ *Selected data* for **4a**: mp 86–87 °C; δ_H 4.2 (CH_2, 2 H, $^3J_{HF}$ 1.9), 7.3 (C_6H_5, 5 H); δ_F 65.7 (SO_2F). For **4b**: bp 102–103 °C/0.05 mbar; δ_H 3.7 (CH_2, 2 H, $^3J_{HF}$ 17.0), 7.3 (C_6H_5, 5 H); δ_F −55.8. For **4d**: bp 125 °C/14 mbar; δ_H 3.9 (CH_2, 2 H, $^3J_{HF}$ 18.0), 7.3 (C_6H_5, 5 H); δ_F − 52.1. For **5**: mp 34–35 °C; δ_H 3.9 (CH_2, 2 H, $^3J_{HF}$ 23.6, $^4J_{HF}$ 1.9), 7.3 (C_6H_5, 5 H); δ_F 51.2 (SO_2F, 2 F, $^3J_{FF}$ 3.7), −139.8 (1 F).

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