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A new reaction of vicinal sulfonyliminocarboxylates with phosphites

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Abstract—The reaction of alkyl trifluoro(organylsulfonylimino)propionates with phosphites occurs with N–C transfer of the RSO_2 group and leads to sulfonyl-substituted trifluoroalanine derivatives. The novel rearrangement is interpreted as cheletropic 1,4-cycloaddition of the phosphite and subsequent 1,2-shift of the sulfonyl group in the intermediate cyclic phosphorane. © 2003 Published by Elsevier Science Ltd.

Polyhaloalkanimines are useful building blocks in the synthesis of biologically important acyclic and heterocyclic compounds.[1–5] Three different pathways are known for the reactions of highly electrophilic azomethines $R_{Hlg}C(X)=NY$ with phosphites: (i) the aza-Perkow-type reaction ($Y=RSO_2$, R_2PO, RCO) involving a halogen atom of the group R_{Hlg} and leading to *N*-phosphorylation or *N*-alkylation products; (ii) the substitution of the nucleofuge X by a phosphoryl group (Arbuzov reaction) and (iii) cycloaddition ($Y=RCO$) with the formation of five-coordinate phosphorus derivatives.[1,4–6]

We have found that a radically new reaction, with a concomitant shift of the organylsulfonyl group from the N to C, is realized in the reaction between alkyl trifluoro(organylsulfonylimino)propionate **1** and phosphite **2**. Thus, the interaction of sulfonylimine **1a** with triisopropyl phosphite **2a** in benzene, at room temperature, over 15–30 min resulted in the formation of iminophosphorane **3a** in a nearly quantitative yield.

The elemental analysis and spectral data were in agreement with the composition and structure proposed for compound **3a** (Table 1). The chemical shift of its ^{31}P NMR signal (–8.0 ppm in C_6D_6) falls within the range expected for iminophosphoranes.[7,8] The singlet for the CF_3 moiety in the ^{19}F NMR spectrum of **3a** (δ_F –70.3 ppm) lies in almost the same region as in the starting imine **1a** (δ_F –70.4 ppm) indicating that the CF_3 group remains unchanged during the reaction. The ^1H NMR spectrum shows the presence of three magnetically equivalent isopropoxy groups at the phosphorus atom in **3a** ([δ_H 1.19 ppm, d (18H, $^3J_{HH}$ 6 Hz, Me); 4.5 ppm, m (3H, OCH)]. Other protons give signals with expected multiplicities, relative intensities and chemical shifts. The most important, for structure identification, are the position and multiplicity of the ^{13}C NMR signals of the carbon atoms of the C–N bond (δ_C 90.4 ppm, dq, $^2J_{CF}$ 29 Hz, $^2J_{CP}$ 3.8 Hz) and the C=O group (δ_C 165.7 ppm, d, $^3J_{CP}$ 9.9 Hz) in **3a**. That is, the imine carbon atom in **1** undergoes sp^2–sp^3 rehybridization in **3** whereas the carbonyl group survives. The structure of **3a** was unequivocally established by XRD analysis.[9] As can be seen from Scheme 1, the transformation discovered is rather general and occurs in arylsulfonylimines with electron-donor (**1a**,**b**) and electron-acceptor substituents on the benzene ring (**1c**,**d**), and in heteroarylsulfonyl- (**1e**) and alkylsulfonylimines (**1f**).

It is apparent that the transformation **1**→**3** is a complex process, but we failed to detect spectrally any intermediates since the interaction with trialkyl phosphites **2a**,**b** is very fast. The reaction of imines **1a**,**c**,**d** with the less nucleophilic triphenyl phosphite **2c** proceeded much more slowly and because of this, the monitoring of the reaction progress by ^{31}P and ^{19}F NMR revealed the formation of two intermediates containing a five-coordinate phosphorus atom (δ_P –28.8 to –29.7 ppm, δ_F –79.7 to –80.3 ppm and δ_P –26.8 to –27.4 ppm, δ_F –80.0 to –80.8 ppm, respectively) which were trans-

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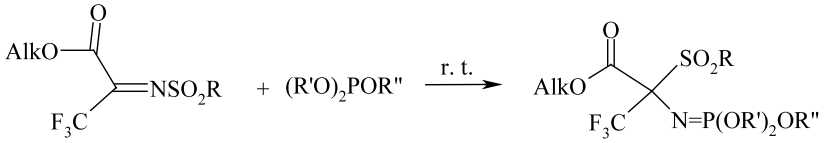
Table 1. NMR spectra of compounds **3a–l** and some of their precursors

Compd	δ_P (C_6D_6), ppm	δ_F (C_6D_6), ppm	Compd	δ_P (C_6D_6), ppm	δ_F (C_6D_6), ppm
3a	−8.0	−70.3[a]	**3i**	−26.2	−69.7
3b	−7.1	−70.0	**3j**[c]	−25.1	−70.2
3c	−6.9[a]	−70.3[a]	**3k**	−24.5	−71.2
3d	−6.3	−70.3	**3l**	−12.7	−69.1
3e[b]	−6.0	−69.0	**4i**[d]	−29.7	−79.7
				−27.4	−80.0
3f	−7.0	−70.0	**4j**[d]	−29.4	−79.9
				−27.0	−80.4
3g	−6.1	−70.2	**4k**[c,d]	−28.8	−80.3
				−26.8	−80.8
3h	−7.5	−70.3	**4l**[d]	−14.4	−78.6
				−11.8	−79.4

[a] In $CDCl_3$.
[b] δ ($F_3CC_6H_4$) −61.9 ppm.
[c] The ^{19}F NMR signals of $F_3CC_6H_4$ in **3k** and **4k** lie between −61.6 and −62.5 ppm.
[d] Substituents in **4i–l** are the same as in **3i–l**.



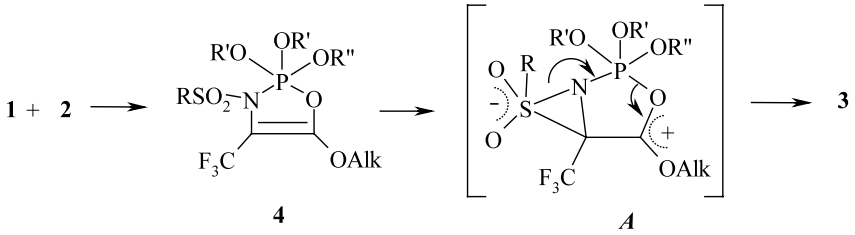
1a-g **2a,b** **3a-l**

1a–g: Alk = Me, R = 4-$MeOC_6H_4$ (a), 4-MeC_6H_4 (b), 4-ClC_6H_4 (c), 3-$CF_3C_6H_4$ (d), 2-thienyl (e), Et (f); Alk = Et, R = Ph (g)

2a–d: R' = R" = *i*-Pr (a), Et (b), Ph (c); R' = Et, R" = 3-pyridyl (d)

Comp.	R	R' = R"	Alk	Comp.	R	R'	R"	Alk
3a	4-$MeOC_6H_4$	*i*-Pr	Me	**3g**	2-thienyl	Et	Me	
3b	4-$MeOC_6H_4$	Et	Me	**3h**	Et	*i*-Pr	*i*-Pr	Me
3c	4-MeC_6H_4	Et	Me	**3i**	4-$MeOC_6H_4$	Ph	Ph	Me
3d	4-ClC_6H_4	Et	Me	**3j**	4-ClC_6H_4	Ph	Ph	Me
3e	3-$CF_3C_6H_4$	Et	Me	**3k**	3-$CF_3C_6H_4$	Ph	Ph	Me
3f	Ph	Et	Et	**3l**	4-$MeOC_6H_4$	Et	3-pyridyl	Me

Scheme 1.



Scheme 2.

formed slowly into the corresponding iminophosphoranes **3i–k** (δ_P −24.5 to −26.2 ppm, δ_F −69.7 to −71.2 ppm). A similar reaction dynamic was also observed in the system composed of imine **1a** and diethyl 3-pyridyl phosphite (**2d**). It is likely that the reaction proceeds via Scheme 2.

The similarity of the transient NMR signals allows one

to assign them to intermediate stereoisomeric phosphoranes of type **4**. It is likely, that the transformation **4→3** involves intramolecular electrophilic attack of the sulfonyl group on the sp^2-C atom, favored by the presence of donor alkoxy and phosphoryloxy substituents at the endocyclic C=C bond of phosphoranes **4**.

It should be noted that the reaction of **1** with phosphites **2c**,**d** is of little preparative use because of side processes and, in particular, the formation of phosphates $(R'O)_2P(O)(OR'')$. This is apparently associated with the lengthy reaction time (several weeks) and low stability of products **3**,**4** under the reaction conditions. Compounds **3a**–**h** are quite stable in a dry inert atmosphere, but they are very sensitive to moisture. Even on running NMR spectra in commercial deuterated solvents, the iminophosphoranes were hydrolyzed. For these reasons compounds **3i**–**l** were not isolated in the pure state, but their NMR spectra (and, obviously, structure) are very similar to those of iminophosphoranes **3a**–**h** (see Table 1).

The following fact also counts in favor of the mechanism proposed for the reaction in question. The replacement of the COOMe group in imine **1a** with a CF_3 group which is close in electron-withdrawing properties to the former (σ_I 0.30 and 0.42, respectively)[10] but is unable to undergo cycloaddition, makes the modified imines $4\text{-}RC_6H_4SO_2N{=}C(CF_3)_2$ (R = MeO, Cl) completely unreactive towards phosphites **2a**,**b** at room temperature or in boiling diethyl ether.

It is evident that the presence of the C=O group in sulfonylimines **1** makes possible the 1,4-cycloaddition of phosphites **2** leading to the formation of phosphoranes **4**, as a necessary prerequisite to accomplish the transformation of **1→3**. Note that the latter includes the formal introduction of the electrophilic RSO_2 group to the electrophilic imine carbon atom in **1**, through the mediation of **2**, and umpolung of this center.

The new reaction can be considered as a phosphite-initiated N–C transfer of a sulfonyl group in vicinal sulfonyliminocarboxylates. Taking into account the simplicity of the procedure, the reaction can find application in the synthesis of biologically active sulfonyl derivatives of trifluoroalanine.[11]

*Iminophosphoranes **3**. Typical procedure*. To a stirred and cooled (5–10°C) solution of **1** in benzene or diethyl ether was added an equimolar amount of **2**. After reacting for 15–30 min at rt, the solvent was evaporated to leave pure **3**.

3a, yield ca. 100%, mp 70–71°C. ^{13}C NMR spectrum (C_6D_6): 23.43 (d, $^3J_{CP}$ 5.5 Hz, $\underline{Me}_2C$), 52.93 (s, COO$\underline{Me}$), 55.29 (s, $\underline{Me}$OAr), 72.34 (d, $^2J_{CP}$ 8.8 Hz, CHO), 90.38 (dq, $^2J_{CF}$ 29 Hz, $^2J_{CP}$ 3.8 Hz, CN), 123.56 (dq, $^1J_{CF}$ 288 Hz, $^3J_{CP}$ 9 Hz, CF_3), 113.57 (s, *m*-C_{Ph}), 129.65 (s, *ipso*-C_{Ph}), 133.65 (s, *o*-C_{Ph}), 164.18 (s, *p*-C_{Ph}), 165.66 (d, $^3J_{CP}$ 9.9 Hz, C=O).

3c, yield. 95%, oil. ^{1}H NMR spectrum (C_6D_6): 1.05 (t, 9H, $^3J_{HH}$ 7 Hz, $\underline{Me}CH_2$), 1.87 (s, 3H, MeAr), 3.96 (m, 6H, CH_2), 6.80 (d, 2H), 8.02 (d, 2H, $^3J_{HH}$ 8.5 Hz) (Ar). ^{13}C NMR spectrum (C_6D_6): 15.98 (d, $^3J_{CP}$ 7 Hz, $\underline{Me}CH_2$), 21.20 (s, MeAr), 53.26 (s, MeO), 64.0 (d, $^2J_{CP}$ 8 Hz, CH_2), 90.43 (dq, $^2J_{CF}$ 30 Hz, $^2J_{CP}$ 4.2 Hz, CN), 123.48 (dq, $^1J_{CF}$ 288 Hz, $^3J_{CP}$ 12 Hz, CF_3), 128.91, 131.59 (s, *o*,*m*-C_{Ph}), 135.89 (s, *ipso*-C_{Ph}), 144.38 (s, *p*-C_{Ph}), 165.85 (d, $^3J_{CP}$ 10.8 Hz, C=O).

3f, yield ca. 100%, oil. ^{1}H NMR spectrum (C_6D_6): 1.2 (m, 12H, Me), 4.1 (m, 6H, CH_2OP), 4.25 (q, 2H, $^3J_{HH}$ 7 Hz, CH_2OC), 7.2 (m, 3H, Ph), 8.3 (m, 2H, Ph). ^{13}C NMR spectrum (C_6D_6): 13.71 (s, $\underline{Me}CH_2OC$), 15.90 (d, $^3J_{CP}$ 7.8 Hz, $\underline{Me}CH_2OP$), 63.23 (s, $\underline{C}H_2OC$), 63.91 (d, $^2J_{CP}$ 7.3 Hz, $\underline{C}H_2OP$), 90.48 (dq, $^2J_{CF}$ 30 Hz, $^2J_{CP}$ 5 Hz, CN), 123.40 (dq, $^1J_{CF}$ 288 Hz, $^3J_{CP}$ 11 Hz, CF_3), 128.11, 131.48 (s, *o*,*m*-C_{Ph}), 133.40 (s, *p*-C_{Ph}), 138.65 (s, *ipso*-C_{Ph}), 165.0 (d, $^3J_{CP}$ 10 Hz, C=O).

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