Notes

Reactions of Bromotrifluoromethane and Related Halides. 8. Condensations with Dithionite and Hydroxymethanesulfinate Salts

Marc Tordeux,† Bernard Langlois,‡ and Claude Wakselman*,†

CNRS-CERCOA, BP 28, 94320 Thiais, France, and
Rhône-Poulenc Research Center, BP 62,
69192 St-Fons, France

Received September 20, 1988

We previously described the synthesis of zinc trifluoromethanesulfinate by the action of the metal to a mixture of sulfur dioxide and trifluoromethyl bromide, under slight pressure in dimethylformamide (DMF).[1,2] In view of the ease of reduction of sulfur dioxide to its anion radical,[3,4] a radical process was considered[2,5] (Scheme I).

In order to confirm the possibility of this one-electron transfer process, we examined the behavior of other well-known sources of $SO_2^{\bullet-}$, like sodium dithionite, $Na_2S_2O_4$, and sodium hydroxymethanesulfinate, NaO_2SCH_2OH.[3,6,7]

As for our first method,[2] precise conditions were necessary for the transformation of the poorly reactive gaseous bromotrifluoromethane by an aqueous suspension of sodium dithionite: use of pressure and dipolar aprotic cosolvents, in order to increase the concentration of this weakly soluble perhalogenomethane. The most convenient solvent was DMF, but dimethylacetamide or *N*-methylpyrrolidone were suitable too. It is preferable to operate at from about 65 to 75 °C at a pressure from 3 to 15 bars. An added base was needed for the neutralization of the sulfur dioxide formed in the reaction in order to avoid the decomposition of sodium dithionite. This base was chosen among alkali metal hydroxides, ammonia, disodium hydrogenophosphate, sodium metabisulfite, and sodium borate. Disodium hydrogenophosphate was very convenient. At the end of the reaction, the solvent was removed, and sodium triflinate was isolated by extraction with ethyl acetate. This method avoids the problem of the separation of zinc salts.[2]

Sodium dithionite can be replaced by hydroxymethanesulfinate salts, known as Rongalite (sodium salt) or Decroline (zinc salt). These reagents were sufficiently soluble in dipolar aprotic solvents (DMF, *N*-methylpyrrolidone, dimethyl sulfoxide) to perform the reaction in anhydrous organic medium. The condensation was performed at a temperature ranging from 20 to 85 °C and a pressure from 3 to 5 bars. Triflinate salts were isolated as before.[8] However, the yield was slightly better with sodium dithionite, and this reagent was chosen to scale up the reaction.

Similar transformations of difluorodihalomethanes CF_2X_2 ($X = Cl, Br$) to their corresponding perhalomethanesulfinate salts were observed. A mechanism analogous to the Scheme I can explain their formation. In the case of sodium dithionite, the sulfinic anion radical $SO_2^{\bullet-}$ is easily formed by the known dissociation:[3]

$$^-SO_2{-}SO_2^- \rightarrow 2SO_2^{\bullet-}$$

Scheme I

$$SO_2^{\bullet-} + CF_3Br \rightarrow SO_2 + CF_3^{\bullet} + Br^-$$

$$CF_3^{\bullet} + SO_2^{\bullet-} \rightarrow CF_3SO_2^-$$

Its formation from hydroxymethanesulfinate salts is less obvious, but its ESR spectrum has also been detected in that case.[6]

Via Scheme I, this anion radical is able to transfer an electron to trifluoromethyl bromide. It was observed very recently that the reduction of CF_3Br takes place at a more negative potential than that of SO_2.[10,11] The electron transfer is likely to occur because reduction of CF_3Br is made irreversible by breaking of the carbon–bromide bond. Capture of a trifluoromethyl radical by an electron-rich aromatic nucleus introduced in the zinc–sulfur dioxide mixture is also compatible with this scheme.[5] The formation of the trifluoromethanesulfinate can be explained by reaction of the trifluoromethyl radical with sulfur dioxide radical anion (Scheme I) or alternatively with dithionite.[12]

$$CF_3^{\bullet} + {}^-O_2SSO_2^- \rightarrow CF_3SO_2^- + SO_2^{\bullet-}$$

To the difference of the reaction of sodium dithionite with usual alkyl halides[13] sulfones have not been observed in our case.[14] Indeed fluorinated perhalogenomethanes are not able to be substituted by hard nucleophiles, like perhalogenomethanesulfinates.[16,17]

---

† CNRS-CERCOA.

‡ Rhône-Poulenc Research Center.

(1) Part 7. Tordeux, M.; Francese, C.; Wakselman, C. *J. Fluorine Chem.*, in press.

(2) Wakselman, C.; Tordeux, M. Eur. Pat. 165135, 1984; *Bull. Soc. Chim. Fr.* **1986**, 868.

(3) Harrison, W. D.; Gill, J. B.; Goodall, D. C. *J. Chem. Soc., Dalton Trans.* **1978**, 1431; **1979**, 847.

(4) Wille, H. J.; Kastening, B.; Knittel, D. *J. Electroanal. Chem.* **1986**, *214*, 221.

(5) Wakselman, C.; Tordeux, M. *J. Chem. Soc., Chem. Commun.* **1987**, 1701.

(6) Rinker, R. G.; Gordon, T. P.; Corcoran, W. H. *Inorg. Chem.* **1964**, *3*, 1467.

(7) Andre, D. L.; Gelbard, G. *Bull. Soc. Chim. Fr.* **1986**, 565.

(8) Recently, the action of sodium hydroxymethanesulfinate–sodium bicarbonate reagent to perfluoroalkyl halides in aqueous DMF was reported to lead to perfluorocarboxylate salts.[9]

(9) Huang, B. N.; Haas, A.; Lieb, M. *J. Fluorine Chem.* **1987**, *36*, 49.

(10) Folest, J. C.; Nedelec, J. Y.; Perichon, J. *Synth. Commun.* **1988**, *18*, 1491.

(11) Gelis, L. Thesis, Paris VII University, 23 September 1988.

(12) We thank a referee for this suggestion.

(13) Matsuo, K.; Kobayashi, M.; Minato, H. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 260.

(14) This behavior is similar to that of 1,1,1-trichloropolyfluoroalkanes and long-chain perfluoroalkyl halides when reacting with sodium dithionite–sodium bicarbonate in aqueous acetonitrile.[15] However, these conditions, used for the sulfinatodehalogenation of liquid perhaloalkanes, are not appropriate for the transformation of gaseous perhalomethane, like CF_3Br. We observed no reaction at atmospheric pressure. This failure is probably due to the poor reactivity of bromotrifluoromethane and its very low solubility in acetonitrile. The same experiment performed under 3 bars was very dangerous: a sudden increase of pressure was observed, which can be due to the formation of carbon dioxide from sodium bicarbonate and sulfur dioxide.

(15) Huang, W. Y.; Huang, B. N.; Chen, J. L. *Acta Chimica Sinica* **1984**, *42*, 1114; *Chem. Abstr.* **1985**, *102*, 78313*g*.

(16) Wakselman, C.; Kaziz, C. *J. Fluorine Chem.* **1986**, *33*, 347.

0022-3263/89/1954-2452$01.50/0 © 1989 American Chemical Society

The various fluorinated sulfinate salts can be transformed to their corresponding sulfonate derivatives: chlorination gives the sulfonyl halides and oxidation by hydrogen peroxide leads to the sulfonic acids.[18] The use of sodium dithionite or sodium hydroxymethanesulfinate allows now the preparation of trifluoromethanesulfonic acid on a large scale.

Experimental Section

Fluorine magnetic resonance spectra were obtained on a Varian EM360L spectrometer (56.4 MHz) and were recorded in ppm (^{19}F) downfield from trichlorofluoromethane (solvents: water, acetone, ethyl acetate); bromotrifluoromethane and sulfur dioxide were purchased from Setic Labo, inorganic bases from Prolabo, sodium dithionite from Fluka, Rongalite from Aldrich, and Decroline from BASF. DMF from Aldrich was distilled in vacuo before use.

For experiments that needed a pressure until 6 bars, a Parr low-pressure hydrogenation apparatus was used. The hydrogen tank was removed, and the bromotrifluoromethane bottle was directly fitted with the manometer. The 250-mL glass bottle was tested for 8 bars and placed in a steel jacket. For experiments up to 20 bars, a Mula 1-L glass reactor, with a double fence, was used. In this case, the mixture was mechanically stirred. This reactor was kept in confinement in a secure polycarbonate box. In both cases, the reaction temperature was controlled by a thermostated water circulation.

Preparation of Sodium Trifluoromethanesulfonate from Sodium Dithionite. A 150-mL portion of water and 32.6 g (0.23 mol) of disodium phosphate was charged as a solution into a 400-mL reactor, followed by 48.3 g (0.24 mol) of 86.5% sodium dithionite and 100 g of dimethylformamide.

After closing the reactor, a vacuum (10 Torr) was created. Trifluorobromomethane was introduced at a pressure of 13 bars. The contents were stirred and heated to 65 °C, and additional CF_3Br was introduced when the pressure dropped to 12 bars.

The total duration of the trial was 70 min. After cooling and degassing, the upper phase was decanted and distilled to dryness. The solid was washed with methylene chloride and extracted with ethyl acetate. After evaporation of the solvent, crude 64% sodium trifluoromethanesulfinate was collected with a yield of 41.7 g (69% based on sodium dithionite).

A 8-g (0.035-mol) portion of crude sodium trifluoromethanesulfinate was dissolved in 25 mL of 35% hydrogen peroxide. Nuclear magnetic resonance measurements (^{19}F) showed that the conversion was complete within 5 h and that a single signal at δ_F −78 ppm remained. Two pieces of pumice were added, and the mixture was brought to reflux to decompose the hydrogen peroxide excess, giving 2.3 L of oxygen. The water was evaporated and the solid was extracted with acetone to give, after evaporation, 7.2 g (0.032 mol) of a crude 77% sodium trifluoromethanesulfonate as a colorless solid.

A mixture of 3 g of sodium trifluoromethanesulfonate and 3 g of 95% sulfuric acid was heated to 140 °C at 0.8 Torr to yield 2.25 g trifluoromethanesulfonic acid monohydrate (mp 45 °C) (lit.[17] mp 45 °C). This material was neutralized with 12.6 mL of IN sodium hydroxide. After the solid was isolated and dried at 80 °C (0.5 Torr), 2.3 g (0.0132 mol) of sodium trifluoromethanesulfonate was obtained as a colorless solid (yield from trifluoromethanesulfinate: 96%); mp 251 °C (lit.[19] mp 248 °C), $\delta_F = -78$ ppm.

Preparation of Trifluoromethanesulfonyl Chloride from Sodium Hydroxymethanesulfinate. A mixture of 50 mL of dimethylformamide, 15.4 g (0.1 mol) of sodium hydroxymethanesulfinate, and 10 g (0.052 mol) of sodium bisulfite was charged in a thick-glass flask. The mixture was placed under 5 Torr, and the temperature was maintained at 20 °C. The flask was stirred at a bromotrifluoromethane pressure ranging from 3 to 5 bars for 3 h or until the gas absorption ceased. The flask was opened. After filtration, the dimethylformamide was distilled under vacuum. The resulting solid was washed with dichloromethane and extracted with ethyl acetate. After evaporation, the solid was dissolved in water. The pH was adjusted to 7. After filtration, the solution was stirred under a chlorine pressure of 3 bars during 2 h with the temperature maintained between 0 and 10 °C. The lower layer was distilled to give 4.7 g (0.028 mol) of trifluoromethanesulfonyl chloride:[19] yield 28%; bp 29–32 °C; δ_F ($CFCl_3$ ext) = −74 ppm.

Preparation of Trifluoromethanesulfonyl Chloride from Zinc Hydroxymethanesulfinate. A mixture of 50 mL of dimethylformamide and 12.7 g (0.05 mol) of zinc hydroxymethanesulfinate was placed in a thick-glass flask. The flask was placed under 5 Torr and heated to 65 °C. The mixture was stirred at a bromotrifluoromethane pressure ranging from 3 to 5 bars for 3 h or until the absorption of gas ceased. The flask was then opened. After filtration, the dimethylformamide was distilled under vacuum; 100 mL of water were added, followed by sufficient sodium hydroxide pellets to get a slightly basic pH. The unsoluble zinc salts were filtered off. The water was evaporated in vacuo. The residual solid was washed with dichloromethane and extracted with ethyl acetate. After evaporation, 100 mL of water was added. The solution was stirred under a chlorine pressure of 3 bars during 2 h, the temperature being maintained between 0 and 10 °C. The lower layer was separated and distilled to give 5.9 g (0.035 mol) of trifluoromethanesulfonyl chloride, yield 35%.

Preparation of Chlorodifluoromethanesulfonyl Chloride from Zinc Hydroxymethanesulfinate. A mixture of 50 mL of DMF and 12.7 g (0.05 mol) of zinc hydroxymethanesulfinate was placed in a thick-glass flask. A vacuum was created in the flask, and then the mixture was stirred for 15 hours at a bromochlorodifluoromethane pressure of 1.2 bars. The flask was opened, the solids were removed by filtration, and 1 g (0.01 mol) of trifluoroethanol was added. The yield of chlorodifluoromethanesulfinate ($\delta_F = -69$ ppm/$CFCl_3$) was determined by ^{19}F nuclear magnetic resonance relative to trifluoroethanol ($\delta_F = -76$ ppm). Yield: 20%. Water (30 mL) was added. The dimethylformamide was extracted with dichloromethane. After filtering, 2 L of chlorine was passed through the aqueous solution, and 3.2 g (0.018 mol) of chlorodifluoromethanesulfonyl chloride[14] ($\delta_F = -58$ ppm) was obtained, bp 84 °C.[20] The yield relative to zinc hydroxymethanesulfinate was 18%.

---

[17] Everett, S. T. *J. Chem. Ed.* **1987**, *64*, 143.

[18] Tordeux, M.; Langlois, B.; Wakselman, C. Fr. Demande 2,593,808, 1986.

[19] Haszeldine, R. N.; Kidd, J. M. *J. Chem. Soc.* **1954**, 4228.

[20] Yarovenko, N. N.; Motornyi, S. P. *Zh. Oshchei Khim.* **1960**, *30*, 4066.

Resolution of Secondary Alcohols Using Lipase in Diisopropyl Ether

H. S. Bevinakatti,* A. A. Banerji, and R. V. Newadkar

Alchemie Research Centre, P.O. Box 155, Belapur Road, Thane-400601, Maharashtra, India

Received August 3, 1988

Since Klibanov et al.[1] discovered enzymatic activity in anhydrous organic solvents, it has become a major field of research. Not only can one now carry out reactions like esterification, transesterification, etc., which otherwise would have been impossible to conduct in the presence of water but also the need to immobilize the enzymes by using tedious procedures is avoided. Enzymes can be separated by filtration and reused.

Lipases are one class of such enzymes that are presently being explored for their stereo- and regioselective esterification and transesterification reactions. They have been successfully used to resolve a host of alcohols[2–5] and for

---

[1] Klibanov, A. M. *CHEMTECH* **1986**, *16*, 354.

[2] Kirchner, G.; Scollar, M. P.; Klibanov, A. M. *J. Am. Chem. Soc.* **1985**, *107*, 7072.

[3] (a) Langrand, G.; Secchi, M.; Buono, G.; Baratti, J.; Triantaphylides, C. *Tetrahedron Lett.* **1985**, *26*, 1857. (b) Langrand, G.; Baratti, J.; Buono, G.; Triantaphylides, C. *Tetrahedron Lett.* **1986**, *27*, 29.