Electrochemical Synthesis of 4,4,4-Trifluoro-2-butanone

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Electrolysis of solutions which contain trifluoroacetate ions generates trifluoromethyl radicals which may either combine to form hexafluoroethane or react with suitable organic cosolutes to form mixtures of trifluoromethylated derivatives.[1-7] When the cosolute is an olefin, it is often found that the principal product is either the corresponding 1,2-bis(trifluoromethyl) derivative[4,5] or a dimeric species resulting from the coupling of two radicals each formed from the olefin by addition of a trifluoromethyl radical at one end of the double bond.[4,6,7] However, it was found in this laboratory that the anodic trifluoromethylation of substrates containing the isopropenyl group leads mainly to monomeric products containing only one trifluoromethyl group.[8] Typically one obtains a mixture of saturated and unsaturated materials, the latter consisting of several isomers, e.g. eq 1 where X = alkyl, CH_2Cl,

$$\underset{1}{\mathrm{CH_2{=}C(CH_3)X}} \rightarrow \underset{2}{\mathrm{CF_3CH_2CH(CH_3)X}} + \underset{3\ (\text{two isomers})}{\mathrm{CF_3CH{=}C(CH_3)X}} + \underset{4}{\mathrm{CH_2{=}C(CH_2CF_3)X}} \quad (1)$$

or $COOCH_3$. If desired, such a mixture can be hydrogenated to convert **3** and **4** to **2** which can then be isolated with a total yield of 15–20%, based on the olefin.

It is now reported that when partially neutralized trifluoroacetic acid is electrolyzed in the presence of isopropenyl acetate, the trifluoromethylated material is almost entirely 4,4,4-trifluoro-2-butanone (**5**). Fluorine NMR spectra of samples taken during the electrolysis indicate that possible intermediates such as the enol acetate of **5** are too short-lived to be easily detected and that only trace amounts of fluorine-containing byproducts are formed if the electrolysis is not excessively prolonged. Compound **5** has been made previously by the hydration of 1,1,1-trifluoro-2-butyne,[9] which, however, is not readily available. The electrochemical method now provides a convenient one-step synthesis of this ketone.

As reported earlier,[9] **5** promptly forms a 2,4-dinitrophenylhydrazone, but it failed to condense with malonic acid or malonic ester under mild conditions in which the unfluorinated analogue, 2-butanone, would react. However, by use of the procedure of Cragoe et al.,[10] **5** could condensed with ethyl cyanoacetate, and hence it can serve as the starting material for the preparation of a variety of other trifluoromethylated compounds.[11]

Experimental Section

Commercial trifluoroacetic acid, isopropenyl acetate, and acetone were used as received. In a typical run, 33 mL (300 mmol) of isopropenyl acetate and 30 mL (389 mmol) of trifluoroacetic acid were dissolved in 180 mL of acetone and 20 mL of water containing 1.6 g (40 mmol) of sodium hydroxide. If the water was not included in the mixture, electrolysis soon caused it to turn dark brown, and the electrodes became coated with a brown resinous material. Electrolyses were carried out with stirring in a 500-mL bottle loosely stoppered with a plug of cotton and cooled in a water bath to keep the temperature from rising much above 25 °C. The electrodes consisted of two spirals of no. 20 platinum wire mounted coaxially and about 0.6 cm apart. It was usually convenient to pass a current of 0.6–0.7 A through the cell for 24 h, providing about 0.6 faradays. The current density could be varied over a wide range without significantly affecting the course of the reaction.

The nearly colorless reaction mixture was poured into 700 mL of water and the product extracted into methylene chloride. The resulting solution contained considerable amounts of acetic and trifluoroacetic acids and was washed with 15% aqueous potassium carbonate until the pH of the aqueous layer was between 7 and 8 and then with water and dried. Such solutions from four identical runs were combined and distilled. When most of the low-boiling material (methylene chloride and acetone) had been removed, 150 mL of *n*-butyl ether was added. Unless such a dilutant was present, the yield was reduced owing to partial pyrolysis of the product during the subsequent distillation. A fraction (25.5 g) boiling from 93 to 98 °C (mostly 94.5–96 °C) consisted of nearly pure **5** (lit.[9] bp 95–96 °C): ^1H NMR ($CDCl_3/Me_4Si$) δ 3.24 (q, J = 10.6 Hz), 2.28 (s). The spectrum indicated a purity of better than 90%; the mixture appeared to contain about 5% *n*-butyl ether and traces of unidentified impurities but no isopropenyl acetate. The initially colorless product gradually turns yellow on storage, even at -15 °C. The ^{19}F NMR of a 1% solution, by volume, in $CHCl_3$ showed the expected triplet (J = 10.6 Hz) 0.59 ppm upfield from external 1,1,2-trichloro-3,3,3-trifluoropropene, the exact shift being strongly solvent and concentration dependent. Distillation of the adjacent fractions gave about 5 g more of similar material, bringing the total yield to about 18%, based on isopropenyl acetate. The 2,4-dinitrophenylhydrazone melted at 130.5–131.5 °C uncor (lit.[9] mp 131–132 °C).

Registry No. 5, 2366-70-3; trifluoroacetic acid, 76-05-1; isopropenyl acetate, 108-22-5.

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(1) Lindsey, R. V., Jr.; Peterson, M. L. *J. Am. Chem. Soc.* **1959**, *81*, 2073.

(2) Renaud, R. N.; Sullivan, D. E. *Can. J. Chem.* **1972**, *50*, 3084.

(3) Renaud, R. N.; Sullivan, D. E. *Can. J. Chem.* **1973**, *51*, 772.

(4) Renaud, R. N.; Champagne, P. J. *Can. J. Chem.* **1975**, *53*, 529.

(5) Renaud, R. N.; Champagne, P. J.; Savard, M. *Can. J. Chem.* **1979**, *57*, 2617.

(6) Brookes, C. J.; Coe, P. L.; Owen, D. M.; Pedler, A. E.; Tatlow, J. C. *J. Chem. Soc., Chem. Commun.* **1974**, 323.

(7) Brookes, C. J.; Coe, P. L.; Pedler, A. E.; Tatlow, J. C. *J. Chem. Soc., Perkin Trans. 1* **1978**, 202.

(8) Muller, N. "Abstracts of Papers", Second Chemical Congress of the North American Continent, San Francisco, Aug 1980; American Chemical Society: Washington, DC, 1980; Abstract FLUO 056.

(9) Haszeldine, R. N.; Leedham, K. *J. Chem. Soc.* **1954**, 1261.

(10) Cragoe, E. J., Jr.; Robb, C. M.; Sprague, J. M. *J. Org. Chem.* **1950**, *15*, 381.

(11) Muller, N., paper in preparation.

High Enantioselectivity in Reductions with a Chiral Polymethylene-Bridged Bis(NADH) Model Compound

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Recently, we reported that the *p*-xylylene-bridged chiral bis(NADH) model compound carrying L-prolinamide as the asymmetric center showed virtually complete stereoselectivity in the asymmetric reduction of ethyl benzoylformate and acetylpyridine. The origin of the enantiospecificity was tentatively ascribed to the specific blockage of diastereotopic faces of the dihydronicotinamide nuclei due to the probable C_2 conformation the model adopts in association with the catalyst magnesium.[1]

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