J. Am. Chem. Soc. 1984, 106, 5544–5546

Generation and Capture of Functionalized Fluorocarbanions[1]

Carl G. Krespan,* Frederic A. Van-Catledge, and Bruce E. Smart

Contribution No. 3369 from the Central Research & Development Department,
E. I. du Pont de Nemours & Company, Experimental Station, Wilmington, Delaware 19898.

Received October 24, 1983

Abstract: Fluorocarbanions that are produced by the addition of nucleophiles to fluoroolefins can be trapped in many cases with CO_2 to form β-substituted polyfluoropropionates directly and in excellent to modest yields. The scope of the reaction encompasses the nucleophiles CN^-, N_3^-, $C_6H_5O^-$, RS^-, $(RO)_2P(O)^-$, $CF_3CH_2O^-$, and even Cl^-, and the fluoroolefins $CF_2{=}CF_2$, $CF_2{=}CFCl$, $CF_2{=}CFOCF_3$, and $CF_2{=}CFOC_3F_7$. Theoretical calculations of the relative energies for rotamers of four fluorocarbanions support the idea that successful trapping of a fluorocarbanion depends upon formation of a relatively stable conformer in which the incoming nucleophile and unshared electron pair are anti.

The addition of nucleophiles to fluoroolefins is a well-established, convenient source of fluorocarbanions.[2-4] Aside from the special case in which fluoride ion is the nucleophile, such fluorocarbanions generally have been trapped with a proton donor or isolated as the fluorolefin after loss of fluoride ion. We have found that carbon dioxide is an efficient trapping agent for many fluorocarbanions, provided that the nucleophile does not first add irreversibly to carbon dioxide.[5] The three-component reaction thus provides β-functionalized polyfluoropropionate salts directly and in excellent to fair yields. Cyanide ion is of particular interest as the nucleophile, since it leads to the formation of two new carbon–carbon bonds (eq 1).

$$NCCO_2^- \underset{CO_2}{\overset{-CO_2}{\rightleftarrows}} NC^- \xrightarrow{CF_2=CF_2} \underset{\mathbf{1}}{NCCF_2CF_2^-} \xrightarrow{CO_2}$$
$$\underset{\mathbf{2a}}{NCCF_2CF_2CO_2^-} \xrightarrow{(CH_3O)_2SO_2} \underset{\mathbf{2b}}{NCCF_2CF_2CO_2CH_3} \quad (1)$$

Optimum conditions for formation of carboxylate salt **2a** involve reacting sodium cyanide with tetrafluoroethylene and carbon dioxide in dimethyl sulfoxide solvent at ≤50 °C under moderate total pressure (<7000 kPa). The product is most conveniently isolated by treating the reaction mixture at 25 °C with dimethyl sulfate, followed by fractional distillation to give the methyl ester **2b** (65–75% yields).[6] Alternatively, acid-catalyzed hydrolysis of **2a** affords directly tetrafluorosuccinic acid (~70%).

Methoxide fails in the reaction since it forms a stable, unreactive adduct with carbon dioxide.[7] Less basic anions, however, are effective replacements for cyanide ion. Phenoxide, methyl mercaptide, and azide ions lead to esters **3–5** in 70–90% yields;

$XCF_2CF_2CO_2CH_3$
3, $X = C_6H_5O$
4, $X = CH_3S$
5, $X = N_3$
6, $X = CF_3CH_2O$

$Cl_2P(O)CF_2CF_2COCl$
7

$NCCF_2CFClCO_2CH_3$
8

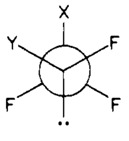
2,2,2-trifluoroethoxide affords 50% of ester **6** after methylation. Sodium dialkyl phosphite also participates to produce a phosphonate, isolated as the acid chloride **7** after reaction with PCl_5. Chloride ion reacts to provide methyl 3-chlorotetrafluoropropionate in low yield after a methylation step, whereas the more weakly nucleophilic bromide ion does not react.[8]

Cyanide also adds to chlorotrifluoroethylene to form a carbanion which is efficiently trapped by carbon dioxide, and subsequent methylation affords ester **8** (64%). However, all attempts to trap the carbanions produced from cyanide and trifluoromethyl trifluorovinyl ether or heptafluoropropyl trifluorovinyl ether gave little or no trapped products. Instead, loss of fluoride ion and perfluoroalkoxy groups perdominated, accompanied by the formation of dark tars. The presence of fluoride ion was indicated by extensive etching reactions, and loss of perfluoropropoxide was established by isolation of methyl pentafluoropropionate (40%) from the reaction with heptafluoropropyl trifluorovinyl ether. This behavior contrasts with that of azide ion, which gives readily trapped carbanions from both trifluorovinyl ethers. Thus, esters **9** and **10** are obtained in 80–90% yields. Phenoxide ion gives results similar to those obtained with azide ion.

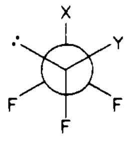
$N_3CF_2CF(OR_f)CO_2CH_3$
9, $R_f = CF_3$
10, $R_f = n\text{-}C_3F_7$

Discussion

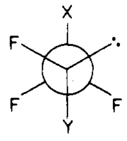
The unexpectedly different results with cyanide ion and azide ion suggest a limited lifetime for the carbanion **11** when X = CN and Y = perfluoroalkoxy. Presumably, the first-formed carbanion has the unshared electron pair anti to the nucleophile X (**11a**). Collapse of this species will merely regenerate the starting olefin. If, however, either the gauche(+) (**11b**) or the gauche(−) (**11c**) form is appreciably populated, carbanion fragmentation would occur by elimination of fluoride ion. This would divert the reaction to pathways that could lead to perfluoroalkoxide elimination.



11a



11b



11c

To clarify this matter, we undertook a theoretical study of the conformational profile for **11** (X = CN, N_3; Y = F, OCF_3). Ab initio SCF–MO calculations were carried out by using the program HONDOG.[9] Standard geometries were generated,[10] assuming a

---

[1] Presented in part at the Sixth Winter Fluorine Conference, Daytona Beach, FL, Feb 6–11, 1983.

[2] Rappoport, Z. *Adv. Phys. Org. Chem.* **1969**, *7*, 1.

[3] Young, J. A. *Fluorine Chem. Rev.* **1967**, *1*, 359.

[4] Chambers, R. D.; Mobbs, R. H. *Adv. Fluorine Chem.* **1965**, *4*, 50.

[5] Polyfluorocarbanions generated from fluoroolefins and fluoride ion are well-known to condense with CO_2 to afford polyfluorocarboxylic acid salts. See: Graham, D. P.; McCormick, W. B. *J. Org. Chem.* **1966**, *31*, 958. To our knowledge, however, the only reported example involving a nucleophile other than fluoride ion is the reaction of $C_6F_5O^-$ with $CF_2{=}CF_2$ to give $C_6F_5OCF_2CF_2CO_2^-$: Quarles, R. W. Ger. Offen. 2 109 979, 1971.

[6] A four-step synthesis of fluorinated ω-cyano esters such as **2b** starting from the corresponding diesters has been described: Dorfman, E.; Emerson, W. E. U. S. Patent 3 535 351, 1970. The present route starts from a readily available fluoroolefin and leads directly to a useful derivative of tetrafluorosuccinic acid in which the two carboxylic functions are differentiated.

[7] Sodium methoxide has been condensed successfully with tetrafluoroethylene in the presence of dimethyl carbonate as a carbanion trap. Acid workup provided methyl 3-methoxy-2,2,3,3-tetrafluoropropionate. See: Wiley, D. W. U.S. Patent 2 988 537, 1961.

[8] The nucleophilic order $Cl^- > Br^-$ in Me_2SO is well-known; see, for example: Rodewald, R. F.; Mahendran, K.; Bear, J. L.; Fuchs, R. *J. Am. Chem. Soc.* **1968**, *90*, 6698.

0002-7863/84/1506-5544$01.50/0

Table I. 4-31G Rotational Profiles for X–CF_2–CFY Carbanions[a,b]

	X = CN, Y = F	X = N_3, Y = F	X = CN, Y = OCF_3[c]	X = N_3, Y = OCF_3[c]
		Maxima		
	8.24 (0)	9.09 (0)	7.35 (359)	8.59 (0)
	5.05 (117)	7.18 (112)	5.64 (122)	7.67 (116)
	5.05 (243)	7.18 (248)	4.96 (244)	7.52 (249)
		Minima		
	1.99 (66)	4.29 (62)	0.63 (64)	3.25 (61)
	0.00 (180)	0.00 (180)	−0.05 (184)	−0.02 (182)
	1.99 (294)	4.29 (298)	1.55 (297)	3.89 (301)
		Fourier Coefficients		
V_1	3.54	4.28	2.14	3.16
V_2	−0.74	1.44	−0.63	1.60
V_3	4.70	4.80	5.20	5.43
V_1'			−0.05	−0.08
V_2'			−0.47	−0.29
V_3'			0.21	0.22

[a] Fourier constants are in kcal/mol. [b] Extrema are in kcal/mol with the dihedral angle in parentheses. [c] The configuration at the carbanionic center is *R*.

tetrahedral carbanion center, ahd the split-valence 4-31G basis set was employed.[11] The (X–C–C–:) dihedral angle was varied in 30° increments over the requisite range, and the resulting energies were fit to a truncated Fourier series.[12] From these fitted data, the locations and relative energies of the extrema were determined. These results are summarized in Table I.

For the symmetric anions (X = CN, N_3; Y = F), the expected butane-like rotational profiles are obtained. The most obvious difference between the two cases is the change in sign for the second-order term. This term has been ascribed to back-donation of the lone pair electrons into ajacent polar bonds.[13,14] Apeloig and Rappoport have shown that back-donation into the C–F bond is preferred relative to the C–CN bond.[15] We have conducted similar studies which show that azide facilitates back-donation better than fluoride. For both X = CN and X = N_3, the anti conformer is sufficiently preferred to ensure that the principal reaction pathway will be carboxylate production. Thus, for X = CN, $E_{\text{gauche}} - E_{\text{trans}} = 2.0$ kcal/mol and $K(\text{trans} \rightleftharpoons \text{gauche}) = 0.034$, whereas for X = N_3, $E_{\text{gauche}} - E_{\text{trans}} = 4.3$ kcal/mol and $K(\text{trans} \rightleftharpoons \text{gauche}) = 0.0007$.

When Y = OCF_3, the Fourier series contains nonzero coefficients for the sine terms, the most important contribution coming from the second-order term. The relative energies of the gauche forms are lowered, with the *g*(+) conformer being lowered more. This effect does not alter significantly the conformational mix when X = N_3 owing to the large initial energy difference.[16] For X = CN, however, the *g*(+) conformer now lies only 0.7 kcal/mol above the anti form (Figure 1), so that carbanion collapse now becomes competitive with trapping by carbon dioxide.[17]

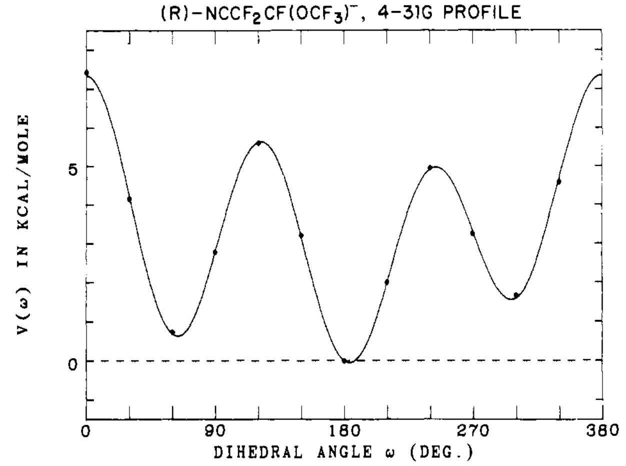


Figure 1. Relative energy as a function of the dihedral angle for the carbanion $NCCF_2CF(OCF_3)^-$, based on SCF–MO calculations using the 4-31G basis set. See text for the definition of the dihedral angle.

Based on these theoretical results, the observed result for X = CN, Y = OR_f can be rationalized by the scheme given in eq 2.

$$\mathbf{11}\ (Y = OR_f) \xrightarrow{-F^-} NC{-}CF{=}CF{-}OR_f \xrightarrow{+B^-} NC{-}\overset{-}{C}F{-}CF(B){-}OR_f \xrightarrow{-R_fO^-} NC{-}CF{=}CF{-}B\ (B = F \text{ or } CN) \xrightarrow{B^-} \text{tars} \quad (2)$$

Experimental Section

General Procedure. A mixture of 0.4–0.5 mol of the anion, usually as the sodium salt, and 150–200 mL of anhydrous Me_2SO is loaded into a 400-mL metal tube. The tube is cooled to −80 °C, evacuated, and charged cold with 0.52–0.75 mol of CO_2 and 0.5 mol of the fluoroolefin. The tube then is shaken while being warmed to room temperature, whereupon a mild exotherm and a sizeable pressure drop occur for most reactions. After 1–4 h at ambient temperature, the tube is heated to 50 °C and maintained there until the pressure no longer drops (1–4 h). With sodium 2,2,2-trifluoroethoxide, a temperature of 100 °C is required for rapid reaction.

The crude reaction mixture is removed from the tube and stirred with 0.45–0.55 mol of dimethyl sulfate for 3 h. The sufficiently volatile products are removed under reduced pressure and purified by fractionation. For the higher boiling products, the reaction mixture is poured into 500 mL of H_2O, and the product layer is removed, washed with H_2O, dried ($CaSO_4$), and fractionated.

Methyl 3-Cyano-2,2,3,3-tetrafluoropropionate (2b). A 400-mL shaker tube containing 24.5 g (0.50 mol) of sodium cyanide and 200 mL of Me_2SO was evacuated and charged at −25 °C with 23 g (0.52 mol) of CO_2 and 50 g (0.50 mol) of tetrafluoroethylene. The reaction mixture was agitated at ~30 °C for 1 h and then at 50 °C for 1 h. The resulting mixture was stirred with 69.3 g (0.55 mol) of dimethyl sulfate at 25 °C for 3 h. The product was removed by warming the mixture at 1 mm. Fractionation of the volatiles afforded 66.6 g (72%) of **2b**: bp 55–57 °C (170 mm); IR identical with that of a sample prepared by the literature[6] method. For the authentic sample: bp 95–97 °C; IR (CCl_4) 3010, 2960,

---

(9) This is the Du Pont version of the General Atomic and Molecular Electronic Structure System (GAMESS) developed by the staff of the National Resource for Computing in Chemistry (NRCC).

(10) (a) Pople, J. A.; Gordon, M. *J. Am. Chem. Soc.* **1967**, *89*, 4253. (b) The required azide parameters were taken from the methyl azide study of: Pauling, L.; Brockway, L. A. *Ibid.* **1937**, *59*, 13. (c) Exploratory calculations have shown that a split-valence basis set is a *minimum* requirement for obtaining realistic rotational profiles.

(11) (a) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1971**, *54*, 724. (b) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *Ibid.* **1972**, *56*, 2257. (c) Hariharan, P. C.; Pople, J. A. *Chem. Phys. Lett.* **1971**, *16*, 217.

(12) The Fourier series used is written so as to define $V(180)$ as zero.

$$V(\omega) = (1/2)\sum_k V_k[1 - (-1)^k \cos k\omega] + \sum_k V_k' \sin k\omega$$

(13) Radom, L.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1972**, *94*, 2371.

(14) Stock, L. M.; Wasielewski, M. R. *Adv. Phys. Org. Chem.* **1981**, *13*, 253.

(15) Apeloig, Y.; Rappoport, Z. *J. Am. Chem. Soc.* **1979**, *101*, 5095.

(16) Presumably for the same reason, the carbanions generated from $C_6H_5O^-$ and $CF_2{=}CFOR_f$ can be successfully trapped with CO_2. The hyperconjugative abilities of CH_3O and OH are reported to be greater than those for either CN or F.[15]

(17) This analysis presumes that internal rotation of the carbanions is slow relative to elimination as well as reaction with CO_2; otherwise the product distributions will be governed by the Curtin–Hammett principle.[18] Although absolute rate data for eliminations from fluorocarbanions are not available, it is reasonable to assume short-lived carbanions. Short-lived carbanion intermediates and hyperconjugative arguments similar to those presented here have been proposed to explain the stereochemistry of nucleophilic addition–elimination reactions of fluoroolefins.[2,15,19,20] The reaction of the trifluoromethyl carbanion with CO_2 in the gas phase has a bimolecular rate constant on the order of 10^{-11} cm^3 $molecule^{-1}$ s^{-1},[21] which corresponds to an activation energy of ca. 4.2 kcal/mol. This compares with the calculated barriers of rotation of 5–8 kcal/mol for the fluorocarbanions in this study and supports the assumption that reaction with CO_2 is faster than internal rotation.

(18) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83.

(19) Texier, F.; Henri-Rosseau, O.; Burgois, J. *Bull. Soc. Chim. Fr., Ser. 2* **1979**, 86.

(20) Normant, J.; Sauvetre, R.; Villieras, J. *Tetrahedron* **1975**, *31*, 891, 897.

(21) McDonald, R. N.; Chowdhury, A. K. *J. Am. Chem. Soc.* **1983**, *105*,, 7267.

2860 (CH), 2250 (CN), 1780 (C═O), and 1200–1100 cm^{-1} (CF); NMR (CCl_4) ^{1}H δ 3.98 (s, OCH_3); ^{19}F ϕ −107.6 (t, J_{FF} = 5.7 Hz, 2 F, CF_2), −119.5 (t, J_{FF} = 5.7 Hz, 2 F, CF_2). Anal. ($C_5H_3F_4NO_2$) C, H, N.

Methyl 3-Azido-2,2,3,3-tetrafluoropropionate (5). A 400-mL tube charged with 26.0 g (0.40 mol) of sodium azide, 150 ml of Me_2SO, 33 g (0.75 mol) of carbon dioxide, and 50 g (0.50 mol) of tetrafluoroethylene was agitated for 4 h at 50 °C. Further heating at 100 °C gave no additional pressure drop. The mixture was stirred with 56.7 g (0.45 mol) of dimethyl sulfate until the mildly exothermic reaction had subsided. The volatiles were then removed under reduced pressure and fractionated to give 73.2 g (91%) of **5**: bp 54 °C (50 mm); IR (CCl_4) 3010, 2960 and 2855 (CH), 2160 (N_3), 1785 (C═O), and 1300–1100 cm^{-1} (CF, C–O); NMR (CCl_4) ^{1}H δ 3.99 (s, OCH_3); ^{19}F ϕ −91.7 (t, J_{FF} = 4.7 Hz, 2 F, CF_2N_3), −120.5 (t, J_{FF} = 4.7 Hz, 2 F, CF_2C═O). Anal. ($C_4H_3F_4N_3O_2$) C, H, N.

Caution: Azidoester **5**, the smallest azide-containing molecule prepared in this work, was handled without incident and appears not to be unduly sensitive to mechanical, thermal, and electrical shock. However, when heated in a closed system to 230–240 °C, **5** detonated *violently*. Appropriate precautions are recommended in handling this and related azides.

Methyl 3-phenoxy-2,2,3,3-tetrafluoropropionate (3): 81% yield; bp 70 °C (1.8 mm); IR (neat) 3070, 3040 (aromatic CH), 2960 (saturated CH), 1780 (C═O), 1590 and 1492 (C═C), 1200–1100 cm^{-1} (CF, C–O); NMR (CCl_4) ^{1}H δ 7.30 (m, 5 H, aromatic CH), 3.95 (s, 3 H, OCH_3); ^{19}F ϕ −85.8 (t, J_{FF} = 4.6 Hz, 2 F, OCF_2), −121.6 (t, J_{FF} = 4.6 Hz, 2 F, CF_2C═O). Anal. ($C_{10}H_8F_4O_3$) C, H.

Methyl 3-(methylthio)-2,2,3,3-tetrafluoropropionate (4): 67% yield; bp 53 °C (10 mm) [lit.[22] bp 83 °C (50 mm)]. Anal. ($C_5H_6F_4O_2S$) C, H, F.

Methyl 2,2,3,3,6,6,6-heptafluoro-4-oxahexanoate (6): 51% yield; bp 68–69 °C (50 mm); IR (neat) 3020, 2980, 2920, 2870 (CH), 1785 (C═O), 1250–1100 cm^{-1} (CF, C–O); NMR (CCl_4) ^{1}H δ 4.21 (q, J_{HF} = 7.7 Hz, 2 H, CH_2), 3.84 (s, 3 H, OCH_3); ^{19}F ϕ −75.6 (t of t, J_{HF} = 7.7 Hz, J_{FF} = 2.3 Hz, 3 F, CF_3), −89.9 (t of q, J_{FF} = 4.3, 2.3 Hz, 2 F, CF_2O), −121.7 (t, J_{FF} = 4.3 Hz, 2 F, CF_2C═O). Anal. ($C_6H_5F_7O_3$) C, H, F.

3-(Dichlorophosphonyl)-2,2,3,3-tetrafluoropropionyl chloride (7): 11% yield (contaminated with ca. 10% CH_3SCCl_3); bp 59–69 °C (20 mm). For **7**: IR (CCl_4) 1800 (C═O), 1310 (P═O), 1250–1100 cm^{-1} (CF); NMR (CCl_4) ^{19}F ϕ −110.6 (m, 2 F, CF_2C═O), −116.0 (d of t, J_{PF} = 113 Hz, J_{FF} = 2.3 Hz, 2 F, CF_2–P).

Methyl 3-cyano-2-chloro-2,3,3-trifluoropropionate (8): 64% yield; bp 58 °C (50 mm); IR (CCl_4) 3020, 2960, 2950 (CH), 2250 (CN), 1770 (C═O), 1250–1100 cm^{-1} (CF); NMR (CCl_4) ^{1}H δ 3.95 (s, OCH_3); ^{19}F ϕ −132.9 (t, J_{FF} = 13.6 Hz, 1 F, CF); −100.2, −103.9 (AB m of m, J_{AB} = 287 Hz; A: d., J = 13.6 Hz; B: d, J = 13.6 Hz, 2 F, CF_2). Anal. ($C_5H_3ClF_3NO_2$) C, H, N.

Methyl 3-azido-2-(trifluoromethoxy)-2,3,3-trifluoropropionate (9): 84% yield, bp 38–41 °C (24 mm); IR (CCl_4) 3010, 2960, 2850 (CH), 2150 (N_3), 1780 (C═O), 1250–1100 cm^{-1} (CF); NMR (CCl_4) ^{1}H δ 3.89 (s, OCH_3); ^{19}F ϕ −56.0 (d, J_{FF} = 8.6 Hz, 3 F, OCF_3), −131.6 (q of t, J_{FF} = 8.6, 5.0 Hz, 1 F, CF); −89.6, −91.8 (AB m of m, J_{AB} = 188 Hz; A: , J_{FF} = 5.0 Hz; B: d, J_{FF} = 5.6 Hz, 2 F, CF_2N_3). Anal. ($C_5H_3F_6N_3O_3$) C, H, N.

Methyl 3-azido-2-(*n*-heptafluoropropoxy)-2,3,3-trifluoropropionate (10): 79% yield; bp 44–45 °C (10 mm); IR (CCl_4) 3010, 2970, 2850 (CH), 2150 (N_3), 1780 (C═O), 1250–1100 cm^{-1} (CF); NMR (CCl_4) ^{1}H δ 3.92 (s, OCH_3); ^{19}F ϕ −82.1 (t, J_{FF} = 7.3 Hz, 3 F, CF_3), −130.3 (d of d of t, J_{FF} = 19.6, 6, 6 Hz, 1 F, CF), −130.4 (s, 2 F, CF_2); −79.9, −87.8 (AB m of m, J_{AB} = 150 Hz; A: d of q, J_{FF} = 19.6, 7.3 Hz; B: q of d, J_{FF} = 7.3, 6 Hz, 2 F, OCF_2); −87.8, −89.9 (AB m of m, J_{AB} = 189 Hz; A: d, J_{FF} = 6 Hz; B: d, J_{FF} = 6 Hz, 2 F, CF_2N_3). Anal. ($C_7H_3F_{10}N_3O_3$) C, H, N.

Methyl 3-phenoxy-2-(trifluoromethoxy)-2,3,3-trifluoropropionate: 58% yield; bp 63 °C (0.5 mm); IR (neat) 3070 (aromatic CH), 2960 (saturated CH), 1785 (C═O), 1590, 1485 (C═C), 1250–1100 cm^{-1} (CF, C–O); NMR (CCl_4) ^{1}H δ 7.23 (m, 5 H, aromatic CH), 3.93 (s, 3 H, OCH_3); ^{19}F ϕ −55.8 (d, J_{FF} = 8.6 Hz, 3 F, OCF_3), −132.8 (q of d, J_{FF} = 8.6, 8.2 Hz, 1 F, CF); −83.3, −85.8 (AB m of m, J_{AB} = 138 Hz; B: d, J_{FF} = 8.2 Hz, 2 F, CF_2). Anal. ($C_{11}H_8F_6O_4$) C, H, F.

Registry No. 2b, 86414-22-4; **3**, 91312-77-5; **4**, 77705-91-0; **5**, 86414-01-9; **6**, 91312-78-6; **7**, 86414-15-5; **8**, 86413-99-2; **9**, 86414-03-1; **10**, 86414-05-3; $NCCF_2CF_2^-$, 91312-80-0; $N_3CF_2CF_2^-$, 91312-81-1; $NCCF_2CF(OCF_3)^-$, 91312-82-2; $N_3CF_2CF(OCF_3)^-$, 91312-83-3; methyl 3-phenoxy-2-(trifluoromethoxy)-2,3,3-trifluoropropionate, 91312-79-7; sodium cyanide, 143-33-9; tetrafluoroethylene, 116-14-3; sodium azide, 26628-22-8.

---

[22] Kimoto et al. (Kimoto, K.; Miyauchi, H.; Ohmura, J.; Ebisawa, M.; Hane, J. U.K. Patent Appl. GB 2051831, 1981) report the preparation of ester **4** by a related route.

Three-Center (Bifurcated) Hydrogen Bonding in the Crystal Structures of Amino Acids

G. A. Jeffrey* and **J. Mitra**

Contribution from the Department of Crystallography, University of Pittsburgh, Pittsburgh, Pennsylvania 15260. *Received December 5, 1983*

Abstract: The hydrogen bonding of the NH_3^+ groups in the crystal structures of the amino acids falls into three distinct classes. Of the 56 structures examined in this analysis, the distribution is as follows. In 10 structures, the NH_3^+ group forms three two-center (linear) hydrogen bonds, in 25, the NH_3^+ group forms two two-center bonds and one three-center bond, and in 14, the NH_3^+ group forms one two-center bond and two three-center bonds. There were no examples of three three-center bonds being formed. There are three examples of four-center (trifurcated) bonds. Two of the four structures with NH_2^+ and NH^+ groups also had three-center hydrogen bonds. This relatively high proportion of three-center bonds is a consequence of a deficiency in the number of functional protons necessary to satisfy the normal acceptor coordination of the carboxylate oxygens, which is two per oxygen, and the chloride ions, which is four.

Three-centered or bifurcated hydrogen bonding of the type **1** was recognized in one of the first amino acid crystal structures to be determined, that of α-glycine.[1] Although 12 well-documented examples of crystal structures containing three-centered hydrogen bonds of the type **1** were identified in 1968,[2] it is only comparatively recently that the concept has become generally accepted.[3-5] A recent metrical survey of 1509 N—H···O═C hydrogen bonds identified 304 as being three-centered.[4]

---

[1] Albrecht, G.; Corey, R. B. *J. Am. Chem. Soc.* **1939**, *61*, 1087–1103.

[2] Donohue, J. In "Structural Chemistry and Molecular Biology"; Rich, A., Davidson, N., Eds.; W. H. Freeman: San Francisco, 1968; pp 443–465.

[3] Newton, M. D.; Jeffrey, G. A.; Takagi, S. *J. Am. Chem. Soc.* **1979**, *101*, 1997–2002.

[4] Taylor, R.; Kennard, O.; Versichel, W. *J. Am. Chem. Soc.* **1984**, *106*, 244–248.

[5] Newton, M. D. *J. Phys. Chem.* **1983**, *87*, 4288–4292.

0002-7863/84/1506-5546$01.50/0