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Anodic Syntheses Involving ω-Monohalocarboxylic Acids[1]

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Representative ω-halocarboxylic acids ($X(CH_2)_nCOOH$) were examined for their ability to undergo the Kolbe electrolytic coupling reaction. Under the conditions employed, fluoroacids ($X = F$; $n \geqslant 4$), chloroacids ($X = Cl$; $n = 2$ or $\geqslant 4$) and bromoacids ($X = Br$; $n \geqslant 10$) gave the normal symmetrical products; iodoacids ($X = I$) on the other hand split out iodine in all instances. 10-Fluorodecanoic acid was shown also to undergo unsymmetrical coupling reactions in the presence of other acids.

A pronounced alternation in toxicity of members of the homologous series of ω-fluorocarboxylic esters, $F(CH_2)_nCOOR$, has been reported[2,3]; those esters the acid moieties of which contain an even number of carbon atoms are toxic, whereas the odd-numbered members are innocuous. More recently, a large number of aliphatic compounds containing an ω-fluorine atom have been prepared[4,5]; the toxic properties of these have been correlated with known metabolic mechanisms, thus affording a simple and clear-cut method of demonstrating *in vivo* conversions of various functional groups in aliphatic compounds. Because of the interesting pharmacological properties of these ω-fluoro compounds, improved methods for obtaining rare, long-chain members were required. Part of the work described in this paper provides one such method,[5] as is illustrated by the preparation of 13-fluorotridecyl chloride, methyl 18-fluorostearate, and seven members of the ω,ω'-difluoroalkane series.

No mention appears in the literature of the Kolbe coupling[6-8] with any fluorine-containing acids other than with trifluoroacetic acid[9,10]; with acids containing the other halogens, only one, 11-bromoundecanoic acid, has been reported to undergo the normal reaction.[11]

Much ingenuity has been displayed in the design of cells for carrying out electrolytic coupling reactions,[8] but refinements such as diaphragms, rotating anodes and flowing mercury cathodes offer little advantage for normal preparative purposes. The cell used in the present work consisted of a water-cooled tube containing two parallel pieces of platinum foil as electrodes. The current density was maintained between 0.11 and 0.16 amp./sq. cm. of anode surface, with the electrodes approximately 1.5 mm. apart.[12] Commercial absolute methanol was used as the solvent, and small amounts of metallic sodium were added. The reactions were continued until the cell contents were just alkaline to litmus; the time for this to occur was usually 50–100% greater than that calculated. In order to test the equipment and conditions, several previously described experiments[12] involving both symmetrical and unsymmetrical couplings were carried out, and in all cases the results were similar to those reported.

As a preliminary study, simple electrolytic coupling of some ω-chlorocarboxylic acids was examined; chloroacetic acid had previously been reported[13,14] to produce none of the expected ethylene chloride. Using the conditions outlined above, 3-chloropropionic, 5-chlorovaleric, 6-chlorohexanoic and 10-chlorodecanoic acids coupled in the normal manner. 4-Chlorobutyric acid however produced no 1,6-dichlorohexane, thus providing a further example of the inherent instability of ω-substituted *n*-butyric acids.

Under the same conditions, bromine was split out from all the lower ω-bromocarboxylic acids, and no other recognizable products were isolated. Only with a chain length of eleven or greater did normal coupling occur. ω-Iodocarboxylic acids in every instance decomposed with very rapid liberation of iodine.

The short chain ω-fluorocarboxylic acids did not undergo symmetrical coupling; thus, fluoroacetic, 3-fluoropropionic and 4-fluorobutyric acids produced no recognizable products, and considerable etching of the cell occurred, indicating liberation of hydrogen fluoride. However, 5-fluorovaleric, 6-fluorohexanoic, 7-fluoroheptanoic, 8-fluoroöctanoic, 9-fluorononanoic, 10-fluorodecanoic and 11-fluoroundecanoic acids formed the expected ω,ω'-difluoroalkanes in satisfactory yield. The product from the 10-fluoroacid, 1,18-difluoroöctadecane, was proved to be identical with the material formed by the fluorination of 1,18-dichloroöctadecane.

The above reactions are summarized in Table I. The reactions represent a new and convenient syn-

TABLE I

SIMPLE COUPLINGS OF ω-HALOCARBOXYLIC ACIDS

Acid: value of n in $X(CH_2)_nCOOH$	Yield (%) of $X(CH_2)_{2n}X$ X = F	X = Cl	X = Br	X = I
1	0	0	0	0
2	0	39	0	0
3	0	0	0	0
4	45	51.5	0	0
5	45	55	0	0
6	57.5	..	..	..
7	64	..	0	..
8	65	..	..	..
9	69	82	0	0
10	61	..	54	0
15	..	..	31	..

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[1] Issued as DRB Report No. SW-6.

[2] B. C. Saunders, *Nature*, **160**, 179 (1947).

[3] F. J. Buckle, F. L. M. Pattison and B. C. Saunders, *J. Chem. Soc.*, 1471 (1949).

[4] F. L. M. Pattison, *Nature*, **172**, 1139 (1953).

[5] F. L. M. Pattison, *ibid.*, **174**, 737 (1954).

[6] H. Kolbe, *Ann.*, **69**, 257 (1849).

[7] A. C. Brown and J. Walker, *ibid.*, **261**, 107 (1891).

[8] B. C. L. Weedon, *Quart. Revs.*, **6**, 380 (1952).

[9] F. Swarts, *Bull. classe sci. Acad. roy. Belg.*, **17**, 27 (1931).

[10] F. Swarts, *Bull. soc. chim. Belg.*, **42**, 102 (1933).

[11] H. Korsching, *Chem. Ber.*, **86**, 943 (1953).

[12] W. S. Greaves, R. P. Linstead, B. R. Shephard, S. L. S. Thomas and B. C. L. Weedon, *J. Chem. Soc.*, 3326 (1950).

[13] F. Kaufler and C. Herzog, *Ber.*, **42**, 3870 (1909).

[14] K. Elbs and K. Kratz, *J. prakt. Chem.*, **55**, 502 (1897).

thesis of difluorides, dichlorides and dibromides containing an even number of carbon atoms, the only limitation being the minimum chain lengths necessary for normal coupling to occur.

Representative unsymmetrical couplings were next examined. In an attempt to form an ω-fluoroalkyl halide, 10-fluorodecanoic acid and 5-chlorovaleric acid were electrolyzed

$$F(CH_2)_9COOH + HOOC(CH_2)_4Cl \longrightarrow F(CH_2)_{13}Cl + 2CO_2 + H_2$$

13-Fluorotridecyl chloride was thus formed in 24% yield. The purification of this material was tedious, due to contamination with esters which codistilled during attempted fractionation. These were finally removed by hydrolyzing the mixture with concentrated hydrochloric acid and purifying the resultant neutral fraction.

An ω-fluorocarboxylic ester was next prepared by the unsymmetrical coupling of 10-fluorodecanoic acid and methyl hydrogen sebacate

$$F(CH_2)_9COOH + HOOC(CH_2)_8COOMe \longrightarrow F(CH_2)_{17}COOMe + 2CO_2 + H_2$$

Methyl 18-fluorostearate was thus obtained. Again, purification of the product constituted the major difficulty, with dimethyl octadecanedioate being the main contaminant. Hydrolysis to the free acids followed by fractional crystallization was ineffective, and chromatography of the esters resulted in no clearly defined fraction. Fractional distillation followed by several recrystallizations from petroleum ether finally produced the pure product in very low yield (5%). The fluoro-ester on hydrolysis formed 18-fluorostearic acid, identical with the acid formed by oxidation of 18-fluorooctadecanol; the preparation of this fluoroalcohol will be described in a later paper.

The L.D. 50 of methyl 18-fluorostearate for mice was 18 mg./kg., and that of the free acid was 5.7 mg./kg.[4] This conforms to the toxicity pattern already reported[2-4] for the ω-fluorocarboxylates. For comparison, 9(10)-fluorostearic acid, $CH_3(CH_2)_nCHF(CH_2)_mCOOH$ ($n = 8$ or 7; $m = 7$ or 8) was prepared from ethyl oleate by addition of anhydrous hydrogen fluoride followed by hydrolysis. Its toxicity was very low (L.D. 50 > 400 mg./kg.). This marked difference between the two isomeric fluorostearic acids emphasizes the high specificity of the ω-fluorine atom for pharmacological activity. The toxicity of the ω,ω′-difluoroalkanes will be reported later.[15]

Experimental[16]

ω-Halocarboxylic Acids. Fluoroacetic Acid.—To technical sodium fluoroacetate (Monsanto "Compound 1080," containing 90% sodium fluoroacetate) (136 g.) was added a mixture of 96% sulfuric acid (318 g.) and 30% fuming sulfuric acid (232 g.). After thorough mixing, the mixture was distilled under reduced pressure, yielding crude fluoroacetic acid, b.p. 75–80° (11–14 mm.). The pure crystalline acid (99.1 g., 93.5%) was obtained by distillation at atmospheric pressure, b.p. 167–168°. Saunders and Stacey[17] report b.p. 167–168.5° and m.p. 31–32°.

3-Fluoropropionic Acid.—3-Fluoropropanol[18] (56.8 g., 0.73 mole) was added dropwise to a vigorously stirred solution of potassium dichromate (225 g., 0.765 mole), sulfuric acid (403 g.) and water (1120 g.), maintained at less than 5°. The mixture was then diluted with an equal volume of water, and continuously extracted with ether for 24 hours. After drying over anhydrous sodium sulfate and removal of the ether, the residue was fractionated yielding 47.7 g. (74%) of 3-fluoropropionic acid, of b.p. 83–84° (14 mm.) and n^{25}_{D} 1.3889. Gryszkiewicz-Trochimowski[19] reports b.p. 78.5–79.5° (12 mm.).

4-Fluorobutyric Acid.—4-Fluorobutanol[20] was oxidized by potassium dichromate, as above, to 4-fluorobutyric acid (68%), b.p. 76–78° (5 mm.), n^{25}_{D} 1.3998. Gryszkiewicz-Trochimowski[19] reports b.p. 60–62° (2 mm.).

Methyl 5-Fluorovalerate.—Dry hydrogen chloride was passed into a solution of 5-fluorovaleronitrile[21] (14.34 g., 0.14 mole) in anhydrous methanol (100 ml.). The mixture was boiled under reflux for one hour, with gradual precipitation of ammonium chloride. After cooling and pouring into an equal volume of water, the ester was extracted with ether. The ether layer was washed once with saturated sodium bicarbonate solution and then three times with water. After drying over anhydrous sodium sulfate and removal of the ether, the residual liquid was distilled under reduced pressure. Methyl 5-fluorovalerate (15.85 g., 83.5%) was thus obtained as a colorless, pleasant-smelling liquid of b.p. 72–74° (25 mm.) and n^{25}_{D} 1.3973.

Anal. Calcd. for $C_6H_{11}O_2F$: C, 53.70; H, 8.26. Found: C, 53.68; H, 7.90.

Methyl 6-fluorohexanoate, b.p. 70–71° (9 mm.), n^{25}_{D} 1.4047, was prepared by the same method from 6-fluorohexanonitrile[21] (166.5 g., 1.45 moles); yield 145.5 g. (68%).

Anal. Calcd. for $C_7H_{13}O_2F$: C, 56.72; H 8.84. Found: C, 56.58; H, 8.66.

5-Fluorovaleric Acid.—A mixture of methyl 5-fluorovalerate (13.76 g., 0.10 mole) and 5% sulfuric acid (120 ml.) was boiled under reflux until homogeneous (*ca.* 10 min.). The cooled solution was extracted with ether, and the extract washed with water. After drying over anhydrous sodium sulfate and removal of the solvent, the residual liquid was fractionally distilled under reduced pressure. After a small forerun of methyl 5-fluorovalerate (1.02 g., b.p. 57–60° (10 mm.), n^{25}_{D} 1.3988), 5-fluorovaleric acid (8.87 g., 77%) was obtained of b.p. 83° (2 mm.) and n^{25}_{D} 1.4080.

Anal. Calcd. for $C_5H_9O_2F$: C, 50.00; H, 7.55. Found: C, 49.75; H, 7.60.

6-Fluorohexanoic acid (96.7 g., 92%), b.p. 114° (6 mm.), n^{25}_{D} 1.4159 was prepared in the same way by hydrolysis of methyl 6-fluorohexanoate (134.5 g., 0.9 mole). Nischk and Müller[22] report b.p. 67–68° (0.6 mm.). A small forerun of the unchanged ester was also obtained.

An experiment omitting purification of the intermediate ester gave 6-fluorohexanoic acid in 71% over-all yield from 6-fluorohexanonitrile.

7-Fluoroheptanoic acid (18.32 g., 90%), b.p. 133–134° (10 mm.), d^{20}_{4} 1.039, n^{25}_{D} 1.4207, was prepared in the same way from 7-fluoroheptanonitrile (17.74 g., 0.14 mole), without purification of the intermediate methyl 7-fluoroheptanoate.

Anal. Calcd. for $C_7H_{13}O_2F$: C, 56.72; H, 8.84. Found: C, 56.93; H, 8.97.

10-Fluorodecanoic Acid.—10-Fluorodecanol[23] (22 g., 0.125 mole) was added dropwise to a vigorously stirred solution of chromium trioxide (50 g., 0.5 mole), glacial acetic acid (450 ml.) and water (50 ml.). The temperature of the mixture was maintained at less than 5° during the addition. Stirring was continued for an additional two hours, and the

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[15] F. L. M. Pattison and W. C. Howell, *J. Org. Chem.*, **21**, in press (1956).

[16] (a) The majority of the microanalyses were performed by Mr. J. F. Alicino, Metuchen, N. J.; (b) the melting points were determined with the Fisher–Johns melting point apparatus; (c) the melting points and boiling points are uncorrected; (d) all ω-halocarboxylic acids not mentioned were purchased commercially.

[17] B. C. Saunders and G. J. Stacey, *J. Chem. Soc.*, 1773 (1948).

[18] F. W. Hoffmann, *J. Org. Chem.*, **15**, 425 (1950).

[19] E. Gryszkiewicz-Trochimowski, *Rec. trav. chim.*, **66**, 430 (1947).

[20] E. Gryszkiewicz-Trochimowski, *ibid.*, **66**, 427 (1947).

[21] F. L. M. Pattison, W. J. Cott, W. C. Howell and R. W. White, THIS JOURNAL, **78**, in press (1956).

[22] G. Nischk and E. Müller, *Ann.*, **576**, 232 (1952).

[23] F. L. M. Pattison, W. C. Howell, A. J. McNamara, J. C. Schneider and J. F. Walker, *J. Org. Chem.*, **21**, in press (1956).

mixture was then allowed to stand at room temperature for 24 hours. The mixture was diluted with water and the product extracted with ether. The combined extract was washed with saturated sodium bicarbonate to dissolve the fluoroacid; the solution was then acidified with hydrochloric acid, and extracted with ether. After drying over anhydrous magnesium sulfate and removal of the ether, 10-fluorodecanoic acid (22 g., 93%) was obtained as a colorless solid. It was purified by recrystallization from low boiling petroleum ether; m.p. 49–49.5°.

Anal. Calcd. for $C_{10}H_{19}O_2F$: C, 63.16; H, 10.00. Found: C, 63.09; H, 10.04.

8-Fluoroöctanoic acid, m.p. 35°, recrystallized from low boiling petroleum ether, was obtained in the same way (78%) by oxidation of 8-fluoroöctanol.[23]

Anal. Calcd. for $C_8H_{15}O_2F$: C, 59.24; H, 9.24. Found: C, 59.66; H, 9.32.

9-Fluorononanoic acid, b.p. 100–101° (0.15 mm.), $n^{25}\mathrm{D}$ 1.4289, was obtained in the same way (87%) by oxidation of 9-fluorononanol.[23]

Anal. Calcd. for $C_9H_{17}O_2F$: C, 61.34; H, 9.72. Found: C, 61.46; H, 9.69.

11-Fluoroundecanoic acid, m.p. 33–34°, recrystallized from low boiling petroleum ether, was obtained in the same way (61%) by oxidation of 11-fluoroundecanol.[23]

Anal. Calcd. for $C_{11}H_{21}O_2F$: C, 64.67; H, 10.36. Found: C, 64.89; H, 10.70.

18-Fluorostearic Acid.—To 18-fluoroöctadecanol[23] (500 mg.) in glacial acetic acid (62 ml.) was slowly added chromium trioxide (750 mg.) in 90% acetic acid (7.5 ml.). The dark solution was allowed to stand at room temperature for 24 hours. Water was then added until precipitation was complete. The acid was filtered, washed with water and dried. The yield of crude 18-fluorostearic acid was 510 mg. (97%). It was purified by two recrystallizations from petroleum ether (60–80°), forming colorless crystals, m.p. 68.5–69°. This was subsequently used to characterize the 18-fluorostearic acid formed by an unsymmetrical coupling reaction.

Anal. Calcd. for $C_{18}H_{35}O_2F$: C, 71.53; H, 11.59. Found: C, 71.44; H, 11.75.

9(10)-Fluorostearic Acid.—Ethyl oleate (15 g.) and finely powdered mercurous chloride (10 mg.) were dissolved in carbon tetrachloride (60 g.) contained in a polyethylene bottle fitted with a polyethylene inlet tube. Anhydrous hydrogen fluoride was bubbled through the mixture for 4 hours. The resultant fuming solution was washed with a large excess of water. Bromine in carbon tetrachloride was added until a permanent orange color persisted. After drying over anhydrous sodium sulfate and removal of the solvent, the residue was distilled slowly. A fraction of b.p. 151–155° (0.004 mm.) was collected as crude ethyl 9(10)-fluorostearate (7.6 g., 48%). A small portion of this was hydrolyzed by boiling with 10% sodium hydroxide for 30 minutes. After cooling and acidifying with sulfuric acid, the solution was extracted with petroleum ether (60–80°). When this extract was cooled to −15°, white crystals separated. These were filtered and recrystallized from petroleum ether (60–80°). 9(10)-Fluorostearic acid was thus obtained as colorless crystals, m.p. 68–69° with slight softening at 43–44° (I. G. Farbenindustrie A.-G.[24] report m.p. 68°).

Anal. Calcd. for $C_{18}H_{35}O_2F$: C, 71.53; H, 11.59. Found: C, 71.26; H, 11.68.

3-Chloropropionic Acid.—A mixture of 3-chloropropionitrile (45 g., 0.435 mole) and concentrated hydrochloric acid (88 ml.) was heated under reflux for 4 hours. After cooling, the product was extracted with ether. The combined extract was washed with saturated sodium bicarbonate to dissolve the chloroacid; the solution was then acidified with hydrochloric acid and extracted with ether. After drying over anhydrous magnesium sulfate and removal of the ether, the residue was fractionated through a modified Podbielniak column, yielding 47 g. (86%) of 3-chloropropionic acid, b.p. 100° (13 mm.), m.p. 40–41°.

4-Chlorobutyric Acid.—4-Chlorobutanol (obtained from 4-chlorobutyl acetate in 60% yield by transesterification using methanol and *p*-toluenesulfonic acid) was oxidized by the method described for 3-fluoropropionic acid, yielding 4-chlorobutyric acid (56%), b.p. 120–125° (15 mm.), $n^{25}\mathrm{D}$ 1.4490. Nischk and Müller[22] report b.p. 84–85° (3 mm.).

5-Chlorovaleric Acid.—5-Chloropentanol (50 g., 0.4 mole) was added dropwise to a vigorously stirred solution of chromium trioxide (85 g., 0.85 mole), glacial acetic acid (450 ml.) and water (50 ml.). The temperature of the mixture was maintained at less than 5° during the addition. Stirring was continued for an additional 2 hours, and the mixture was then allowed to stand at room temperature for 24 hours. After dilution with water, the acid was isolated as described for 3-chloropropionic acid. The neutral fraction yielded 10 g. of recovered 5-chloropentanol, and the acidic fraction yielded 5-chlorovaleric acid (41.5 g., 76% conversion, 92% yield) of b.p. 99–100° (2 mm.) and $n^{25}\mathrm{D}$ 1.4515. Nischk and Müller[22] report b.p. 102° (2 mm.).

By this procedure, 6-chlorohexanol was oxidized in 72% yield to **6-chlorohexanoic acid**, b.p. 120–122° (3 mm.), $n^{25}\mathrm{D}$ 1.4530 [Nischk and Müller[22] report b.p. 116–117° (1.3 mm.)]; and 10-chlorodecanol[23] was oxidized in 51% to **10-chlorodecanoic acid**, m.p. 39–39.5°, recrystallized from low boiling petroleum ether.

Anal. Calcd. for $C_{10}H_{19}O_2Cl$: C, 58.10; H, 9.26; Cl, 17.16. Found: C, 57.94; H, 9.13; Cl, 16.97.

4-Bromobutyric acid was prepared from 4-phenoxybutyric acid by the method of Marvel and Birkhimer.[25]

8-Bromoöctanoic acid was prepared by degradation of silver methyl azelate with bromine[26] to methyl 8-bromooctanoate, followed by hydrolysis (dil. sulfuric acid) to the acid, m.p. 36–37°. Hunsdiecker and Hunsdiecker[26] report m.p. 37°.

10-Bromodecanol.—Decamethylene glycol (80 g., 0.453 mole) and 42% hydrobromic acid (650 ml.) were mixed in a liquid-liquid extractor. Using petroleum ether (boiling range 100–120°), the mixture was continuously extracted at 95–100° for 24 hours. The petroleum ether was then separated and shaken with granular potassium carbonate. After filtering off the solid and removal of the solvent, the residue was distilled through a 30 cm. Vigreux column, yielding 10-bromodecanol (74.0 g., 68%), a colorless liquid of b.p. 166–169° (10 mm.) and $n^{25}\mathrm{D}$ 1.4817. Chuit[27] reports b.p. 153–155° (8 mm.).

10-Bromodecanoic Acid.—By the method described above for the preparation of 5-chlorovaleric acid, 10-bromodecanol was oxidized in 31% yield to 10-bromodecanoic acid, a colorless solid of m.p. 37–38°, recrystallized from low boiling petroleum ether. Paulshock and Moser[28] report m.p. 35–38°.

5-Iodovaleric Acid.—A mixture of 5-chlorovaleric acid (26 g., 0.191 mole) and sodium iodide (57.0 g., 0.38 mole) in acetone (200 ml.) was heated under reflux for 16 hours. The mixture was cooled and filtered, and the acetone reremoved by distillation. The residue was diluted with water and extracted with ether. The extract was washed with dilute sodium thiosulfate and then with water, and dried over anhydrous sodium sulfate. After removal of the ether, the solid residue was recrystallized from low boiling petroleum ether (30–60°) to yield 5-iodovaleric acid (29.0 g., 66.5%), beautiful colorless leaflets, m.p. 56–57°. Hunsdiecker and Hunsdiecker[26] report m.p. 56°.

Similarly, 4-chlorobutyric acid was converted in 61% yield to **4-iodobutyric acid**, m.p. 37–38°, recrystallized from low boiling petroleum ether (30–60°) (Henry[29] reports m.p. 40–41°); and 6-chlorohexanoic acid was converted in 71% yield to **6-iodohexanoic acid**, m.p. 43–43.5°, recrystallized from low boiling petroleum ether (30–60°).

Anal. Calcd. for $C_6H_{11}O_2I$: C, 29.77; H, 4.58; I, 52.43. Found: C, 29.84; H, 4.50; I, 52.55.

Similarly, 10-chlorodecanoic and 11-bromoundecanoic acids were converted, in 67 and 71% yields, respectively, to **10-iododecanoic acid**, m.p. 49–50°, and **11-iodoundecanoic acid**, m.p. 64–65°, both recrystallized from petroleum ether (30–60°). Hunsdiecker and Hunsdiecker[26] report m.p. 53 and 66°, respectively.

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(24) I. G. Farbenindustrie A.-G., French Patent 799,432 (June 12, 1936); *C. A.*, **30**, 7585 (1936).

(25) C. S. Marvel and E. R. Birkhimer, THIS JOURNAL, **51**, 260 (1929).

(26) H. Hunsdiecker and Cl. Hunsdiecker, *Ber.*, **75B**, 291 (1942).

(27) P. Chuit, *Helv. Chim. Acta*, **9**, 264 (1926).

(28) M. Paulshock and C. M. Moser, THIS JOURNAL, **72**, 5073 (1950).

(29) Henry, *Compt. rend.*, **102**, 369 (1886).

TABLE II

SYMMETRICAL COUPLING REACTIONS

Product	Reactant (g.)		Sodium (g). in methanol (ml.)		Current, amp.	Time, hr.	Yield, %	B.p.		M.p., °C. or $n^{25}D$	Analytical results, %					
											Carbon		Hydrogen		Halogen	
								°C.	Mm.		Calcd.	Found	Calcd.	Found	Calcd.	Found
1,8-Difluoroöctane	5-Fluorovaleric acid	(10.0)	0.1	80	1.5	3	45	75–75.5	13	1.3933	63.97	63.87	10.74	10.48		
1,10-Difluorodecane	6-Fluorohexanoic acid	(10.0)	.085	80	1.5	2.7	45	98	12	1.4060	67.36	67.47	11.31	11.61		
1,12-Difluorododecane	7-Fluoroheptanoic acid	(10.0)	.08	80	1.5	2.5	57.5	120	10	1.4170	69.90	70.01	11.65	11.76		
1,14-Difluorotetradecane	8-Fluoroöctanoic acid	(10.0)	.07	80	1.5	2.2	64	148	11	1.4218	71.80	71.57	11.97	11.93		
1,16-Difluorohexadecane[a,b]	9-Fluorononanoic acid	(10.0)	.065	80	1.5	2.0	65	138	2.7	1.4268; m.p. 22.5–23	73.28	73.30	12.21	12.05		
1,18-Difluoroöctadecane[a,b,c]	10-Fluorodecanoic acid	(10.0)	.05	60	1.5	1.3	69	163–164	9	39–39.5	74.49	74.58	12.42	12.39		
1,20-Difluoroeicosane[b,d]	11-Fluoroundecanoic acid	(3.2)	.02	80	1.0	0.83	61			46–46.5	75.48	75.75	12.58	12.61		
1,4-Dichlorobutane[b]	3-Chloropropionic acid	(12.0)	.2	50	1.5	3	39	161–162		1.4501						
1,8-Dichloroöctane[b,e]	5-Chlorovaleric acid	(10.0)	.2	40	1.4	2.5	51.5	115–116	11	1.4570						
1,10-Dichlorodecane[b,f]	6-Chlorohexanoic acid	(15.0)	.12	80	1.5	3.5	55	140–142	10	1.4585						
1,18-Dichloroöctadecane[b,g]	10-Chlorodecanoic acid	(10.0)	.05	60	1.0	2.75	82			53.5–54	66.85	66.78	11.22	10.93	Cl, 21.93	Cl, 21.89
1,20-Dibromoeicosane[b,h,i,j]	11-Bromoundecanoic acid	(10.0)	.046	80	0.5–1.0	3	54			66.5–67						
1,30-Dibromotriacontane[b,h,i]	16-Bromohexadecanoic acid	(2.0)	.007	80	0.3–1.0	1.08	31			80–80.5	62.07	61.96	10.35	10.20	Br, 27.58	Br, 27.79

[a] Recrystallized from petroleum ether (30–60°). [b] The procedure for the removal of esters by heating with concd. hydrochloric acid was not carried out. [c] 1,18-Difluoroöctadecane was also obtained by fluorination of 1,18-dichloroöctadecane with potassium fluoride in diethylene glycol at 175° for six hours (40% yield), b.p. 110–112° (0.02 mm.), m.p. 39–40°. Mixed m.p. undepressed. [d] Recrystallized from methanol. [e] Huber[30] reports b.p. 118–119° (14 mm.) and $n^{25}D$ 1.4572. [f] Huber[30] reports b.p. 115–120° (4 mm.) and $n^{25}D$ 1.4586. [g] Recrystallized from methanol and from ethanol. Bennett and Gudgeon[31] report m.p. 54°. [h] As the reaction proceeded, the solid product settled on the electrodes, causing a marked drop in current; frequent changes of polarity were therefore necessary. [i] Recrystallized from methanol and from petroleum ether (30–60°). [j] Korsching[11] reports m.p. 67.4–68°.

Anodic Syntheses.—The cell used for all the electrolyses consisted of a water-jacketed 6-inch tube of diameter 1.5 inches. The cell was stoppered with a rubber stopper fitted with a dropping funnel, a reflux condenser and two platinum foil electrodes (5 cm. × 2.5 cm.). In the case of *symmetrical coupling reactions*, the acid, dissolved in commercial absolute methanol, was placed in the cell together with enough sodium to neutralize approximately 5% of the acid. After placing the electrodes about 1–2 mm. apart, a current of 1.0–2.0 amp. was passed for about twice the theoretical time, *i.e.*, until the electrolyte became slightly alkaline to litmus; a d.c. supply of 110 volts was used as the electrical power source. The temperature was maintained at 50° or less. In the case of *unsymmetrical coupling reactions*, 25% of the non-fluorinated material was dissolved in methanol and placed in the cell together with the required amount of sodium. After the electrolysis was started under the conditions described above, a methanolic solution of the remaining non-fluorinated material and the other acid component was added by means of the dropping funnel, at such a rate as to maintain the current at 1.5 amp. or greater. As soon as the electrolyte became slightly alkaline, the current was stopped. In order to isolate the products, the methanolic solutions were diluted with water, neutralized with glacial acetic acid and extracted with ether several times. The combined extracts were washed twice with 5% aqueous sodium carbonate to remove unreacted starting materials and then dried over anhydrous sodium sulfate or magnesium sulfate overnight. Finally, the ether was removed and the products isolated by fractional distillation through a modified Podbielniak column.

The apparatus and conditions were tested by carrying out the following preparations: dimethyl octadecanedioate (66%, from methyl hydrogen sebacate); diethyl octadecanedioate (65%, from ethyl hydrogen sebacate); *n*-decane (67%, from hexanoic acid); methyl hexanoate (isolated as the free acid, 42%, from methyl hydrogen adipate and acetic acid); and methyl decanoate (61%, from methyl hydrogen adipate and hexanoic acid).

(a) **Symmetrical Couplings.**—The general procedure, as outlined above, was essentially the same for all the symmetrical coupling reactions. The preparation of 1,8-difluoroöctane is representative, and is described below. The details of the other reactions, together with significant variations in technique, are given in Table II.

1,8-Difluoroöctane.—5-Fluorovaleric acid (10 g., 0.083 mole) was added to a cooled solution of sodium (0.1 g., 0.0043 mole) in methanol (80 ml.). A current of 1.5 amp. was passed for 3 hours. After isolation of the neutral fraction as described above and removal of the solvent, the residue was heated under reflux for one hour with concd. hydrochloric acid (50 ml.) to remove any esters (notably methyl 5-fluorovalerate formed during the electrolysis) which might have contaminated the product. The mixture was then cooled and extracted with ether. The extracts were washed with 5% aqueous sodium carbonate and with water. After drying and removal of the solvent, 2.8 g. (45%) of 1,8-difluoroöctane was obtained.

By essentially the same procedure, but usually under even milder conditions (lower current and greater dilution of reactants), the following acids produced none of the expected coupled products; the fluoroacids liberated hydrogen fluoride, while the bromo- and iodoacids formed the free halogen in most instances.

Fluoroacetic acid
3-Fluoropropionic acid
4-Fluorobutyric acid
Chloroacetic acid
4-Chlorobutyric acid
Bromoacetic acid
3-Bromopropionic acid
4-Bromobutyric acid
5-Bromovaleric acid
6-Bromohexanoic acid
8-Bromoöctanoic acid
10-Bromodecanoic acid
Iodoacetic acid
3-Iodopropionic acid
4-Iodobutyric acid
5-Iodovaleric acid
6-Iodohexanoic acid
10-Iododecanoic acid
11-Iodoundecanoic acid

(b) **Unsymmetrical Couplings of 10-Fluorodecanoic Acid. 13-Fluorotridecyl Chloride.**—10-Fluorodecanoic acid (10 g., 0.053 mole) and 5-chlorovaleric acid (14.4 g., 0.105 mole) were electrolyzed by the general procedure for unsymmetri-

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(30) W. F. Huber, THIS JOURNAL, **73**, 2730 (1951).

(31) G. M. Bennett and H. Gudgeon, *J. Chem. Soc.*, 1679 (1938).

cal electrolyses as outlined above. 5-Chlorovaleric acid (4.0 g.) and sodium (0.15 g., 0.0066 mole) were dissolved in methanol (50 ml.), and a current of 2.0 amp. applied. As the current started to drop, a methanolic solution of the remainder of the starting materials was slowly added to maintain the current at about 2.0 amp. Total time of the electrolysis was 2.6 hours. After the usual isolation, fractionation through a modified Podbielniak column yielded crude 13-fluorotridecyl chloride. This fraction was heated under reflux for one hour with concentrated hydrochloric acid (20 ml.) and then separated into neutral and acidic portions. The neutral fraction, upon distillation through the same column, yielded 3.05 g. (24.4%) of 13-fluorotridecyl chloride of b.p. 160.5° (14 mm.) and $n^{25}\text{D}$ 1.4407.

Anal. Calcd. for $C_{13}H_{26}ClF$: C, 65.97; H, 11.00; Cl, 15.01. Found: C, 65.74; H, 10.85; Cl, 14.98.

Methyl 18-Fluorostearate.—Methyl hydrogen sebacate (3.0 g., 0.014 mole) was added to a solution of sodium (0.15 g., 0.0066 mole) in methanol (50 ml.). A current of 1.5 amp. was applied. A solution of methyl hydrogen sebacate (11.4 g., 0.053 mole) and 10-fluorodecanoic acid (10 g., 0.053 mole) was added at such a rate as to maintain the current at 1.5 amp. The reaction was complete after 2.8 hours. After the usual isolation procedure, crude methyl 18-fluorostearate was obtained, of b.p. 143–148° (0.6 mm.), which solidified on standing. This was recrystallized from petroleum ether (60–80°) yielding 0.8 g. (4.8%) of pure methyl 18-fluorostearate, m.p. 33–34°. A small portion of this was hydrolyzed with 10% sodium hydroxide to 18-fluorostearic acid, which after recrystallization from petroleum ether had m.p. 68–69°. An equal mixture of the samples obtained by this method and by the oxidation of 18-fluoroöctadecanol (see above) had m.p. 68–69°.

Anal. Calcd. for $C_{19}H_{37}O_2F$: C, 72.14; H, 11.70. Found: C, 72.25; H, 11.48.

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LONDON, ONTARIO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

The Isomerization by Base of Alkyl Allyl Sulfides to Alkyl Propenyl Sulfides. The Mechanism of the Reaction[1]

BY D. S. TARBELL AND WILLIAM E. LOVETT

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Allyl *n*-hexyl sulfide is isomerized to *n*-hexyl propenyl sulfide by refluxing with 3.7 *M* alcoholic sodium ethoxide; allyl *t*-butyl sulfide behaves similarly. Allyl *n*-hexyl ether is recovered after similar treatment. Diallyl sulfide is isomerized to dipropenyl sulfide, and is also converted in part to an unsaturated mercaptan, 3-mercapto-1,5-hexadiene, by a rearrangement of an allyl group. N-Sodiochloro-*p*-bromobenzenesulfonamide has been found to be superior to chloramine-T for characterization of sulfides by formation of sulfilimines. Isomerization of allyl *n*-hexyl sulfide by sodium ethoxide in deuteroethanol gives *n*-hexylpropenyl sulfide containing (by mass spectrometric analysis) considerable quantities of mono- and dideuterated products, indicating that the isomerization proceeds through a carbanion which can exchange with the solvent. The results of the study emphasize the ability of sulfide sulfur, not attached to an aromatic ring, to stabilize a negative charge on the adjacent carbon, presumably through contributions from resonance forms with a decet of electrons around sulfur.

It was shown previously[2] that aryl allyl sulfides (I, R = aryl or 2-pyridyl) are readily isomerized by aqueous or alcoholic base to the corresponding propenyl sulfides II. This behavior was interpreted as an indication of the ability of the sulfur atom to stabilize the carbanion III by contributions from resonance forms with a decet of electrons around sulfur. It was obviously desirable to know if the isomerization required the presence of an aromatic (or heterocyclic) group attached to sulfur; such groups might contribute to the stability of the carbanion by resonance involving the aromatic nucleus. In the present paper it is shown that the isomerization of alkyl allyl sulfides to alkyl propenyl sulfides does in fact occur readily. Experiments on the isomerization in deuteroethanol indicate that the reaction probably proceeds through a carbanion III which can exchange deuterium with the solvent.

The allyl sulfides I were prepared and characterized by analysis, refractive index, spectroscopic properties and by catalytic reduction to the corresponding *n*-propyl sulfides IV. The isomerization was followed by observing the refractive index, and the propenyl sulfides II were characterized by analysis, spectroscopic properties, preparation of crystalline sulfilimines and by catalytic reduction to the *n*-propyl sulfides IV. These were shown to be identical with authentic samples of the *n*-propyl sulfides by mixed melting points of the crystalline sulfilimines.

It was found in this work that sulfilimines V prepared from N-sodiochloro-*p*-bromobenzenesulfonamide[3] were uniformly higher melting and more desirable as derivatives than the corresponding ones (VI) prepared from chloramine-T.

The *n*-hexyl propenyl sulfide (IIa) obtained by isomerization was apparently a mixture of *cis* and *trans* isomers, as was phenyl propenyl sulfide,[2] because the sulfilimine melted over a range (75–85°),

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(1) This research was supported in part by the United States Air Force, through the Office of Scientific Research of the Air Research and Development Command.

(2) D. S. Tarbell and M. A. McCall, THIS JOURNAL, **74**, 48 (1952).

(3) R. R. Baxter and F. D. Chattaway, *J. Chem. Soc.*, **107**, 1814 (1915).