THE ELECTROLYSIS OF ω-BROMOCARBOXYLIC ACIDS

II. PREPARATION OF LONG-CHAIN ω-BROMOCARBOXYLIC ESTERS BY MIXED COUPLING REACTIONS[1]

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ABSTRACT

An attempt to synthesize long-chain ω-bromocarboxylic esters from the mixed electrolyses of ω-bromocarboxylic acids and half-esters is described. Methyl 15-bromopentadecanoate was successfully prepared in this way in 37% yield, but other reactions producing methyl 16-bromohexadecanoate (by two different routes) and methyl 14-bromotetradecanoate gave low yields (6–18%) and difficulties in purification of products. The product analysis of these electrolyses (symmetrical and unsymmetrical coupling products, methyl esters of starting materials) is given. It is concluded that this method is more likely to be of specific rather than general use.

The use of halogenated carboxylic acids for Kolbe electrolysis reactions has received little study (1). Most of the successful reactions have involved ω-chloro- and ω-bromocarboxylic acids (2–4). Under appropriate conditions the ω-chloro- and ω-bromo-acids with chains of six or more carbon atoms couple normally to produce ω,ω′-dihalides in good (usually 60–70%) yield. The preparation of 1,28-dibromooctacosane by electrolysis of 15-bromopentadecanoic acid is an example (see Experimental section). This dibromide has not been made previously by the Kolbe reaction.

The number of reported mixed electrolyses involving halogenated acids to produce long-chain esters and halides is small. Pattison *et al.* (3) produced 13-fluorotridecyl chloride in 24% yield from the electrolysis of 10-fluorodecanoic acid and 5-chlorovaleric acid. A series of esters have been produced by mixed coupling reactions of ω-fluoroacids (3, 5, 6). However, fluorine is not a typical halogen. The only mixed electrolysis of an ω-bromoacid is the preparation of 1-bromo-2,4-dimethyldocosane from 3,5-dimethyl-6-bromohexanoic acid and stearic acid but no experimental details are given (7).

ω-Bromo-acids and esters are useful as intermediates in multi-step syntheses (e.g. the bromodocosane just mentioned), but their preparation often involves long, tedious routes and low overall yields. Thus a study of the mixed electrolysis of some ω-bromoacids and half-esters seemed appropriate as a possible method offering a one-step route to the longer chain ω-bromoesters. A promising initial reaction seemed to be a mixed electrolysis of 11-bromoundecanoic acid (I; $n = 10$) and methyl hydrogen adipate (II; $m = 4$), both of which are commercially available as fairly inexpensive compounds.

$$\underset{\text{I}}{\mathrm{Br(CH_2)_{\mathit{n}}COOH}} + \underset{\text{II}}{\mathrm{HOOC(CH_2)_{\mathit{m}}COOCH_3}} \xrightarrow[\text{d-c. current}]{\mathrm{CH_3OH}\ \text{solvent}}$$

$$\underset{\text{III}}{\mathrm{Br(CH_2)_{\mathit{n}+\mathit{m}}COOCH_3}} + \underset{\text{IV}}{\mathrm{Br(CH_2)_{2\mathit{n}}Br}} + \underset{\text{V}}{\mathrm{CH_3OOC(CH_2)_{2\mathit{m}}COOCH_3}}$$

$$+ \underset{\text{VI}}{\mathrm{Br(CH_2)_{\mathit{n}}COOCH_3}} + \underset{\text{VII}}{\mathrm{CH_3OOC(CH_2)_{\mathit{m}}COOCH_3}}$$

This reaction produced the primary reaction products III ($n + m = 14$), IV ($n = 10$), and V ($m = 4$) and, in addition, the products VI ($n = 10$) and VII ($m = 4$), methyl

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[1] *For Part I, see reference 4.*

esters of the starting materials, resulted from attack of the carboxylate radicals on the solvent. Control reactions showed a negligible tendency to form esters under the reaction conditions if no current were passed. The desired long-chain ω-bromoester, methyl 15-bromopentadecanoate (III; $n + m = 14$) was easily separated from the other products by distillation. The yield of 37% (Table I) is good, considering the number of products possible and bearing in mind that there are few recorded examples in which mixed coupling products are produced in significantly better yields. Moreover, the reaction represents a simpler and more effective means of obtaining this bromoester than hitherto reported (8).

It was previously shown (4) that experimental conditions have to be carefully controlled in reactions of long-chain ω-bromoacids to avoid the almost complete esterification of starting material. Further work indicates that the most critical factor is the temperature of reaction. At temperatures above ca. 54° the yield of coupled product is lowered considerably. Other factors normally considered critical, such as current density, concentration, and solvent, do not affect this yield nearly so much. Therefore, in the present experiments, the temperature was kept between 45 and 54°, while maintaining as high a current density as possible.

The success of this mixed coupling reaction led to its extension to other ω-bromoacids and half-esters. A number of possible combinations were ruled out because of anticipated difficulties in separating products, especially the long-chain bromoester, by distillation. Three reactions were tried: 8-bromooctanoic acid (I; $n = 7$) and methyl hydrogen sebacate (II; $m = 8$) to give methyl 16-bromohexadecanoate (III; $n + m = 15$); 6-bromohexanoic acid (I; $n = 5$) and methyl hydrogen sebacate (II; $m = 8$) to give methyl 14-bromotetradecanoate (III; $n + m = 13$); and 12-bromododecanoic acid (I; $n = 11$) and methyl hydrogen adipate (II; $m = 4$) to give also methyl 16-bromohexadecanoate. In these cases the products IV and V were usually obtained in greater yield, and separation of the products was much more difficult than in the previous reaction producing methyl 15-bromopentadecanoate. A summary of product yields is given in Table I.

TABLE I

Mixed coupling reactions of ω-bromocarboxylic acids

Reagents		Product yield (%)				
I	II	III	IV	V	VI	VII
$n = 10$	$m = 4$	37	39	39	11	5
$n = 11$	$m = 4$	6	21	51	34	1
$n = 5$	$m = 8$	18	23	1	51	50
$n = 7$	$m = 8$	7	24	6	32	30

It must be concluded that, while specific reactions of ω-bromoacids and half-esters may produce a successful mixed coupling, e.g. the preparation of methyl 15-bromopentadecanoate (and thus 15-bromopentadecanoic acid), the method is not likely to be a good general one for the preparation of pure long-chain ω-bromoesters in reasonable yield.

EXPERIMENTAL

General

Melting points, which were corrected, were recorded on a Leitz hot-stage microscope. Boiling points were uncorrected. Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, New York.

A previous article (4) describes the commercial sources or the preparations of ω-bromoacids, methyl hydrogen adipate, and authentic reference samples used in the present work. The electrolytic cell was also fully described, as well as the general method of working up the reaction products into neutral and acidic fractions. Methyl hydrogen sebacate was prepared by half-esterification of sebacic acid. Following standard procedure in mixed electrolyses, the half-ester was usually in 1–2 molar excess, so as to improve chances for optimum yield of mixed coupling product. Percentage yields for the mixed electrolyses are recorded in Table I and are based on moles of bromoacid or half-ester reacting (in each case, on whichever was the limiting reagent).

Gas chromatographs used were a Beckman GC-2A and an F and M model 720 with TC3 fraction collector; columns were 6–8 ft Carbowax 20, diethylene glycol succinate, and silicone rubber on Chromosorb-W or its equivalent. Infrared spectra were obtained with a Beckman model IR-5.

Mixed Electrolysis of 11-Bromoundecanoic Acid and Methyl Hydrogen Adipate

11-Bromoundecanoic acid (50 g, 0.19 mole), methyl hydrogen adipate (100 g, 0.63 mole), and sodium (0.9 g, 0.04 g-atom) were dissolved in 95% methanol (130 ml). A current of 1.5–1.7 A was passed for 42 hours (3 × theoretical) at a temperature of 45–50°. A negligible amount of unreacted acid was isolated.

Distillation of the neutral fraction through a short Vigreux column yielded the following fractions: (i) b.p. 80–100° (0.6 mm), 13.8 g; (ii) b.p. 108–111° (0.6 mm), n_D^{25} 1.4346, 28.0 g; (iii) 125–130° (0.6 mm), n_D^{25} 1.4630, 6.0 g; (iv) 130–168° (0.6 mm), 29.5 g; and an undistilled residue of 15.8 g.

Fraction (i) was shown, by gas chromatography, to contain dimethyl adipate, 5.7 g. Fractions (ii) and (iii) were shown by gas chromatography and infrared spectrum analysis to be dimethyl sebacate and methyl 11-bromoundecanoate respectively; Trent *et al.* (9) give b.p. 175° (20 mm), n_D^{25} 1.4342 for dimethyl sebacate, and methyl 11-bromoundecanoate has b.p. 112–116° (0.3 mm), n_D^{25} 1.4630 (4). Fraction (iv) was methyl 15-bromopentadecanoate and was redistilled to yield a white solid, 23.4 g, of b.p. 142–147° (0.25 mm), m.p. 36.5–38.5°. Recrystallization from methanol yielded a solid with m.p. 38.5–39.5°. Anal. Calc. for $C_{16}H_{31}BrO_2$: C, 57.32; H, 9.32; Br, 23.84. Found: C, 57.41; H, 9.32; Br, 23.60. The infrared spectrum was consistent with the structure assumed. The original residue from distillation plus a 3.1 g residue from redistillation of fraction (iv) was recrystallized from methanol to yield 1,20-dibromoeicosane (16.3 g) of m.p. 66.5–68°; Korsching (2) reports m.p. 67.4–68°. A mixed melting point with an authentic sample showed no depression.

Mixed Electrolysis of 12-Bromododecanoic Acid and Methyl Hydrogen Adipate

12-Bromododecanoic acid (23.6 g, 0.085 mole), methyl hydrogen adipate (40.6 g, 0.25 mole), and sodium (0.040 g., 0.017 g-atom) were dissolved in methanol (100 ml) and electrolyzed at 2.0 A for 21 hours (4 × theoretical) at 50–54°. The neutral extract was 46.9 g, and unreacted acids were 5.7 g (1.8 g bromoacid and 6.3 g half-ester, by gas chromatography).

Distillation of the neutral extract and redistillation of each fraction gave the following: (i) b.p. 110–113° (13 mm), n_D^{25} 1.4264, 1.1 g; (ii) b.p. 108–110° (0.6 mm), n_D^{25} 1.4346, 14.1 g; (iii) b.p. 130–135° (0.6 mm), n_D^{25} 1.4625, 7.5 g; (iv) b.p. 152–157° (0.6 mm), m.p. 24–26°, 1.5 g; (v) undistilled residue, 5.4 g.

Gas chromatography and infrared spectrum analysis showed fraction (i) to be dimethyl adipate, fraction (ii) to be dimethyl sebacate, and fraction (iii) to be methyl 12-bromododecanoate; Hunsdiecker and Hunsdiecker (8) give b.p. 130° (0.5 mm). Fraction (iv) was methyl 16-bromohexadecanoate. Seven recrystallizations from methanol gave a white solid of m.p. 28–29° which could not be raised further; Hunsdiecker and Hunsdiecker (8) give m.p. 31°. For fraction (iv) Anal. Calc. for $C_{17}H_{33}BrO_2$: C, 58.46; H, 9.52; Br, 22.88. Found: C, 58.31; H, 9.43; Br, 22.90. Fraction (v) was recrystallized from petroleum ether (30–60°) and methanol to give a white solid (3.6 g) of m.p. 69–70°, undepressed on admixture with authentic 1,22-dibromodocosane.

Mixed Electrolysis of 8-Bromooctanoic Acid and Methyl Hydrogen Sebacate

8-Bromooctanoic acid (40.0 g, 0.18 mole), methyl hydrogen sebacate (78.0 g, 0.36 mole), and sodium (0.21 g, 0.009 g-atom) were dissolved in methanol (150 ml) and electrolyzed at 1.0–1.5 A for 40 hours (3 × theoretical) at 40–50°. At the end of this time the reaction mixture was thick with a solid white precipitate and the temperature could no longer be held below 50°. Gas chromatography showed the recovered acids to be 13.0 g 8-bromooctanoic acid and 25.0 g methyl hydrogen sebacate.

The neutral extract of 44.2 g was distilled and the main fractions redistilled. The following fractions were collected: (i) b.p. 88–90° (0.7 mm), n_D^{25} 1.4605, 8.7 g; (ii) 105–110° (0.6 mm), n_D^{25} 1.4348, 16.7 g; (iii) b.p. 155–160° (0.4 mm), m.p. 24–26°, 2.8 g; (iv) b.p. 165–172° (0.2 mm), m.p. 45–47°, 5.2 g; (v) residue in distilling flask, 2.3 g.

Fraction (i) was shown by gas chromatography and infrared spectrum analysis to be methyl 8-bromooctanoate; Cavanna and Ställberg-Stenhagen (10) give b.p. 91° (0.8 mm). Fraction (ii), identified in the same way, was dimethyl sebacate. Recrystallization of fraction (iii) from methanol gave a white solid of m.p. 28–29°, undepressed on admixture with authentic methyl 16-bromohexadecanoate. Recrystallization of fraction (iv) from petroleum ether (30–60°) gave a solid of m.p. 47.5–48.0°, undepressed on mixing with authentic 1,14-dibromotetradecane. The residue, fraction (v), on recrystallization from low-boiling petroleum ether gave a white solid of m.p. 59–60°, undepressed on admixture with authentic dimethyl 1,16-hexadecanedicarboxylate.

Mixed Electrolysis of 6-Bromohexanoic Acid and Methyl Hydrogen Sebacate

6-Bromohexanoic acid (25.0 g, 0.13 mole), methyl hydrogen sebacate (83.0 g, 0.39 mole), and sodium (0.6 g, 0.025 g-atom) were dissolved in 150 ml of 1:1 methanol–water. Electrolysis was carried out at 1.5–3.5 A for 28 hours (3 × theoretical) at 45–54°. Products were a neutral extract of 65.5 g and unreacted acids 6-bromohexanoic acid, 1.8 g, and methyl hydrogen sebacate, 6.3 g.

The neutral extract was fractionated and the fractions redistilled to yield: (i) b.p. 66–69° (0.3 mm), n_D^{25} 1.4625, 12.9 g; (ii) 95–102° (0.3 mm), 43.4 g; (iii) 145–150° (0.6 mm), 6.9 g; (iv) undistilled residue, 0.7 g.

Fraction (i) was shown by gas chromatography and infrared spectrum analysis to be methyl 6-bromohexanoate; Skinner, Johnston, and Fisher (11) give b.p. 72° (1 mm), n_D^{22} 1.4635. Fraction (ii) was shown by gas chromatography to be a mixture of 1,10-dibromodecane (4.1 g) and dimethyl sebacate (39.3 g). Fraction (ii) could not be separated further by distillation, but fractionation by gas chromatography yielded small samples of the two compounds; these had the expected infrared spectrum and the correct physical constants: n_D^{25} 1.4265 for dimethyl sebacate, and n_D^{28} 1.4914, m.p. 25–26° for 1,10-dibromodecane (melting point undepressed on admixture with an authentic sample). Fraction (iii) was identified by gas chromatography and infrared spectrum analysis to be methyl 14-bromotetradecanoate; Hunsdiecker and Hunsdiecker (8) give b.p. 164° (0.8 mm), m.p. 22°. Careful recrystallization from methanol gave m.p. 23–23.5°. Fraction (iv), on recrystallization from petroleum ether (30–60°), gave 0.6 g of a white solid of m.p. 59–60°, undepressed on admixture with authentic dimethyl 1,16-hexadecanedicarboxylate.

15-Bromopentadecanoic Acid

Methyl 15-bromopentadecanoate (6.0 g, 0.016 mole) was dissolved in 150 ml of 4 *N* hydrogen bromide in glacial acetic acid and heated under reflux for 24 hours. 5.3 g (95%) of 15-bromopentadecanoic acid of m.p. 65–66° (from low-boiling petroleum ether) was isolated; Hunsdiecker and Hunsdiecker (8) report m.p. 66°. Because of the low solubility of this ester in aqueous systems, attempts to use 48% hydrobromic acid in glacial acetic acid gave less than 0.5% hydrolysis in the same time period.

1,28-Dibromooctacosane

15-Bromopentadecanoic acid (2.00 g, 0.0006 mole) in methanol (50 ml) was electrolyzed at 0.8 A for 10 hours at 45–50°. There was 0.24 g of unreacted acid. The neutral fraction was recrystallized from methanol to yield 0.70 g (51%) of 1,28-dibromooctacosane of m.p. 78–79°. Anal. Calc. for $C_{28}H_{56}Br_2$: C, 60.84; H, 10.23; Br, 28.93. Found: C, 60.54; H, 10.21; Br, 28.62. Gas chromatography of the recrystallization residue indicated 0.38 g, 21%, of the ester methyl 15-bromopentadecanoate.

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