Electrochemical Synthesis of Diethyl 2,3-Bis-*p*-halogenophenylsuccinates; Reduction of α-Bromo-*p*-halogenophenylacetates[1]

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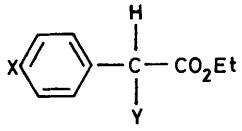
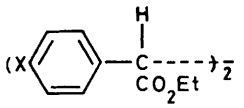
The reductive electrochemical dimerization of ethyl α-bromo-*p*-halogenophenylacetates, (ABr) (**1**)—(**3**), to the corresponding racemic and *meso* succinates (AA) (**7**)—(**9**) is reported. Monoesters AH (**4**)—(**6**) and epoxides (**11**)—(**13**) were also isolated. An excess of racemic isomer for (**7**)—(**9**) is observed, decreasing in the order of the F, Cl, and Br substituent in the phenyl group. Voltammetric experiments show only slight differences between the reduction potentials of the isomeric *meso* and racemic compounds (**8**), whereas in the case of the isomeric *p*-bromo-substituted compounds (**9**) the reduction potentials are almost identical. The *meso* compounds can be distinguished from the DL isomers by n.m.r. spectroscopy. This feature is also observed in the n.m.r. spectra of epoxides (**11**)—(**13**).

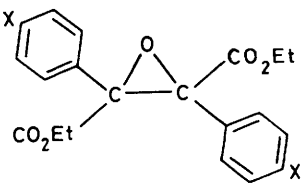
The electrochemical reductive dimerization of ethyl α-bromo-*p*-halogenophenylacetates ABr (**1**)—(**3**) to give the corresponding succinates AA (**7**)—(**9**) is reported. In principle, symmetrical succinic acids or esters are obtainable, chemically, by Würtz-type reactions,[2] by dimerization of thermally or photochemically generated radicals from azoalkanes,[3] by dimerization of radicals generated by hydrogen abstraction,[4] and by oxidative coupling reactions.[5] Electrochemical reductive dimerization of alkyl α-aryl-α-halogenoacetates AHal at a glassy carbon electrode in aprotic solvents offers an alternative route to the desired compounds.[6–9] Electrochemical reduction of AHal can be controlled by choosing a definite, constant potential for electrolysis. Thus, over-reduction of the products, expected if chemical methods using metals are employed, can be avoided.



(**1**) X = F, Y = Br (**4**) X = F, Y = H
(**2**) X = Cl, Y = Br (**5**) X = Cl, Y = H
(**3**) X = Y = Br (**6**) X = Br, Y = H



(**7**) X = F (**9**) X = Br
(**8**) X = Cl (**10**) X = H
a; *meso*
b; DL



(**11**) X = F
(**12**) X = Cl
(**13**) X = Br
a; *meso*
b; DL

Our results are interesting because (i) the *p*-halogeno-substituent is preserved during the preparative procedure; (ii) *meso* and DL structures of the products can be assigned to particular diesters on the basis of the n.m.r. spectra; (iii) an excess of the DL isomer relative to the corresponding *meso* isomer is obtained, starting from (**1**)—(**3**); (iv) the *p*-halogeno esters (**5**) and (**6**), as well as (**2**), are important intermediates in synthesis of pharmaceutical compounds[10a] and various other chemicals;[10b] [similar uses for (**7**)—(**9**) are conceivable]; and (v) of the relevance to carbon–carbon bond-forming and related catalytic electrochemical reduction of simple alkyl halides.[11] The importance of steric factors in determining the selectivity of biochemical recognition processes has recently been stressed.[12]

Experimental

Preparations.—Ethyl 4-fluorophenylacetate (**4**)[13] was obtained by the standard method ($EtOH–H_2SO_4$) from 4-fluorophenylacetic acid (K and K). Ethyl 4-chlorophenylacetate (**5**)[14] and 4-bromophenylacetate (**6**)[15] were prepared in the same manner from the corresponding acids (K and K or Aldrich): (**4**), $\delta_H(CCl_4)$ 1.1 (3 H, t, *J* 7.5 Hz, CH_3), 3.4 (2 H, br s, CH_2), 4.0 (2 H, q, *J* 7.5 Hz, OCH_2), and 6.7—7.4 (4 H, m, ArH); (**5**), δ_H (neat liquid) 1.0 (3 H, t, *J* 7 Hz, CH_3), 3.4 (2 H, s, CH_2), 4.0 (2 H, q, *J* 7 Hz, OCH_2), and 7.1 (4 H, apparently s, ArH); $\delta_H(CDCl_3)$ for (**5**) are all shifted 0.1 p.p.m. to lower field; (**6**), δ_H (neat liquid) 1.1 (3 H, t, *J* 7 Hz, CH_3), 3.4 (2 H, s, CH_2), 4.0 (2 H, q, *J* 7 Hz, OCH_2), 7.2 (4 H, ABq, δ_{H_A} 7.0, δ_{H_B} 7.4, J_{AB} 10 Hz,*

* The large *cis* coupling constant ($J_{o,m}$ 10 Hz) indicates that the double bond is more of the ethylene type than benzoid. Further splitting, *ca.* 2 Hz, of the lines, due to long-range coupling with CH, is also observed.[17]

ArH); all data were consistent with literature data for the corresponding acids.

Ethyl α-bromo-4-fluorophenylacetate (**1**), ethyl α-bromo-4-chlorophenylacetate (**2**),[16] and ethyl α-bromo-4-bromophenylacetate (**3**) were prepared *via* bromination with *N*-bromosuccinimide of the corresponding esters (**4**)—(**6**) respectively.

Ethyl α-bromo-4-fluorophenylacetate (**1**). This was obtained as a liquid, $\delta_H(CCl_4)$ 1.20 (3 H, t, *J* 7.5 Hz, CH_3), 4.13 (2 H, q, *J* 7.5 Hz, CH_2), 5.20 (1 H, s, CH), and 6.8—7.9 (4 H, m, AB prt of ABX, X = F, system, δ_{H_A} 7.00, δ_{H_B} 7.5, J_{AB} 10,* J_{AX} 20, J_{BX} 8 Hz, ArH), *m/z* (70 eV) 261 and 259 (*M* − H), 216 and 214 (*M* − EtOH), 189 and 187 (*M* − CO_2Et), 181 (*M* − Br), 153 (*M* − Br − Et + H), 109 (*M* − Br − CO_2Et + H), 95 (*M* − $CHBrCO_2Et$), and 81 and 79 (Br).

Ethyl α-bromo-4-chlorophenylacetate (**2**). This was obtained as a liquid, $\delta_H(CCl_4)$ 1.20 (3 H, t, *J* 7.5 Hz, CH_3), 4.16 (2 H, q, *J* 7.5 Hz, CH_2), 5.30 (1 H, s, CH), 7.1—7.6 (4 H, q, AB system, δ_{H_A} 7.2, δ_{H_B} 7.5, J_{AB} 10 Hz,* ArH). Peaks in the mass spectrum are at *m/z* 277 and 275 (*M* − H), 248 and 246 (*M* − H − Et), 205 and 203 (*M* − CO_2Et), 197 (*M* − Br), 123 (*M* − Br − HCO_2Et), and 89 (*M* − Br − Cl − CO_2Et).

Ethyl α-bromo-4-bromophenylacetate (**3**). This was obtained as a liquid, $\delta_H(CCl_4)$ 1.20 (3 H, t, *J* 7.5 Hz, CH_3), 4.17 (2 H, q, *J* 7.5 Hz, CH_2), 5.30 (1 H, s, CH), and 7.40 (4 H, AB system, apparent triplet, $\Delta\delta_{AB} < J_{AB}$ = 10 Hz, ArH), *m/z* 324, 322, and 320 (1:2:1, M^+), 251, 249, and 247 (*M* − CO_2Et), 243 and 241 (*M* − Br), 171 and 169 (*M* − Br − CO_2Et + H), 162 (*M* − 2Br), and 134.

NN-Dimethylformamide (DMF) (Riedel de Haen spectroanalytical) and Et_4NClO_4 (Fluka) were purified as described previously.[6–9] All other chemicals were commercially available and of the highest purity.

Apparatus and Procedures.—Voltammetric measurements and controlled-potential electrolyses were carried out at ambient temperature with the arrangement described in refs. 6—9 and 18. Routine ^1H n.m.r. spectra were obtained at 60 MHz using a Varian EM 360 instrument, with tetramethylsilane as internal standard. Chemical shifts are expressed in δ values. Occasionally, 80 MHz spectra were obtained in the Fourier transform mode using a Bruker 80 FT apparatus. Mass spectra were determined using a VG model ZAB-2F apparatus. All compounds were reduced at −1.60 V *versus* s.c.e. and the products separated by column chromatography, thin layer chromatography, and/or h.p.l.c. with the apparatus and procedures already described.[6–9,18] M.p.s were determined on a Kofler or Büchi apparatus and are uncorrected.

Constant-potential Electrolysis of Ethyl α-Bromo-4-fluorophenylacetate (**1**).—Ethyl α-bromo-4-fluorophenylacetate (**1**) (2.071 g, 7.9×10^{-3} mol) in DMF (155 ml) containing Et_4NClO_4 (0.1M) was electrolysed on reticulated vitreous carbon. The substance was added in small portions, so that the concentration was never higher than 10^{-2}M. The initial current was 40—50 mA and the final current was *ca.* 2 mA. After conventional work-up to remove DMF and Et_4NClO_4, the viscous mixture (1.2 g, 86% current yield) of products was analysed by t.l.c. and ^1H n.m.r. showing the presence of at least four products, among them monoester (**4**) and diesters (**7a** and **b**). This mixture was subjected to column chromatography (SiO_2; 2.2 × 80 cm; prepared in n-hexane) with ethyl acetate–hexane as eluant. In the order of increasing percentage of ethyl acetate the following products were obtained: monoester (**4**) [354 mg, 1.95×10^{-3} mol, 25% based on ABr (**1**)]; dimer (**7a**) (*meso*) (178 mg, 5×10^{-4} mol) impure (n.m.r.); dimer (**7b**) (DL), pure (n.m.r.) (265 mg, 7.4×10^{-4} mol, 19%); epoxide (**11b**) (33 mg, *ca.* 2%). The other fractions contained (n.m.r.) unidentified and/or polymeric material (172 mg). The column efficiency was *ca.* 81%. The crystalline fraction containing *meso*-dimer (**7a**) was further separated by preparative h.p.l.c. [$CHCl_3$–n-hexane; SiO_2 column (Merck); i.d. ½ in; *h* 25 cm] thus obtaining pure (**7a**) (30 mg), a further crop (30 mg) of a mixture of (**7a** and **b**) (1:1), epoxide (**11a**) (15 mg), and an unidentified product (15 mg) showing a sharp singlet, δ 6.05, in the n.m.r. spectrum, in addition to signals pertaining to the *p*-fluorophenyl and CO_2Et groups. Coulometry of a 10^{-2}M solution of (**1**) gave n_{app} 1.1.

meso-*Diethyl* 2,3-*bis*-p-*fluorophenylsuccinate* (**7a**).†—This had m.p. 94—96 °C, $\delta_H(CDCl_3)$ 0.95 (6 H, t, *J* 7.5 Hz, 2 × CH_3), 3.85 (4 H, q, *J* 7.5 Hz, 2 × CH_2), 4.2 (2 H, s, 2 × CH), and 6.6—7.4 (8 H, m, AB part of ABX, X = F, system, δ_{H_A} 7.2, δ_{H_B} 7.5, J_{AB} 10, J_{AX} 20, J_{BX} 8 Hz, 2 × ArH), *m/z* (70 eV) 362 (M^+, $C_{20}H_{20}F_2O_4$), 316 (*M* − EtOH), 288 (*M* − EtOH − CO), 245 (*M* − OEt + H − CO_2Et), 225 (*M* − OEt − CO_2Et − F), and 216 (*M* − $2CO_2Et$), 197 (*M* − $2CO_2Et$ − F), 181 (*M*/2), 153, 149, 137, 123, 110, and 95.

DL-*Diethyl* 2,3-*bis*-p-*fluorophenylsuccinate* (**7b**).†—This had m.p. 77—70 °C, $\delta_H(CDCl_3)$ 1.2 (6 H, t, *J* 7.5 Hz, 2 × CH_3), 4.05 (4 H, q, *J* 7.5 Hz, 2 × CH_2), 4.1 (2 H, s, 2 × CH), and 6.6—7.1 (8 H, m, AB part of ABX, X = F, system, δ_{H_A} 6.8, δ_{H_B} 6.9, J_{AB} 10, J_{AX} 20, J_{BX} 8 Hz, 2 × ArH), *m/z* (70 eV) 362 (M^+), 360, 316 (*M* − EtOH), 288, 245, 225, 214 (*M* − 2H − $2CO_2Et$), 195 (*M* − 2H − $2CO_2Et$ − F), 181 (*M*/2) 153, 136, 120, 110, and 97.

cis-*Diethyl* 2,3-*bis*-(4-*fluorophenyl*)*oxirane*-2,3-*dicarboxylate* (**11a**).‡—This had m.p. 105—106 °C, $\delta_H(CDCl_3)$ 0.9 (6 H, t, *J* 7.5 Hz, 2 × CH_3), 3.8 (4 H, q, *J* 7.5 Hz, 2 × CH_2), and 6.9—7.9 (8 H, m, AB part of ABX system, δ_{H_A} 7.1, δ_{H_B} 7.7, J_{AB} 10, J_{AX} 20, J_{BX} 8 Hz, 2 × ArH), *m/z* (70 eV) 376 (M^+), 375, 360 (28), 332 (5), 314 (5), 303 (*M* − CO_2Et, 7), 287 (16), 259 (10), 214 (41), 123 (C_6H_4FCO, 25), 95, 69, and 44 (100).

trans-*Diethyl* 2,3-*bis*-(4-*fluorophenyl*)*oxirane*-2,3-*dicarboxylate* (**11b**).‡—This had m.p. 91—93 °C, $\delta_H(CDCl_3)$ 1.30 (6 H, t, *J* 7.5 Hz, 2 × CH_3), 4.20 (4 H, q, *J* 7.5 Hz, 2 × CH_2), and 6.7—7.6 (8 H, m, AB part of ABX system, X = F, δ_{H_A} 6.8, δ_{H_B} 7.3, J_{AB} 10, J_{AX} 20, J_{BX} 8 Hz, 2 × ArH), *m/z* 376 (M^+, $C_{20}H_{18}F_2O_5$), 303 (*M* − CO_2Et), 275 (*M* − CO_2Et − Et + H), 257, 225, 201 (*M* − C_6H_4F − Et + H − Et + H), 181, 153, 136, 124, 107, and 95.

Constant-potential Electrolysis of Ethyl α-Bromo-p-chlorophenylacetate (**2**).—Preparative electrolysis on ester (**2**) was performed twice. In the first experiment (**2**) (2.00 g, 7.2×10^{-3} mol) in DMF (155 ml) with Et_4NClO_4 (0.1M) was electrolysed as described for compound (**1**). Coulometry of a solution of (**2**) (10^{-2}M) gave n_{app} 1.0. After conventional work-up, a mixture of products (1.24 g, current yield 89%) was found (t.l.c. and n.m.r.). This consisted of at least four products, the main ones

* See p. 847.

† The assignments of the *meso* and DL structures to compounds (**7a** and **b**) respectively rests on the n.m.r. chemical shifts of the CH_3 and CH_2 groups of the CO_2Et group: $\delta_{CH_3}(meso) < \delta_{CH_3}(DL)$ for the related compounds (**10a** and **b**) respectively, of known stereochemistry (see ref. 6).

‡ The stereochemistry of compound (**11b**), as well as of (**11a**), is unknown. However, we have assigned the *cis*(*meso*) structure to (**11a**) and the *trans*(DL) structure to (**11b**) on the basis of the n.m.r. signals of the CH_3 and CH_2 groups in the CO_2Et group: $\delta_H CH_3(meso) < \delta_H CH_3(DL)$ as for compounds (**10a** and **b**), respectively.

being (n.m.r.) monoester (**5**), *meso* and DL dimers (**8a** and **b**) respectively, and epoxide (**12**). The mixture was subjected to column chromatography with the same column and eluants as before. The following products were obtained (in the order of increasing percentage of ethyl acetate): a crystalline mixture of monoester (**5**) (220 mg) containing two other products; crystalline (**8a**) (75 mg) containing two other products; crystalline (**8b**) (440 mg) (pure by n.m.r.); and finally four unidentified crystalline products (4, 90, 48, and 54 mg) with singlets at δ 5.1—5.2 in the n.m.r. spectrum, in addition to the signals for the *p*-chlorophenyl and CO_2Et groups.

The fraction containing monoester (**5**) as the main product was subjected to h.p.l.c. (conditions as before) thus giving pure (**5**) (50 mg), and a crystalline mixture of (**5**), (**8a**), and (**12**). The fraction containing dimer (**8a**) was subjected to h.p.l.c. obtaining pure (**8a**) (28 mg), pure (Fourier transform n.m.r.) epoxide (**12**) (5 mg), and an unidentified product (11 mg) showing m.p. 130 °C and a singlet at δ 6.0, in addition to signals for the *p*-chlorophenyl and CO_2Et groups.

In the second experiment, (**2**) (2.28 g, 8.2 × 10^{-3} mol) was electrolysed as described before in DMF–Et_4NClO_4 (0.1M, 155 ml) giving a mixture of products (1.54 g, current yield 95%), mainly (**8a** and **b**), as in the first experiment. A first chromatographic separation (SiO_2; n-hexane–ethyl acetate) gave products (1.34 g), thus distributed, in order of elution: monomer (**5**) plus *meso* dimer (**8a**) (1.5:1 mol/mol) (210 mg); (**5**) (380 mg) contaminated with (**8a**) (4:1 mol/mol; n.m.r.); crystalline DL dimer (**8b**) (430 mg); a mixture of (**8a** and **b**) (320 mg); and (**12**). This last crop was subjected to a second column chromatographic separation to give finally (**8a**) (108 mg), (**8b**) (43 mg), and epoxide (**12b**) (110 mg).

meso-*Diethyl* 2,3-*bis*-p-*chlorophenylsuccinate* (**8a**).* This had m.p. 148 °C, $\delta_H(CDCl_3)$ 1.00 (6 H, t, *J* 7.0 Hz, 2 × CH_3), 3.90 (4 H, q, *J* 7 Hz, 2 × CH_2), 4.2 (2 H, s, 2 × CH), and 6.9—7.4 (8 H, q, 2 × ArH), *m/z* 396 and 394 ($C_{20}H_{20}Cl_2O_4$) (2:3), 348 (*M* − EtOH), 316, 306, 279, 248 (*M* − $2CO_2Et$), 216, 197 (*M*/2), and 113 and 111 consistent with the assigned structure.

DL-*Diethyl* 2,3-*bis*-p-*chlorophenylsuccinate* (**8b**).* This had m.p. 115—118 °C, $\delta_H(CDCl_3)$ 1.20 (6 H, t, *J* 7.0 Hz, 2 × CH_3), 4.0 (4 H, q, *J* 7.0 Hz, 2 × CH_2), 4.10 (2 H, s, 2 × CH), and 6.8—7.2 (8 H, q, 2 × ArH), *m/z* 396 and 394 ($C_{20}H_{20}Cl_2O_4$) (2:3), 348 (*M* − EtOH), 320, 277, 248 (*M* − $2CO_2Et$), 212, and 197 (*M*/2).

cis-*Diethyl* 2,3-*bis*-(4-*chlorophenyl*)*oxirane*-2,3-*dicarboxylate* (**12a**). † This had $\delta_H(CDCl_3$; 80 MHz) 0.92 (6 H, t, *J* 7.1 Hz, 2 × CH_3), 3.90 (4 H, q, *J* 7.1 Hz, 2 × CH_2), and 7.5 (8 H, q, AB system, δ_{H_A} 7.35, δ_{H_B} 7.68, J_{AB} 9.7 Hz, 2 × ArH), *m/z* 407 (*M* − H, 1), 393 and 391 (*M* − OH, 2), 334 (*M* − H − CO_2Et, 3), 320 and 318 (2), 307, 290, 243, and 241 (20), 176 (10), 141 and 139 (ClC_6H_4CO, 100, 1:3), and 111 (25).

trans-*Diethyl* 2,3-*bis*-(4-*chlorophenyl*)*oxirane*-2,3-*dicarboxylate* (**12b**).† This had m.p. 78—80 °C, $\delta_H(CDCl_3)$ 1.3 (6 H, t, *J* 7.5 Hz, 2 × CH_3), 4.2 (4 H, q, *J* 7.5 Hz, 2 × CH_2), and 7.0 (8 H, q, AB system, 2 × ArH), *m/z* 409 (12%) and 407 (18) (*M* − H), 396 (33), 395, 394, and 393 (82), 320 and 318 (10), 247 (18) and 245 (27), 214 and 212 (12), 176 (27), 141 (48) and 139 (57) (ClC_6H_4CO), 113 and 111, and 43 (100); $\nu_{max.}$(KBr) 3 000—2 900 (w), 1 720 (s, ester CO), 1 600 (w), 1 490 (m), 1 275, 1 240, 1 190, 1 090, 1 050, 1 020, and 840 (m) cm^{-1}.

*Constant-potential Electrolysis of Ethyl α-Bromo-*p*-bromophenylacetate* (**3**).—Compound (**3**) (2.6 g, 8.07 × 10^{-3} mol) in DMF–Et_4NClO_4 (0.1M, 100 ml) was electrolysed by the procedure described for the α-bromo derivatives (**1**) and (**2**), obtaining, after work-up to remove solvent and electrolyte, a mixture (1.8 g) consisting (t.l.c., n.m.r.) of four main products. The n.m.r. spectrum of the mixture showed the presence of monoester (**6**) and *meso* and DL dimers (**9a** and **b**). Column chromatography as described before gave, in the order of elution: (**6**) and (**9a**) (135 mg) (2:1 mol/mol), (**6**) and (**9a**) (173 mg) (5:1), a mixture of (**6**) and (**9a**) (98 mg) (*ca.* 5:4) plus traces of an unknown product with δ_H 6.0 [see analogous compounds obtained in the electrolysis of (**1**) and (**2**)], pure *meso* dimer (**9a**) (20 mg), pure DL dimer (**9b**) (445 mg), and finally a mixture of epoxides (**13**) (180 mg) (n.m.r.).‡ H.p.l.c. of the mixture (135 mg) containing the *meso* dimer (**9a**) gave another crop of pure (**9a**) (53 mg) and of pure (**6**) (*ca.* 60 mg).

meso-*Diethyl* 2,3-*bis*-p-*bromophenylsuccinate* (**9a**). This had m.p. 155—157 °C, $\delta_H(CDCl_3)$ 1.00 (6 H, t, *J* 7.0 Hz, 2 × CH_3), 3.80 (4 H, q, *J* 7 Hz, 2 × CH_2), 4.2 (2 H, s, 2 × CH), 7.2—7.5 (8 H, q, AB system, 2 × ArH), *m/z* 484, 482, and 480 (1:2:1, *M* − 2H), 440, 438, and 436 (1:2:1, *M* − EtOH), 404 and 402 (1:1, *M* − HBr), 360 and 358 (1:1, *M* − Br − OEt), 328 (*M* − HBr − CO_2Et), 317 and 315, 281, 277, 252 (*M* − Br − CO_2Et + H), 244 (*M*/2 + H), 243, 242, and 241.

DL-*Diethyl* 2,3-*bis*-p-*bromophenylsuccinate* (**9b**). This had m.p. 119—122 °C, $\delta_H(CDCl_3)$ 1.20 (6 H, t, *J* 7.0 Hz, 2 × CH_3), 4.10 (4 H, q, *J* 7.0 Hz, 2 × CH_2), 4.20 (2 H, s, 2 × CH), and 6.8—7.4 (8 H, q, AB system, 2 × ArH), *m/z* 486, 484, and 482 (1:2:1, M^+), 440, 438, and 436 (1:2:1, *M* − EtOH), 412, 410, and 408 (1:2:1, *M* − HCO_2Et), 340, 338, and 336 (1:2:1, *M* − $2CO_2Et$), and 243 and 241 (1:1, *M*/2).

Diethyl 2,3-*bis*-(4-*bromophenyl*)*oxirane*-2,3-*dicarboxylate* (cis + trans) (**13a** + **b**). This had m.p. 79—82 °C, $\delta_H(CDCl_3)$ 1.05 and 1.30 (6 H, 2 × t, *J* 7.0 Hz, 2 × CH_3), 3.90 and 4.30 (4 H, 2 × q, *J* 7 Hz, 2 × CH_2), and 6.9—7.45 (8 H, q, AB system, 2 × ArH), *m/z* 502 (0.2%), 428 (*M* + 2 − CO_2Et, 12), 400 (*M* − Et + H − CO_2Et + H, 10), 354 (*M* − CO_2Et + 2H, 20), 281 (19), 221 (20), 147 (30), and 73 (100).

Table 1. Results of electrochemical reduction of α-bromo-*p*-halogenophenylesters (**1**)—(**3**) (ABr) on a reticulated vitreous carbon electrode in DMF–Et_4NClO_4 solution

ABr	Product	Yield (%)[a]	Product ratio DL:*meso*	D.e. (%)[b]	n_{app}[c]
(**1**)	(**4**)	25			1.1
	(**7a**)	3.2	6:1	71	
	(**7b**)	19.5			
	(**11**)	3			
	Various	18			
(**2**)	(**5**)	21			1.0
	(**8a**)	17	2.3:1	39	
	(**8b**)	39			
	(**12**)	6			
(**3**)	(**6**)	12			1.2
	(**9a**)	14	1.6:1	23	
	(**9b**)	23			
	(**13**)	8			

[a] Based on ABr. [b] D.e. = Diastereoisomeric excess. [c] n_{app} = Numbers of faradays per mol of substrate ABr consumed in the electrolysis; room temperature; *E* −1.6 V.

* For the assignment of the *meso* and DL structures to (**8a** and **b**), respectively, the criterion for compounds (**7a** and **b**) was followed.

† For the assignments of the *cis*(*meso*) and the *trans*(DL) structures to (**12a** and **b**), respectively, the criterion for compounds (**11a** and **b**) was followed.

‡ We were not able to separate the *cis* and *trans* isomers in this mixture; the product ratio *trans*:*cis* was *ca.* 3:1 (n.m.r.).

Table 2. Voltammetric data for α-bromoesters ABr (**1**)—(**3**), for esters AH (**4**)—(**6**), and for diesters AA (**7**)—(**9**) (all 1 × 10^{-3}M) in DMF–Et_4NClO_4 (0.1M) solutions. Potential sweep-rate v 0.2 V s^{-1}; glassy carbon (GC) and mercury (Hg) electrode; E/V *versus* s.c.e.

ABr	E'_p (GC)	AH	E_p (GC)	E_p (Hg)	AA	E_p (GC)	E_p (Hg)
(**1**)	−1.23	(**4**)			(**7a, b**)		
(**2**)	−1.23	(**5**)	−2.62	−2.56	(**8a**)	−2.53	−2.45
(**3**)	−1.25	(**6**)	−2.52	−2.46	(**8b**)	−2.59	−2.48
					(**9a**)	−2.54	
					(**9b**)	−2.51	

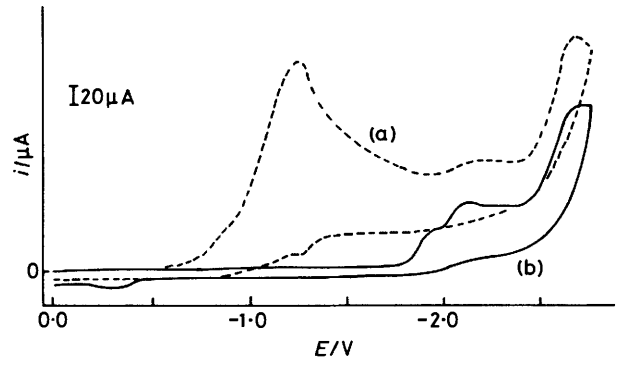


Figure 1. (a) Cyclic voltammograms for bromoester (**2**) (1.0 × 10^{-2}M) in DMF containing Et_4NClO_4 (0.1M) as supporting electrolyte; (b) same solution after controlled-potential electrolysis at E −1.60 V. Sweep rate 200 mV s^{-1}, glassy carbon electrode, E/V *versus* s.c.e.

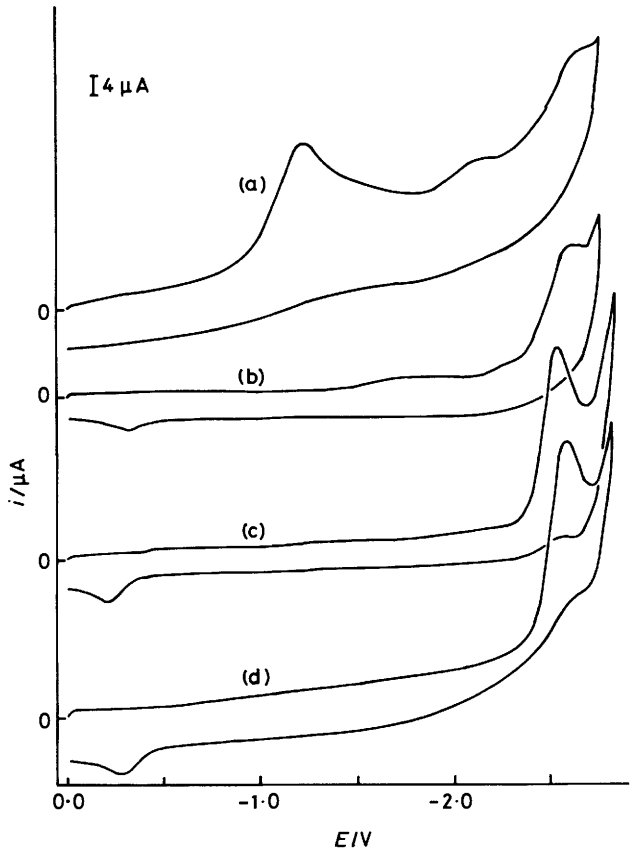


Figure 2. Cyclic voltammograms for (a) ester (**2**) (1 × 10^{-3}M), (b) ester (**5**), (c) ester (**8a**), (d) ester (**8b**) all 1 × 10^{-3}M. Same conditions as in Figure 1

Results and Discussion

Electrochemistry.—The voltammetric behaviour of ethyl α-bromo-*p*-fluorophenylacetate (**1**) consists in a single, irreversible reduction wave with E_p −1.23 V (v 200 mV s^{-1}, glassy carbon electrode). This accords with the fact that the main products of reduction of (**1**) (Table 1) are monoester (**4**) and diesters (**7**), which cannot be reduced in the potential range available. An analogous wave, E_p −1.23 V at v 200 mV s^{-1}, can be observed in the case of the α-bromo-*p*-chlorophenylacetate (**2**) (Figures 1a and 2a) and for the α-bromo-*p*-bromophenylacetate (**3**) (Table 2). For (**2**) and (**3**) the main reduction products (Table 1) are reducible (Table 2). The peak currents of the wave at E −1.23 V are of the order expected for a one-electron process, compared with the values obtained in previous studies on other α-bromoaryl acetates.[6–9,18] In fact, controlled-potential electrolysis (c.p.e.) performed for coulometric purposes at a constant potential E of −1.6 V, so as to prevent reduction of the electroactive products, gave n_{app} *ca.* 1 for (**1**)—(**3**). Preparative electrolysis at the same potential results in the formation mainly of monoesters AH (**4**)—(**6**) and of diesters AA (**7**)—(**9**) (Table 1). Having prepared pure monoesters AH, chemically or electrochemically, and diesters *meso* and DL AA, electrochemically from the corresponding ABr, the voltammetric behaviour of (**5**), (**6**), and (**7a, b**)—(**9a, b**) can be studied, as exemplified in Figure 2b, c, d for the *p*-chloro derivatives. Similar voltammograms were obtained for the *p*-bromo derivatives. Thus, the most negative peak displayed in the forward *i*–*E* curve of (**2**) (Figures 1a and 2a) and of (**3**) [voltammograms for (**3**) are similar, see data in Table 2] are to be assigned to overlapping AH and AA (*meso* + DL) reduction. This happens because the reduction potentials for AHs are very close to the corresponding potentials for the dimeric AAs (Table 2). No corresponding peak is found if ABr is (**1**) owing to the fact that the corresponding AHs and AAs are inactive. Two small waves occurring between the first, more positive ABr reduction peak and the last (AH and AA) reduction peak are connected with the formation of epoxides and/or unidentified products, which are formed in addition to AH and AA (see Table 1 and Experimental section).

Some distinctive features of the voltammetric behaviour of the particular compounds can be observed. As far as the ABrs is concerned, the peak potential for reduction of the C–Br bond is practically insensitive to the *p*-halogeno substituent in the phenyl group (Table 2). The *p*-chloro-substituted monoester (**5**) is reduced, as expected, 100 mV more negative than the corresponding *p*-bromo-substituted AH (**6**), either on a glassy carbon or on a mercury electrode. A small anodic wave at *ca.* −0.3 V in Figure 2b for ester (**5**), and similarly for (**6**), is probably due to traces of A^- stemming from interaction of AH with electrogenerated base. A similar anodic peak was found at E −0.4 V when dealing with the voltammetric curves of 1- and 2-naphthylsuccinates.[9]

meso- and DL-bis-*p*-chlorophenylsuccinates (**8a** and **b**), respectively, are reduced at slightly more positive potentials than the corresponding monomer AH (**5**). For the *meso*-compound (**8a**) E_p is 60—30 mV more positive than E_p of the corresponding DL compound (**8b**). The *p*-substituted dimers (**9a** and **b**) show a 30 mV difference in favour of (**9b**) in the voltammetric peak potentials; the monomeric *p*-bromoester AH (**6**) is reduced at the same potential (Table 2). Thus, *para*-substitution with bromine in the phenyl group seems to produce a levelling effect in the reduction potentials of AH and AA.

For the epoxides (**11**)—(**13**) (a tentative mechanism for their formation is described below), the voltammetric behaviour of

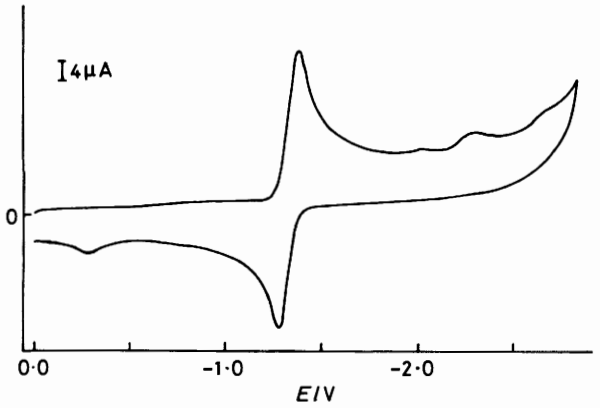


Figure 3. Cyclic voltammogram for epoxide (**12b**) (1×10^{-3}M) in DMF–Et_4NClO_4 (0.1M). Sweep rate 200 mV s^{-1}. Glassy carbon electrode, i.d. 3.24 mm. *E*/V *versus* s.c.e.

(**12b**), the *p*-chlorophenyl derivative, was investigated. Others, *e.g.* (**11a** and **b**), were obtained in too small an amount for voltammetric measurements; (**13a** and **b**) were obtained as an inseparable mixture. Compound (**12b**) exhibits a quasi-reversible 1e voltammetric reduction peak (Figure 3) to its radical-ion, E_{pc} −1.37, E_{pa} −1.28 V, i_{pa}/i_{pc} 0.85, followed by two small reduction waves between −2.0 and −2.30 V. Further investigations were hampered by the small amount of material at our disposal. However, the very early reduction potential of (**12b**) and the notable persistence of its radical ion are worthy of mention. The value of E_p found for (**12b**) is consistent with the data obtained by Boujlel and Simonet [19] for stilbene epoxide in comparable conditions, if the additional two CO_2Et groups in (**12b**) are considered.

A few comments are needed about the distribution of products (Table 1). Dimeric products (**7**)—(**9**) are usually the consequence of the overall electrode process (1). Routes (2) and

$$ABr + e \longrightarrow \tfrac{1}{2}\,AA + Br^- \quad (1)$$

$$ABr + 2e \longrightarrow A^- + Br^- \quad (2)$$

(3) to AA are to be considered. Path (3a), *i.e.* the intermediacy of

$$A^- + ABr \xrightarrow[b]{a} \begin{matrix} 2A^\cdot \longrightarrow AA \\ AA \end{matrix} \quad (3)$$

radicals as a solution process in the overall electrode reaction was first postulated by us [7] and by others.[11] The main consequence is that hydrogen abstraction (4) from solvent HS

$$A^\cdot + HS \longrightarrow AH + S^\cdot \quad (4)$$

can compete with proton abstraction (5) for the formation of the

$$A^- + HS \longrightarrow AH + S^- \quad (5)$$

monomeric esters (**4**)—(**6**). In addition, if hydrogen or proton abstraction may occur from ABr itself, other routes are available to account for the by-products formed. In this respect, it can be observed that formation of epoxides seems to be roughly correlated with the formation of the corresponding AH: an increase in AH is accompanied by a decrease in epoxides (Table 1). The first question is, of course, where does the oxygen originate. It seems that epoxides are formed, albeit in low yield, during electrolysis of ABr (*cf.* Figure 1a and b). The simplest way is to think in terms of a Darzens [20] type condensation of *p*-$XC_6H_4C(Br)CO_2Et^-$ with *p*-$XC_6H_4C(O)CO_2Et$. Anion *p*-X-$C_6H_4C(Br)CO_2Et^-$ could arise by proton abstraction from ABr by A^-. Ketone *p*-X-$C_6H_4C(O)CO_2Et$ may be formed in a manner analogous to that for the formation of fluorenone when 9-bromo- or 9-chloro-fluorene is electrolysed in aprotic solvents.[21] Preparative electrolyses were performed at a potential just more negative than that needed for reduction of ABr and for the (reversible) formation of epoxide radical ions. When exposed to air for work-up, radical ions will be reoxidized to the corresponding neutral compounds and as such they will be found together with the main products AA and AH.

N.m.r. Spectroscopy and Stereochemistry of Products.—As described in the Experimental section, the stereochemistry of the *p*-halogenophenylsuccinates series can be assigned. In fact, the ^1H chemical shifts are in the following order: $\delta(CH_3)$(*meso*)-$< \delta(CH_3)$(DL) for the CO_2Et group; in addition, the AB patterns in the phenyl groups are very different, the two doublets for the DL compound being well developed, $\Delta\delta_{AB}$(DL) $> \Delta\delta_{AB}$(*meso*). These last differences are more prominent for the *p*-fluoro-substituted compounds where further coupling of the phenyl hydrogens with fluorine is present. These spectroscopic features are undoubtedly connected with the symmetry characteristics, bond angles, bond lengths, torsional angles, and conformational preferences of the isomers concerned. These in turn will control the relative stability of *meso* and DL isomers.[22] In this respect, it is interesting to note the DL diastereoisomeric excess found for the diphenylsuccinates, which decreases in the order *p*-F > *p*-Cl > *p*-Br. The same trend in the n.m.r. spectra observed for (**7**)—(**9**) is present also for the rigid compounds (**11**)—(**13**). A self-consistent picture of the relative position of the attached groups in the preferred conformations of non-rigid (**7**)—(**9**) can thus be drawn.

The meaning of the figures for diastereoisomeric excess are to be considered with caution, because, for example, one diastereoisomer could be preferentially consumed in side reactions. However, we are unable to speculate about the nature of such reactions for the conditions of the electrochemical experiments and during the separation procedures.

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