564. *Optically Active Forms of* 3′ : 2″-*Dibromo*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic Acid, and their Stability.*

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The presence of two bromine atoms enables this acid (VI; R = Br, R′ = H) to be obtained in optically active form with a half-life of 32 hr. at 22° in chloroform solution. In absence of the bromine or in presence of smaller substituents only mutarotation or partial resolution had previously been achieved. The identity of the compound has been confirmed by comparison of its ultraviolet absorption spectrum with those of compounds containing similar and related ring systems.

The molecule of 3 : 4-5 : 6-dibenzophenanthrene is twisted into a helical shape by overcrowding.[1] Because of the resulting asymmetry Bell and Waring[2] were able to detect mutarotation in solutions of the morphine salt of 3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylic acid (VI; R = R′ = H) and partially to resolve 1′ : 3′ : 2″ : 4″-tetramethyl-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylic acid (VI; R = R′ = Me). This showed that methyl groups in the 3′ and 2″ positions decrease the rate of racemisation, presumably by interfering with the passage from one isomer to the other through the planar position. To confirm this and to obtain stable isomers an acid (VI; R = Br, R′ = H) containing larger groups, namely bromo, in the interfering 3′ and 2″ positions has been prepared. Weidlich's method[3] for the synthesis of this ring system was used with appropriate modifications.

The acid passes very readily into its anhydride. When the acid is required the orange anhydride is dissolved in hot potassium hydroxide solution giving a colourless solution, from which dilute hydrochloric acid precipitates the orange-yellow acid. After filtration and washing it can be dried under reduced pressure at room temperature. The product

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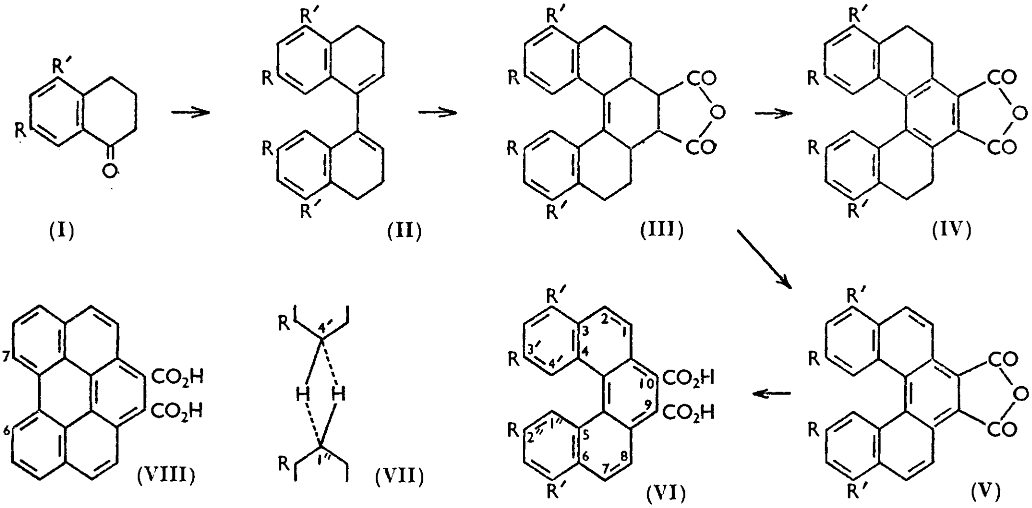
[1] McIntosh, Robertson, and Vand, *J.*, 1954, 1661.

[2] Bell and Waring, *J.*, 1949, 2689.

[3] Weidlich, *Ber.*, 1938, **71**, 1203.

melts about 130° but sets again to the anhydride, m. p. 338°. The equivalent weight indicates about $\frac{1}{2}H_2O$ more than formula (VI). Reversion to the anhydride does not take place under ordinary moist atmospheric conditions but very readily on heating, recrystallising, or on dissolving in such solvents as chloroform or even acetic acid. This change was followed conveniently by observing the infrared absorption of a chloroform solution. Chloroform does not absorb between 2000 and 1600 cm.$^{-1}$; in this region the anhydride is responsible for two characteristic peaks at 1845 and 1775 cm.$^{-1}$ respectively, whereas the acid absorbs at 1705 cm.$^{-1}$ only. The solid acid suspended in Nujol shows the latter peak, the two anhydride peaks being present only to a minute extent. In chloroform solution, however, all three are shown intensively. The acid peak at 1705 cm.$^{-1}$ vanishes on boiling the solution, indicating complete conversion into anhydride. At room temperature nearly one day is required for this peak to disappear.


(I) (II) (III) (IV) (VIII) (VII) (VI) (V)

The acid was resolved by use of morphine. The following procedures were used: (*a*) By working quickly so that the ethanol solution containing the morphine salts was not kept long above room temperatures, two distinct morphine salts were obtained of $[\alpha]_D^{22} = -220°$ and $+497°$ which gave respectively acids of $[\alpha]_D^{22} = -712°$ and $+745°$. (*b*) By dissolving the acid in chloroform, adding morphine suspended in chloroform, and concentrating at room temperature, four fractions of morphine salt were obtained. From the first fraction active acid of $[\alpha]_D^{25} = +589°$ and from the fourth of $[\alpha]_D^{25} = -394°$ was obtained. (*c*) By refluxing the ethanol solution of morphine salts for some time and allowing it to cool slowly only dextro-rotatory salts were obtained. Recrystallisation of the fraction of highest rotation followed by decomposition gave an acid of $[\alpha]_D^{25} = +1238°$. Obviously an asymmetric transformation had taken place in the last case resulting in extensive conversion of the lævo- into dextro-rotatory acid.

The active and partially active acids appeared to be optically stable in the solid state but racemised slowly in chloroform solution with half-lives of 32 hr. at 22° or 20 hr. at 25°. The reversion of the active acid to its anhydride in chloroform is superimposed on the racemisation. The two, however, are distinct processes as complete racemisation to zero rotation takes from 4 to 7 days whereas conversion into the anhydride is complete in less than one day. The smoothness of the decay curves in the initial stages shows that the specific rotations of anhydride and acid cannot differ widely. Anhydride formation therefore does not affect the arguments developed below about optical stability and its relationship to overcrowding in the neighbourhood of the bromine atoms. Freshly precipitated active acid is also orange-yellow. From C, H, and Br analyses after drying under reduced pressure at room temperature the acid contains from $\frac{1}{2}$ to 1 molecule of water additional to that required by formula (VI). When heated it softens at 127° but sets again to the anhydride which is orange with m. p. 338°.

It appears that by the aid of morphine partial resolution of the acid can be achieved giving both optical isomers. By asymmetric transformation the pure dextro-rotatory acid results. The nature of this transformation was not examined further as our purpose was to find the effect of large substituents on the optical stability of this overcrowded system. It is clear that the introduction of bromine into these interfering positions has the expected effect of lowering the racemisation rate. The hydrogen atoms in positions 4′ and 1″ with their considerable overlap (1·2 Å) do not seem to offer much resistance to racemisation. Substitution by methyl groups in positions 3′ and 2″ with an extra overlap of only 0·6 Å produces mutarotation in morphine salts.[2] The overlap of two bromine atoms is 1·4 Å and it brings a fair measure of optical stability. If racemisation does take place through a planar state it is surprising that the massive interpenetration of atoms, or alternatively the far-reaching bending of bonds necessarily occurring in that state, permits racemisation at all. It is now suggested that the transition state for racemisation of such molecules is one in which carbon atoms 1″ and 4′ are tetrahedral (VII). Some support for this is to be found in the racemisation of diaryls by tetrahedralisation of carbon.[4,5] This mechanism would require much less activation energy and would minimise atom interpenetration. It would also account for the marked effect of overlapping 3′ and 2″ substituents compared with the negligible hindrance to racemisation offered by overlapping 4′ and 1″ hydrogen atoms.

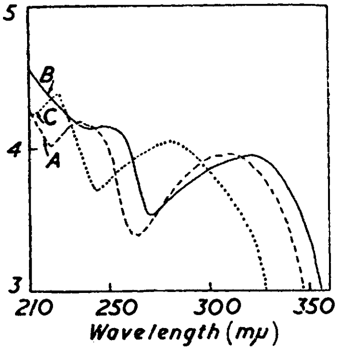


FIG. 1. *Ultraviolet spectra.*

A, Potassium 1 : 2 : 7 : 8 : 9 : 10 : 11 : 14-octahydro-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate (from high-melting anhydride) in water. $\lambda_{\text{max.}}$ 234, 239, 308 mμ ($\varepsilon_{\text{max.}}$ 15,360, 14,720, 9160); $\lambda_{\text{min.}}$ 221, 263 mμ ($\varepsilon_{\text{min.}}$ 10,750, 2450).

B, Potassium 3′ : 2″-dibromo-1 : 2 : 7 : 8 : 9 : 10 : 11 : 14-octahydro-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate in water. $\lambda_{\text{max.}}$ 249, 322 mμ ($\varepsilon_{\text{max.}}$ 14,400, 9000); $\lambda_{\text{min.}}$ 240, 271 mμ ($\varepsilon_{\text{min.}}$ 14,000, 3400).

C, *cis*-Stilbene (ref. 8). $\lambda_{\text{max.}}$ 224, 280 mμ ($\varepsilon_{\text{max.}}$ 24,400, 10,450).

The adduct (III; R = Br, R′ = H) was first obtained in a form of m. p. 260°. Subsequent preparations had m. p. 290°. Both forms gave the same acid from which only the low-melting anhydride could be obtained. It is possible that these are *endo* and *exo* forms. Both gave the same dehydrogenation products. Weidlich [3] obtained the unsubstituted adduct (III; R = R′ = H) with m. p. 256°. In repeating this to obtain samples for comparison of ultraviolet spectra, two forms of this adduct also were obtained of m. p. 237° and 262° in about equal amounts and readily separated by their different solubilities in acetic acid. Both gave the same dehydrogenation products. Methods of structure allocation are being sought.

Ultraviolet Spectra.—The vigorous methods of dehydrogenation used in this synthesis could conceivably result in the formation of 1 : 12-benzoperylene-1′ : 2′-dicarboxylic acid (VIII) or its derivative which could not definitely be discounted by carbon and hydrogen analysis. Moreover substitution in the 6- and 7-positions of (VIII) by bromine would give rise to enantiomorphous forms. The ultraviolet absorption spectra of the compounds produced at each stage in the synthesis, however, when compared with the spectra of the

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[4] Crawford and Smyth, *Chem. and Ind.*, 1954, 346.

[5] Crawford and Smyth, *J.*, 1954, 3464.

unsubstituted compounds, whose structures have been established, show that the final product (VI; R = Br, R′ = H) is not a benzoperylene derivative and allow the stages of dehydrogenation to be clearly followed. All acids were examined in the form of their potassium salts in aqueous solution, and anhydrides as potassium salts of the corresponding acids.

The two adducts (III) absorb very similarly (Fig. 1). They possess an unsaturated system resembling that of *cis*-stilbene,[6,7] but absorbing at longer wavelength with somewhat less intensity. The spectra of the two intermediate compounds (IV) also agree closely. The absorption (Fig. 2) is more intense than that of (III) owing to the 2-phenyldiphenyl system present.

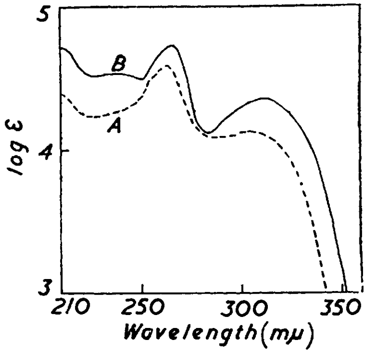

FIG. 2. *Ultraviolet spectra.*

A, Potassium 1 : 2 : 7 : 8-tetrahydro-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate in water. $\lambda_{\text{max.}}$ 263, 305 mμ ($\varepsilon_{\text{max.}}$ 39,200, 13,500); $\lambda_{\text{min.}}$ 288 ($\varepsilon_{\text{min.}}$ 12,600).

B, Potassium 3′ : 2″-dibromo-1 : 2 : 7 : 8-tetrahydro-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate in water. $\lambda_{\text{max.}}$ 266, 312 ($\varepsilon_{\text{max.}}$ 54,800, 22,900); $\lambda_{\text{min.}}$ 285 ($\varepsilon_{\text{min.}}$ 13,200).

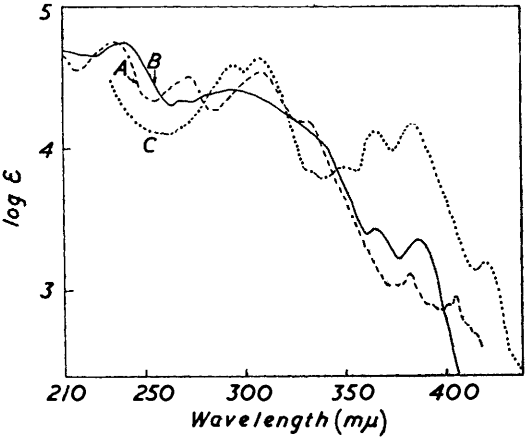

FIG. 3. *Ultraviolet spectra.*

A, Potassium 3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate in water. $\lambda_{\text{max.}}$ 235, 272, 310, 328, 382, 405 mμ ($\varepsilon_{\text{max.}}$ 56,000, 32,700, 34,200, 15,800, 1300, 890); $\lambda_{\text{min.}}$ 216, 253, 284, 375, 397 mμ ($\varepsilon_{\text{min.}}$ 35,800, 21,500, 19,000, 11,000, 738).

B, Potassium 3′ : 2″-dibromo-3 : 4-5 : 6-dibenzophenanthrene-9 : 10-dicarboxylate in water. $\lambda_{\text{max.}}$ 240, 270, 292, 365, 385 mμ ($\varepsilon_{\text{max.}}$ 56,000, 22,200, 26,000, 2700, 2280); $\lambda_{\text{min.}}$ 225, 264, 274, 360, 376 ($\varepsilon_{\text{min.}}$ 44,800, 20,300, 21,800, 2500, 1700).

C, Potassium 1 : 12-benzoperylene-1′ : 2′-dicarboxylate (ref. 8) in water. $\lambda_{\text{max.}}$ 295, 308, 330, 350, 365, 384, 420 mμ ($\varepsilon_{\text{max.}}$ 38,900, 43,700, 7080, 7410, 13,180, 15,140, 1580).

The fully dehydrogenated compounds (VI) are also alike in absorption (Fig. 3) but the unsubstituted one exhibits more fine structure, possibly owing to nearer approach to uniplanarity. As all five rings are aromatic the spectra show many more peaks but are still distinct from that of the corresponding benzoperylene acid (VIII).[8]

EXPERIMENTAL

7 : 7′-*Dibromo*-3 : 3′ : 4 : 4′-*tetrahydro*-1 : 1′-*dinaphthyl* (II; R = Br, R′ = H).—Aluminium foil (8 g.) and mercuric chloride (0·5 g.) were added to a solution of 7-bromo-1-tetralone (25 g.) in dry ethanol (200 ml.) and " AnalaR " benzene (140 ml.). Dry ethanol (60 ml.) was added after 3 hours' refluxing and the cooled mixture, after a further 6 hours' refluxing, decomposed with ice-water containing hydrochloric acid. The two layers were separated, the aqueous layer

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[6] Gillam and Stern, " An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," 2nd Edn., Arnold, London, 1957, p. 268.

[7] Beale and Roe, *J.*, 1953, 2755.

[8] Clar, *Ber.*, 1932, **65**, 846.

was extracted four times with benzene, and the combined benzene layers were washed successively with dilute hydrochloric acid and saturated brine. Removal of the benzene left the pinacol as a sticky brown solid which was dehydrated by four hours' boiling with acetic acid (200 ml.). On concentration of the solution the colourless crystalline *diene* (17 g.) separated, white plates, m. p. 212°, from acetic acid (Found: C, 58·0; H, 4·0; Br, 38·2. $C_{20}H_{16}Br_2$ requires C, 57·7; H, 3·9; Br, 38·4%).

3′ : 2″-*Dibromo*-1 : 2 : 7 : 8 : 9 : 10 : 11 : 14-*octahydro*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic Anhydride* (III; R = Br, R′ = H).—A solution of the foregoing diene (14 g.) and maleic anhydride (4 g.) in nitrobenzene (100 ml.) was refluxed for 3 hr. Removal of most of the solvent left a light-brown solid which was filtered off, dried thoroughly, and dissolved in hot chloroform with addition of charcoal. On addition of an equal volume of ethanol, filtering and cooling, the *anhydride* (15 g.) separated, large colourless plates, m. p. 260°, from chloroform–ethanol (Found: C, 56·0; H, 3·7; Br, 31·6. $C_{24}H_{18}O_3Br_2$ requires C, 56·0; H, 3·5; Br, 31·1%). The corresponding *acid* was precipitated on acidification of a solution of the anhydride in hot potassium hydroxide solution, m. p. 146° followed by resolidification and second m. p. 255°. In all subsequent preparations a form of the anhydride of m. p. 290° was obtained (Found: C, 56·1; H, 4·4; Br, 30·2%). The corresponding acid had m. p. 146° and second m. p. 255°. Reconversion into the anhydride gave the low-melting form.

Dehydrogenation of the foregoing anhydride. (*a*) When the anhydride, low-melting form (1 g.), and lead tetra-acetate (2 g.) in acetic acid (40 ml.) and acetic anhydride (40 ml.) were heated for 1 hr. yellow crystals separated (0·7 g.). Recrystallisation from acetic acid–acetic anhydride gave colourless prisms, m. p. 306°. This appears to be an *acetoxy-derivative* of unknown orientation (Found: C, 55·9; H, 3·5; Br, 29·2. $C_{26}H_{20}O_4Br_2$ requires C, 56·1; H, 3·6; Br, 28·8%). (*b*) The anhydride, either form (15 g.), in acetic acid was treated slowly with bromine (10 g., 2 mol.) in acetic acid and warmed. Hydrogen bromide was evolved and the colour changed to bright yellow. On concentrating and standing, 3′ : 2″-*dibromo*-1 : 2 : 7 : 8-*tetrahydro*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic anhydride* (IV; R = Br, R′ = H) crystallised out, bright yellow plates, m. p. 284°, from acetic acid (Found: C, 56·7; H, 2·6; Br, 31·2. $C_{24}H_{14}O_3Br_2$ requires C, 56·5; H, 2·7; Br, 31·1%). The corresponding acid is colourless, m. p. *ca.* 140°. (*c*) The octahydro-anhydride, either form (5 g.), in boiling acetic acid was treated slowly with bromine (6·6 g., 4 mol.) in acetic acid. Hydrogen bromide was evolved immediately and bright orange crystals quickly separated out. On 10 minutes' refluxing and cooling overnight the crystals of 3′ : 2″-*dibromo*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic anhydride* (V; R = Br, R′ = H) were filtered off and recrystallised twice from acetic anhydride, fine orange needles, m. p. 338° (Found: C, 56·8; H, 2·0. $C_{24}H_{10}O_3Br_2$ requires C, 56·9; H, 2·0%). Infrared absorption in Nujol suspension and in chloroform solution: sharp twin peaks 1845 cm.$^{-1}$ and 1775 cm.$^{-1}$.

Stability of 3′ : 2″-*Dibromo*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic Acid* (VI; R = Br, R′ = H).—The anhydride (1 g.) was boiled with potassium hydroxide solution until dissolved. To the colourless solution dilute hydrochloric acid was added until all acid was precipitated. After filtration and washing with water it was dried for 24 hr. at room temperature under reduced pressure. On standing in contact with air there was only a very slight variation in weight, possibly due to changes in humidity [Found: equiv. (after 7 days by titration), 533·7, 535·0. Calc. for $C_{24}H_{12}O_4Br_2$: equiv., 524·2]. The material consisted of orange-yellow crystals, m. p. *ca.* 130° resetting and melting again at 338°. Infrared absorption: in Nujol suspension a characteristic peak at 1705 cm.$^{-1}$; in chloroform this peak and the twin anhydride peaks appeared with equal intensity, but within 24 hr. the peak at 1705 cm.$^{-1}$ had disappeared. On one occasion when the acid was dried for 3 hr. instead of 24 hr. the peak at 1705 cm.$^{-1}$ took 40 hr. to disappear. It also disappeared immediately on boiling the chloroform solution.

1 : 2 : 7 : 8 : 9 : 10 : 11 : 14-*Octahydro*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic Anhydride* (III; R = R′ = H).—This was prepared according to Weidlich [3] except that the solid left after removal of solvent was recrystallised from acetic acid. Two fractions were obtained of which the first after several recrystallisations from acetic anhydride gave the high-melting *anhydride*, plates, m. p. 262° (Found: C, 80·7; H, 6·0. $C_{24}H_{20}O_3$ requires C, 80·9; H, 5·7%). The second fraction treated similarly gave the low-melting *anhydride*, needles, m. p. 237° (Found: C, 80·5; H, 5·7%).

Partial Resolution of 3′ : 2″-*Dibromo*-3 : 4-5 : 6-*dibenzophenanthrene*-9 : 10-*dicarboxylic Acid*

—The acid (1·5 g.) suspended in boiling ethanol (50 ml.) was treated with morphine (0·91 g.). The orange-red colour faded with formation of a white precipitate, which was dissolved by adding ethanol (250 ml.) and refluxing. Cooling after filtration produced a crop of colourless crystals (0·8 g.). Concentration of the mother liquor under reduced pressure yielded three further crops. Only the first and the fourth (0·5 g.) were used.

(*a*) Several recrystallisations of the first crop from ethanol gave a morphine salt (0·22 g.), $[\alpha]_D^{22}$ (ethanol) = $-220°$, which on decomposition with hydrochloric acid afforded the orange-yellow *active acid* (0·12 g.), $[\alpha]_D^{22}$ (chloroform) = $-712°$, m. p. 330° after shrinkage at 120° representing conversion into the anhydride (Found: C, 56·9; H, 2·1. $C_{24}H_{10}O_3Br_2$ requires C, 56·9; H, 2·0%).

(*b*) Recrystallisation of the fourth crop from ethanol gave a morphine salt (0·35 g.), $[\alpha]_D^{22}$ = $+497°$ (ethanol), which on decomposition afforded the acid (0·2 g.), $[\alpha]_D^{22}$ (chloroform) = $+745°$.

Racemisation.—The foregoing active acids in chloroform solution at 22° racemised with a half-life of 32 hr.:

t (hr.)	0	2¼	24	26	36	87	97
α_D	+3·28°	+2·98°	+2·08°	+1·92°	+1·52°	+0·60°	+0·49°
t (hr.)	0	13	23	49	71	95	111
α_D	−1·64°	−1·24°	−0·97°	−0·59°	−0·40°	−0·30°	−0·20°

Alternative Partial Resolution.—To the acid (1·789 g.) dissolved in chloroform morphine (1·088 g.) suspended in chloroform was added, with stirring. On concentrating the resulting solution at room temperature under reduced pressure four fractions of morphine salt were obtained. On recrystallisation and decomposition the first fraction (0·825 g.) gave the acid $[\alpha]_D^{25}$ = $+589°$ and the last fraction (0·936 g.) gave the acid of $[\alpha]_D^{25}$ = $-394°$.

Asymmetric Transformation.—The acid (0·896 g.) and morphine (0·545 g.) were refluxed in ethanol (100 ml.). On cooling, four fractions of morphine salt were obtained of total weight 1·288 g. and decomposed with acid:

Fraction	1	2	3	4
Weight (g.)	0·336	0·156	0·395	0·401
$[\alpha]_D^{25}$ after recrystallisation from ethanol	+541°	—	—	—
$[\alpha]_D^{25}$ of acid obtained on decomp.	+1078°	+1150°	+1238°	+1211°

A sample of *acid* from another run was purified by reprecipitation at 10° and dried at reduced pressure. It had $[\alpha]_D^{25}$ = $+1203°$, m. p. 127° then 338° (Found: C, 53·8; H, 2·7; Br, 27·7. $C_{24}H_{12}O_4Br_2,H_2O$ requires C, 53·2; H, 2·6; Br, 29·5%).

Racemisation of Dextro-rotatory Acid.—A sample of active acid obtained from a transformation was allowed to racemise in chloroform solution at 25°. The half-life from the following data is 20 hr.:

t (hr.) ...	0	3	8	21	27	34	45	57
α_D^{25}	+3·205°	+2·902°	+2·390°	+1·523°	+1·245°	+0·967°	+0·669°	+0·418°
t (hr.) ...	70½	81	93	104	117	141	165	
α_D^{25}	+0·280°	+0·198°	+0·136°	+0·100°	+0·068°	+0·025°	0°	

In another racemisation in chloroform the starting solution absorbed strongly in the infrared region at 1705 $cm.^{-1}$. After 40 hr. this peak had vanished (the longer time required was due to the acid's not having been dried for so long). When fully racemised the recovered anhydride had m. p. 331° and showed the characteristic absorption peaks at 1845 and 1775 $cm.^{-1}$.

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