# 775. *Alkyl–Oxygen Fission in Carboxylic Esters. Part XVI.* Influence of the Ethoxyl Group on the Reactivity of 4-Ethoxydiphenylmethanol.*

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4-Ethoxydiphenylmethanol has been obtained by reduction of the corresponding ketone, which was prepared by a Friedel–Crafts reaction. The alcohol was resolved by fractional crystallisation of the quinidine salt of its hydrogen phthalate.

The incidence of alkyl–oxygen fission has been studied for this ester by formation of (*a*) the bisdiarylmethyl phthalate in dilute alkali, (*b*) the *p*-tolyl sulphone by reaction with sodium toluene-*p*-sulphinate, and (*c*) the methyl ether by reaction with methanol, and the course of racemisation during this process. It is concluded that for these the promotion of alkyl–oxygen fission by electron-release is greater for the ethoxy- than for the methoxy-group.

ALKYL–oxygen fission has been observed in the reactions of the hydrogen phthalates of alcohols which contain electron-releasing groups, *e.g.*, 4-methoxy-[1] and 4,4′-dimethoxydiphenylmethanol.[2] We have studied the influence of the ethoxy-group on the reactivity of diphenylmethanol.

4-Ethoxydiphenylmethanol reacts very slowly with phthalic anhydride in the presence of pyridine, but readily in the presence of triethylamine at room temperature. This supports the suggestion [2] that the stronger base overcomes the effect of the electron-releasing

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* Part XV, *J.*, 1957, 3158.

[1] Balfe, Doughty, Kenyon, and Poplett, *J.*, 1942, 605.
[2] Balfe, Kenyon, and Thain, *J.*, 1951, 386.

*p*-ethoxy-group in hindering the separation of the proton from the hydroxyl group during ester formation.

$$\mathrm{EtO\cdot C_6H_4\cdot CHPh\cdot OH + NEt_3 \rightleftharpoons EtO\cdot C_6H_4\cdot CHPh\cdot O^- + NHEt_3^+}$$

$$\mathrm{EtO\cdot C_6H_4\cdot CHPh\cdot O^- + \mathit{o}\text{-}C_6H_4(CO)_2O \longrightarrow \mathit{o}\text{-}{}^-O_2C\cdot C_6H_4\cdot CO\cdot O\cdot CHPh\cdot C_6H_4\cdot OEt}$$

4-Ethoxydiphenylmethyl hydrogen phthalate has a greater tendency to undergo alkyl–oxygen fission than does the methoxy-analogue.[1] This is shown by the rapid formation of (±)-4-ethoxydiphenylmethyl *p*-tolyl sulphone when (—)-4-ethoxydiphenylmethyl hydrogen phthalate in an equivalent of 0·3N-sodium hydroxide reacts with the molecular proportion of sodium toluene-*p*-sulphinate and by the rapid dismutation of bis-(—)-4-ethoxydiphenylmethyl phthalate.

Further, (±)-, (+)-, or (—)-4-ethoxydiphenylmethyl hydrogen phthalate, on crystallisation from polar or non-polar solvents at room temperature, rapidly gives phthalic acid and neutral phthalate. This indicates that the influence of the *p*-ethoxy-group in favouring alkyl–oxygen fission is greater than that of the *p*-methoxy-group, since the acid *p*-methoxy-ester has been purified by crystallisation from carbon disulphide.[1]

This effect is also shown by the fact that the optically pure hydrogen phthalate decomposed a little even in the dry, crystalline condition in several months, resulting in the formation of a little phthalic acid and neutral ester. The pure ester, $[\alpha]_D^{22}$ —19·1° (*c* 2·75 in MeOH, *l* 2) and —20·9° (*c* 5 in $\mathrm{COMe_2}$, *l* 2), had $[\alpha]_D^{25}$ —15·6° (*c* 2·75 in MeOH, *l* 2) after five months and $[\alpha]_D^{22}$ —15·7° (*c* 5·62 in $\mathrm{COMe_2}$, *l* 1) after 54 weeks. The optically pure (—)-ester had m. p. 82—84° (decomp.), but after 54 weeks it had an indefinite m. p., softening at 84°; no such observation has been mentioned for the 4-methoxy-analogue.[1]

The rate of change of rotation of (—)-4-ethoxydiphenylmethyl hydrogen phthalate in methanol at 25° has been measured; racemisation by solvolysis was approximately of the first order ($k = 0{\cdot}086$ hr.$^{-1}$). For the (+)-4-methoxy-compound [1] an approximate value is 0·011 hr.$^{-1}$. The factor of 8 times provides a measure of the greater electron-release by the ethoxy- than by the methoxy-group.

That the mixed-ether formation involves an $S_N1$ mechanism is demonstrated by the absence of methyl hydrogen phthalate and 4-ethoxydiphenylmethanol from the product.

The mixed ether obtained in the reaction is highly racemised but contains a little optically active ether opposite in sign of rotation to the parent hydrogen phthalate. This suggests that in the ether formation the mechanism $A_{AL}1$ (the weaker acid methanol acting as a catalyst) is mainly operative, and by analogy [3] it can be inferred that mixed-ether formation is accompanied by a little inversion. That such ether formation involves alkyl–oxygen fission has been shown by previous workers.[1,4,5]

The formation of the mixed ether with the inverted configuration predominating may be ascribed to dissymmetric shielding of the carbonium ion by the receding phthalate group. Substantial shielding is attributed to the strong electron-releasing power of the ethoxy-group which increases the electron density at the alkyl-carbon atom and thus makes it less easy to remove the (alkyl)C–O electrons from the oxygen atom; this is manifested in a stronger electrostatic force in the $\overset{\delta+}{\mathrm{C}}\overset{\curvearrowright}{\text{——}}\overset{\delta-}{\mathrm{O}}$ group. This in turn slows down complete separation of the carbonium ion from the phthalate group, making it possible for the methoxide ion to attack from the opposite side and leading thus to a preponderance of the inverted configuration in the mixed ether.

No such observation has been made in the solvolysis of 4-methoxydiphenylmethyl hydrogen phthalate [1] in methanol. This may be due to the weaker electron-releasing

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[3] Hughes, Ingold, *et al.*, *J.*, 1937, 1196, 1201, 1208, 1243, 1252.

[4] Arcus and Kenyon, *J.*, 1938, 1912.

[5] Hammond and Rudesill, *J. Amer. Chem. Soc.*, 1950, **72**, 2769; Cohen and Schneider, *ibid.*, 1941, **63**, 3382.

power which, on the above mechanism, permits rapid formation of the long-lived carbonium ion and so gives rise to the racemic product.

In free 4-ethoxydiphenylmethanol the promotion of alkyl–oxygen fission is shown in the formation of bis-4-ethoxydiphenylmethyl ether in the presence of concentrated hydrochloric acid, and in the formation of the racemic sulphone by the interaction of the optically active alcohol and sodium-*p*-toluene sulphinate in 90% formic acid.

## EXPERIMENTAL

4-*Ethoxybenzophenone* (cf. Gattermann [6]).—To a stirred solution of phenetole (30·5 g.) and benzoyl chloride (36·2 g.) in dry carbon disulphide (250 c.c.) at $<0°$ aluminium chloride (40 g.) was added in 3 hr. Stirring was continued until evolution of hydrogen chloride had ceased (4—5 hr.). The carbon disulphide was then decanted from the reddish-brown solid which had separated. This solid was washed with carbon disulphide and worked up in the usual manner, giving 4-ethoxybenzophenone as thick plates (82%) (from aqueous ethanol or acetic acid), m. p. 47·5—48° (lit.,[7] 47—48°).

4-*Ethoxydiphenylmethanol*.—A suspension of zinc dust (30 g.) in a 96% ethanolic solution (200 c.c.) of sodium hydroxide (25 g.) and the ketone (44·9 g.) was heated for 5—6 hr., then concentrated and diluted with water, giving, in almost quantitative yield, 4-ethoxydiphenylmethanol, needles, m. p. 40—41° [from ether–light petroleum (b. p. 40—60°)]. Montagne [8] records m. p. 40·75° (corr.).

(±)-4-*Ethoxydiphenylmethyl Hydrogen Phthalate*.—The alcohol (41·6 g.), phthalic anhydride (27 g.), triethylamine (20 g.), and pyridine (3 c.c.) were mixed and, next day, dissolved in acetone and decomposed by addition of a slight excess of dilute hydrochloric acid, followed by water. The precipitated oil, washed with water and then benzene, gave the acid *ester* (57 g.), m. p. 109·5—111° (decomp.) (Found, on rapid titration with 0·1N-NaOH, equiv., 372. $C_{23}H_{20}O_5$ requires equiv., 376). This ester was satisfactory for the subsequent resolution. Attempts to recrystallise it from benzene, methylene chloride, chloroform, ethanol, or methanol resulted in separation of phthalic acid.

(−)-4-*Ethoxydiphenylmethyl Hydrogen Phthalate*.—A solution of the (±)-ester (75·2 g.) and quinidine (64·9 g.) in acetone (350 c.c.) slowly deposited the quinidine salt of the lævorotatory phthalate, which was collected after three days. This, after five recrystallisations from hot acetone, yielded optically pure (−)-quinidine salt (42·5 g.), needles, m. p. 153—155° (decomp.). Decomposition of this salt (37·5 g.) in acetone gave (−)-4-ethoxydiphenylmethyl hydrogen phthalate (18·5 g.), m. p. 82—84° (decomp.) (Found, as above: equiv. 380). For [α] see Table 1. Attempts to recrystallise this ester led to dismutation.

TABLE 1.

| Solvent | $c$ | $l$ | Temp. | $\alpha_{5893}$ | $\alpha_{5461}$ | $\alpha_{4358}$ | $[\alpha]_{5893}$ | $[\alpha]_{5461}$ | $[\alpha]_{4358}$ |
|---|---|---|---|---|---|---|---|---|---|
| $CS_2$ ............ | 0·260 | 2 | 22° | −0·32° | −0·40° | −0·68° | −61·5° | −77° | −131° |
| $C_6H_6$ ......... | 2·715 | 2 | 22 | −2·25 | −2·69 | −5·04 | −41·4 | −49·5 | −93 |
| $Me_2CO$ ...... | 5·00 | 2 | 22 | −2·09 | −2·52 | −4·8 | −20·9 | −25·2 | −48 |
| MeOH ...... | 2·75 | 2 | 22 | −1·05 | −1·29 | −2·29 | −19·1 | −23·5 | −41·6 |

(−)-4-*Ethoxydiphenylmethanol*.—The (−)-ester (5·64 g.) was dissolved in a solution from sodium (0·7 g.) in 96% ethanol (15 c.c.) and very gently warmed for ~5 min. Addition of water after cooling gave the (−)-alcohol (3·2 g.), m. p. 40—41°. It separated from ether–light petroleum (b. p. 40—60°) in needles, m. p. 41—42°. $[\alpha]_D$ values are given in Table 2.

TABLE 2.

| Solvent | $c$ | $l$ | Temp. | $\alpha_{5893}$ | $\alpha_{5461}$ | $\alpha_{4358}$ | $[\alpha]_{5893}$ | $[\alpha]_{5461}$ | $[\alpha]_{4358}$ |
|---|---|---|---|---|---|---|---|---|---|
| $CS_2$ ............ | 0·615 | 2 | 21° | −0·54° | −0·65° | −1·15° | −43·9° | −53·2° | −94° |
| $C_6H_6$ ......... | 1·525 | 2 | 22 | −0·42 | −0·56 | −0·98 | −13·7 | −18·5 | −32·1 |

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[6] Gattermann, *Ber.*, 1889, **22**, 1130.
[7] Montagne, *Rec. Trav. chim.*, 1920, **39**, 344.
[8] Montagne, *Rec. Trav. chim.*, 1920, **39**, 345; 1922, **41**, 717.

*Action of Dilute Sodium Hydroxide on the* (−)-*Ester*.—A solution of the ester (0·714 g.) in cold 0·3N sodium hydroxide (6·6 c.c.) became turbid in 5 min. and after 4—5 hr. the neutral ester had separated. Next day phthalic acid (0·14 g.) was recovered from the aqueous layer.

The neutral ester, when extracted with ether, gave material of $[\alpha]_D^{24}$ −21·6° in $CS_2$. Its molecular weight was determined by hydrolysis with 0·5N-sulphuric acid (Found: *M*, 583. $C_{38}H_{34}O_6$ requires *M*, 586).

The neutral ester, on hydrolysis with a solution from sodium in 96% ethanol on a water-bath for 15 min., gave optically active, oily alcohol, with $[\alpha]_D^{24}$ −15·7° in $CS_2$.

*Interaction of the* (−)-*Ester and Sodium Toluene*-p-*sulphinate*.—The acid ester (0·543 g.) was mixed with a solution of sodium toluene-*p*-sulphinate (0·32 g.) containing 0·3N-sodium hydroxide (6 c.c.). The mixture became turbid in 4 min. After 40 hr. the crystalline *sulphone* was collected and dried (0·40 g.; m. p. 158·5—160°). It separated from acetone in prisms, m. p. 168°, $[\alpha]_D^{22}$ ±0° in $COMe_2$ (Found, S, 8·7. $C_{22}H_{22}O_3S$ requires S, 8·75%).

A solution of the (−)-alcohol (0·67 g.) in 90% formic acid (3 c.c.) was mixed with a solution of sodium toluene-*p*-sulphinate (0·67 g.) in 90% formic acid (5 c.c.). Turbidity appeared within 30 sec. and crystals separated within 1 min. The sulphone was collected (1·03 g.; m. p. 163—164°). It had $[\alpha]_D^{24}$ ±0° in $CHCl_3$ (*c* 3·58; *l* 1). It separated from acetone in prisms, m. p. 168° alone or when mixed with the analysed sample.

*Bis*-4-*ethoxydiphenylmethyl Ether*.—An ethereal solution of the (±)-alcohol (11 g.) was shaken with concentrated hydrochloric acid for about 10 min. and then washed with water several times till free from acid. The dried ethereal layer, when concentrated and diluted with light petroleum (b. p. 40—60°), yielded *bis-4-ethoxydiphenylmethyl ether* as rhombs, m. p. 104—105° (Found: C 81·6; H 6·9. $C_{30}H_{30}O_3$ requires C, 82·1; H, 6·9%).

*Reaction* of (±)-p-*Ethoxydiphenylmethyl Hydrogen Phthalate with Methanol*.—The (±)-ester (9 g.) was dissolved in methanol (50 c.c.). The resulting solution deposited phthalic acid on being kept overnight. (±)-*p*-Ethoxydiphenylmethyl methyl ether (4 g.), b. p. 120°/0·2 mm., $n_D^{25}$ 1·5568 was isolated (Found: C, 78·85; H, 7·45; "–OMe," 24·7; $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·5%. Found: O from the "methoxy" value, 12·75; calculated 13·2%.)

The combined aqueous and alkaline washings yielded phthalic acid (3·5 g.), calculated yield 3·97 g.

*Reaction of the* (−)-*Acid Ester with Methanol*.—When the (−)-ester was dissolved in methanol and its specific rotatory power determined at intervals, it was found to fall, $[\alpha]_D$ ±0° being reached in about 24 hr. It then became dextrorotatory (see Table 3).

TABLE 3.

Reaction of the acid ester with methanol (*c* 2·75, *l* 2, 25°). *k* is the first-order reaction constant.

| Time (hr.) | $\alpha_D$ | $[\alpha]_D$ | *k* (hr.$^{-1}$) | Time (hr.) | $\alpha_D$ | $[\alpha]_D$ | *k* (hr.$^{-1}$) |
|---|---|---|---|---|---|---|---|
| 0 | −0·86° | −15·6° | — | 32·5 | +0·06° | +1·1° | 0·0857 |
| 8·5 | −0·36 | −6·5 | 0·0842 | 48 | +0·1 | +1·9 | 0·085 |
| 21·5 | −0·03 | −0·6 | 0·086 | 50 | +0·12 | +2·2 | — |
| 24 | ±0 | ±0 | 0·087 | 38 days | +0·12 | +2·2 | — |
| 25·5 | +0·01 | +0·02 | 0·0866 | | | | |

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