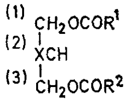
Nucleophilic Substitution in Glycerol Derivatives. Reaction of Acylglycerols with Triphenylphosphine and Carbon Tetrachloride†

By Rajindra Aneja,* Alan P. Davies, and Jeffery A. Knaggs
(*Lipid Chemistry Group, Unilever Research Laboratory Colworth/Welwyn, The Frythe, Welwyn, Herts.*)

Summary The reaction of PPh_3–CCl_4 with acylglycerols carrying a hydroxy-group at C-2 proceeds without concomitant acyloxy-migration and gives an enantiomeric 2-chlorodeoxy-derivative.

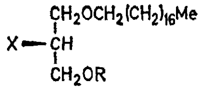
Nucleophilic substitution at C-2 in acylglycerols (glycerides) normally proceeds with concomitant migration of a participating acyloxy-group from a neighbouring carbon atom (C-1 or C-3) to C-2.[1] We now report the first examples in which such neighbouring acyloxy-group participations and migrations do not occur.

The reaction of 1,3-distearoylglycerol (I)[2] with PPh_3–CCl_4[3,4] under reflux gave 2-chlorodeoxy-1,3-distearoylglycerol (II) (95%), m.p. 53·0, containing only a trace amount of the 3-chlorodeoxy-isomer. The stereochemical course of the reaction was followed using 3-benzoyl-1-octadecyl-*sn*-glycerol (III),[5] m.p. 47·5°, $[\alpha]_D + 1{\cdot}8°$, as the substrate. Reaction of (III) with PPh_3–CCl_4 gave (IV) (96%), m.p. −5 to −3°, $[\alpha]_D + 9{\cdot}08°$, which was identical‡ with an authentic sample, m.p. −3 to −2° $[\alpha]_D + 8{\cdot}92°$ prepared by an unequivocal sequence of reactions which included the action of LiCl on the monotoluene-*p*-sulphonate (V), m.p. 26·5, $[\alpha]_D - 2{\cdot}33°$, as the key step. Thus in the reaction of (I) and (III), with PPh_3–CCl_4, substitution of the C-2 hydroxy-group by chloride proceeds without acyloxy-migration and for (III), results in inversion of configuration at C-2.



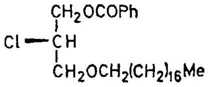
$$\begin{array}{ll} (1) & CH_2OCOR^1 \\ & | \\ (2) & XCH \\ & | \\ (3) & CH_2OCOR^2 \end{array}$$

(I) $R^1 = R^2 = C_{17}H_{35}$, $X = OH$
(II) $R^1 = R^2 = C_{17}H_{35}$, $X = Cl$
(VI) $R^1 = C_{15}H_{31}$, $R^2 = C_{17}H_{35}$, $X = p\text{-}MeC_6H_4SO_3$
(VII) $R^1 = C_{15}H_{31}$, $R^2 = C_{17}H_{35}$, $X = Cl$



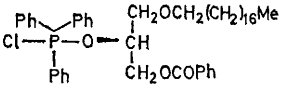
$$\begin{array}{l} \quad CH_2OCH_2(CH_2)_{16}Me \\ \quad | \\ X - CH \\ \quad | \\ \quad CH_2OR \end{array}$$

(III) $X = OH$, $R = PhCO$
(V) $X = p\text{-}MeC_6H_4SO_3$, $R = H$



$$\begin{array}{l} \quad CH_2OCOPh \\ \quad | \\ Cl - CH \\ \quad | \\ \quad CH_2OCH_2(CH_2)_{16}Me \end{array}$$

(IV)



$$\begin{array}{l} \quad Ph \quad Ph \qquad CH_2OCH_2(CH_2)_{16}Me \\ \quad\; \backslash\,/ \qquad\quad\;\; | \\ Cl - P - O - CH \\ \quad\;\; | \qquad\qquad | \\ \quad\; Ph \qquad\;\; CH_2OCOPh \end{array}$$

(VIII)

---

† For a previous paper in this series see ref. 1.

‡ By mixed m.p., R_F in thin layer chromatograms, and i.r., and 220 MHz ^1H n.m.r. spectroscopy.

In contrast, and as expected from our earlier work,[1] reaction of (VI)[1] with LiCl in solution in refluxing anhydrous MeCN gave (VII) (3·6%), 1-chlorodeoxy-2-palmitoyl-3-stearoylglycerol (28%), and 3-chlorodeoxy-1-palmitoyl-2-stearoylglycerol (28%). In this case the departure of the sulphonate group from (VI) is assisted by intramolecular attack by the neighbouring carboxylic ester groups and this takes precedence over attack by external chloride ions. For reasons which have been discussed earlier,[1] the reaction proceeds *via* dioxolenium ion intermediates which suffer regioselective attack by Cl^- ion at the terminal carbon atoms (C-3 and C-1).

The data support the results of Weiss and Snyder,[4] but are not consistent with their view that in the decomposition of the chloroalkoxytriphenylphosphorane intermediate [*e.g.* (VIII)], cleavage of the P–Cl bond precedes the cleavage of the C–O bond. The complete absence of participation by the neighbouring carboxylate ester group shows that ion pairs, even "very tight ion pairs" are ruled out, and the formation of the C–Cl and P=O bonds and fission of the C–O and P–Cl bonds are synchronous, and presumably concerted.

Elemental analysis and spectral data for all new compounds were in accord with the structures shown. The ratio of the isomeric chlorodeoxy-derivatives was determined by 220 MHz ^{1}H n.m.r.

(*Received*, *4th December* 1972; *Com.* 2021.)

---

[1] R. Aneja and A. P. Davies, *Tetrahedron Letters*, **1972**, 4497, and references therein.

[2] F. J. Baur and W. Lange, *J. Amer. Chem. Soc.*, 1951, **73**, 3926; A. Crossley, I. P. Freeman, B. J. F. Hudson, and J. H. Pierce, *J. Chem. Soc.*, 1959, 760.

[3] I. M. Downie, J. B. Lee, and M. F. S. Matough, *Chem. Comm.*, 1968, 1350; A. J. Burn and J. I. G. Cadogan, *J. Chem. Soc.*, 1963, 5788; See G. W. Brown, in 'The Chemistry of the Hydroxyl Group,' ed. S. Patai, Interscience, Part I, 1971, p. 606.

[4] R. G. Weiss and E. I. Snyder, *J. Org. Chem.*, 1970, **35**, 1627; R. G. Weiss and E. I. Snyder, *J. Org. Chem.*, 1971, **36**, 403.

[5] Prepared from commercial selachyl alcohol (ex dogfish liver oil), $[\alpha]_D$ −4·3°, lit. $[\alpha]_D$ −4·5°, see E. Baer, H. O. L. Fischer, and L. J. Rubin, *J. Biol. Chem.*, 1947, **170**, 337.