A New Procedure for the Identification, Analysis, and Isolation of Long Chain Alcohols and Acids having Alkene Unsaturation in Positions 3,4, or 5

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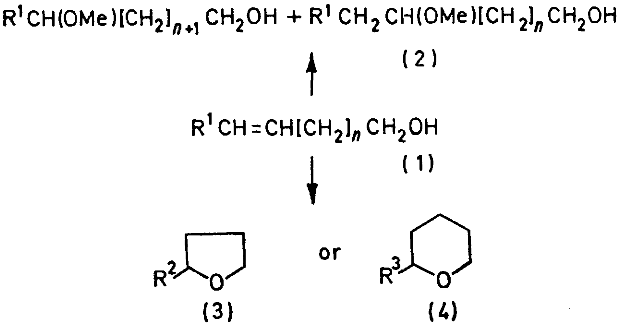
Summary The oxymercuration–demercuration of mono- or poly-enoic long-chain alcohols with Δ^3 (*trans*), Δ^4 (*cis* or *trans*), or Δ^5 (*cis* or *trans*) unsaturation to give 2-alkyl cyclic ethers provides a convenient procedure for the identification and/or isolation of these alcohols and of the corresponding acids after reduction.

WHEN unsaturated alcohols of the general formula (**1**) are treated with mercuric acetate and methanol and then reduced with sodium borohydride, the product is either a mixture of two methoxy-alcohols (**2**) or the cyclic ether (**3**) and/or (**4**) depending on the value of *n* and on the configuration of the double bond.[1,2] If the reaction is conducted in a non-participating solvent such as dimethylformamide (DMF), reaction does not occur unless a cyclic ether can be formed. With the octadecenols, 2-alkyltetrahydrofurans (THF) and/or 2-alkyltetrahydropyrans (THP) were formed with the *trans*-3 (THF, 100%), *cis*-4 (THF 92%), *trans*-4 (THF, 88% and THP, 12%), *cis*-5 (THP, 100%), and *trans*-5 (THP, 100%) enols only, whether the reaction is carried out in a participating or non-participating solvent. The latter is preferred since the products resulting from polyene alcohols are simpler. Ethyl arachidonate (**5**), for example, after reduction to the alcohol and oxymercuration–demercuration in DMF solution, gave the triunsaturated C_{20} tetrahydropyran (**6**). The high yields of these cyclic ethers and their favourable chromatographic properties make this reaction of great potential for the identification, analysis, and isolation of long-chain alcohols having unsaturation in these positions. The cyclic ethers are readily separated from one another and from any unchanged alcohols by g.l.c. and by t.l.c. Since acids, esters, and aldehydes are readily reduced to alcohols they can also be examined by this procedure.

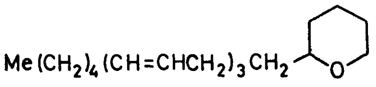


$$R^1CH(OMe)[CH_2]_{n+1}CH_2OH + R^1CH_2CH(OMe)[CH_2]_nCH_2OH \quad (2)$$

$$R^1CH{=}CH[CH_2]_nCH_2OH \quad (1)$$

(3) or (4)

$Me(CH_2)_4(CH{=}CHCH_2)_3CH{=}CH(CH_2)_3CO_2Et$ (5)



$Me(CH_2)_4(CH{=}CHCH_2)_3CH_2$–THP (6)

The value of this reaction is illustrated in the following examples:

(i) The seed oil of *Thalictrum flavum* contains acids with Δ^5 unsaturation (information supplied by Dr. I. A. Wolff, then of Peoria, along with a sample of methyl esters). After reduction of the esters and oxymercuration–demercuration of the resulting alcohols in DMF solution, cyclic ethers were prepared in 35% yield by preparative t.l.c. These were shown by g.l.c. to be tetrahydropyrans derived from 16:1 (4%), 18:1 (24%), 18:2 (15%), and 18:3 (57%) alcohols. The seed oil thus contains four acids with unsaturation at Δ^5. The position of any additional double bond is not indicated by these experiments.

(ii) A sample of tall oil fatty acids (supplied by Mr. J. A. Ashley of B.O.C.) similarly furnished tetrahydropyrans (10%) derived from 16:1 (1%), 18:2 (11%), 18:3 (69%), 20:2 (10%), and 20:3 (9%) acids having Δ^5 unsaturation.

(iiia) The total acids derived from rat liver lipids furnished two cyclic ethers. One of these (4% of the reaction product, e.c.l.† 22·7 before and 19·8 after hydrogenation) is a C_{22} pentaene tetrahydrofuran which must be derived from a 22:6 alcohol having Δ^4 unsaturation (or, less likely, Δ^3-*trans*). The second cyclic ether (13% of the reaction product, e.c.l. 18·5 before and 17·0 after hydrogenation) was identical with that (**6**) obtained from ethyl arachidonate. The rat liver lipids therefore contain 4% of 22:6 (probably the $\Delta^{4,7,10,13,16,19}$ isomer) and 13% of 20:4 ($\Delta^{5,8,11,14}$) along with traces of other Δ^5 acids.

(iiib) The mercury-containing cyclic ethers, before sodium borohydride reduction, were separated by t.l.c. from unchanged alcohols and then regenerated with methanolic hydrochloric acid. These regenerated alcohols, as trimethylsilyl ethers, showed two major peaks on g.l.c. at e.c.l. 18·9 (76%, 20:4) and 21·8 (24%, 22:6).

(iv) This procedure also gives useful information about fish oils and hydrogenated fish oils which contain polyenoic acids with Δ^4 or Δ^5 unsaturation. For example, cod liver oil and pilchard oil were shown to contain 20:5 (5·0% and 12·7%, respectively) and 22:6 (5·0% and 4·1%, respectively). Since the C_{20} acids gave a tetrahydropyran and the C_{22} acid a tetrahydrofuran they are probably the $\Delta^{5,8,11,14,17}$ and $\Delta^{4,7,10,13,16,19}$ acids, respectively, both of which belong to the linolenic or $\omega 3$ series.

When necessary, the alcohols were prepared by reduction of acids, esters, or glycerides with lithium aluminium hydride in ether. Oxymercuration–demercuration was carried out as already described using DMF in place of methanol[1] and cyclic ethers were separated from unchanged alcohols by preparative t.l.c. on layers of silica using petroleum and diethyl ether (70:30) as developing solvent. Packed DEGS columns were used for g.l.c. This procedure had advantages over the complementary m.s. method recently reported.[3] Full details will be published elsewhere.

(*Received, November 1st*, 1971; *Com.* 1887.)

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† Equivalent chain length—a method of indicating retention data (g.l.c.) of long chain esters and related compounds (T. K. Miwa, M. L. Mikolajczak, F. R. Earle, and I. A. Wolff, *Anal. Chem.*, 1960, **32**, 1739).

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[2] H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 1959, 227.
[3] P. Abley, F. J. McQuillin, D. E. Minnikin, K. Kusamran, K. Maskens, and N. Polgar, *Chem. Comm.*, 1970, 348.