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THE REACTION OF LEAD TETRA-ACETATE WITH SOME ACYCLIC HYDROXY-ETHERS[1,2]

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Abstract—By means of lead tetra-acetate in refluxing benzene open-chain 1,2-, 1,3-, 1,4- and 1,5-hydroxy-ethers are mainly converted to the corresponding five-membered or six-membered cyclic products. Thus, 2-alkoxy-1-ethanols afford 2-substituted 1,3-dioxolanes in 50–53% yield and 4-ethoxy-1-butanol gives 2-ethoxytetrahydrofuran in 52% yield; 3-alkoxy-1-propanols are oxidized to the corresponding 2-substituted 1,3-dioxans in 26–40% yield and 5-ethoxy-1-pentanol cyclizes to 2-ethoxytetrahydropyran in 46% yield. 2-Phenoxyethanol undergoes ring closure to 1,4-benzodioxan in 15% yield.

INTRODUCTION

DIALKYL ethers,[4–6] benzylphenyl ethers, [7–9] dibenzyl ether[5] (I), and tetrahydrofuran and its derivatives[6] are primarily attacked by lead tetra-acetate, in different solvents, at the α-carbon atoms to give as intermediates the corresponding α-carbon radicals (II), which can then further react with the oxidizing agent or stabilize themselves in different ways, mainly by conversion to α-acetoxy derivatives.[10]

$$\underset{\text{I}}{RCH_2{-}O{-}R'} \xrightarrow{Pb(OAc)_4} \underset{\text{II}}{R\dot{C}H{-}O{-}R'}$$

[1] Paper VIII in the series *Reactions with lead tetra-acetate.*

[2] For paper VII see M. Lj Mihailović, Ž. Čeković and D. Jeremić, *Tetrahedron* **21**, 2813 (1965).

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[4] M. S. Kharasch, H. N. Friedlander and W. H. Urry, *J. Org. Chem.* **16**, 533 (1951).

[5] J. Jadot, A. David and J. Kasperszyck, *Bull. Soc. Roy. Sci., Liège* **29**, 196 (1960).

[6] W. Frass, Ph.D. Thesis, Karlsruhe (1960).

[7] H. E. Barron, G. W. K. Cavill, E. R. Cole, P. T. Gilham and D. H. S. Solomon, *Chem. & Ind.* 76 (1954).

[8] G. W. K. Cavill, F. M. Dean, A. McGookin, B. M. Marshall and A. Robertson, *J. Chem. Soc.* 4573 (1954).

[9] G. W. K. Cavill and D. H. Solomon, *J. Chem. Soc.* 1404 (1955).

[10] Benzyl phenyl ethers (III) undergo, in addition to α-hydrogen atom abstraction (IV), a competitive reaction, i.e. radical formation in the *para* position of the phenyl group (V), with subsequent acetoxylation.[7,9]

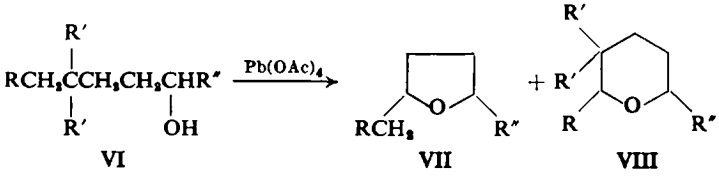
$$\underset{\text{III}}{C_6H_5CH_2{-}O{-}C_6H_5} \xrightarrow{Pb(OAc)_4} \underset{\text{IV}}{C_6H_5\dot{C}H{-}O{-}C_6H_5} + \underset{\text{V}}{C_6H_5CH_2{-}O{-}\langle\bigcirc\rangle}.$$

Alkyl aryl (phenyl or naphthyl) ethers containing one alkoxy group are predominantly attacked by lead tetra-acetate on the aromatic moiety (to give intermediate aryl carbon radicals of type V),[9,11] whereas more highly substituted compounds, such as dimethoxy- and trimethoxybenzenes, undergo reaction both on the methoxy groups and on the benzene ring (to give intermediate carbon radicals of type IV and V, respectively).[12]

[11] F. Wessely, J. Kotlan and W. Metlesics, *Monatsh.* **85**, 69 (1954); J. Jadot and M. Neuray, *Bull. Soc. Roy. Sci., Liège* **29**, 138 (1960).

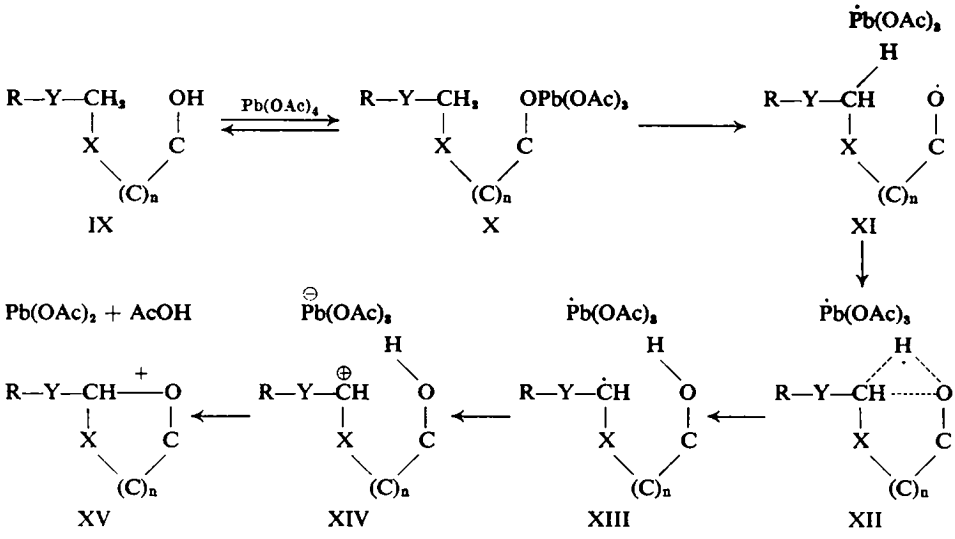
[12] M. M. Bokadia, B. R. Brown and W. Cummings, *J. Chem. Soc.* 3308 (1960); F. R. Preuss and R. Menzel, *Arch. Pharm.* **291**, 350, 377 (1958); F. R. Preuss and L. Tan, *Ibid.*, **293**, 505 (1960); F. R. Preuss and I. Janshen, *Ibid.*, **293**, 933 (1960).

On the other hand it was recently shown[13,14] that unbranched primary and secondary aliphatic alcohols (VI; R′ = H) with nonactivated δ- and ε-methylene groups react with lead tetra-acetate in nonpolar solvents (e.g. refluxing benzene) to give as major products (33–50% yield) 2-alkyl- or/and 2,5-dialkyl-tetrahydrofurans (VII), accompanied by small amounts (1–4% yield) of the isomeric six-membered cyclic ethers (VIII; R′ = H).



VI VII VIII

The formation of tetrahydropyran derivatives (VIII) is not favoured in oxidations with lead tetra-acetate since in alcohols, such as 4,4-dimethyl-1-alkanols (VI; R′ = CH_3, R″ = H), which cannot afford substituted tetrahydrofurans (VI ↛ VII), the yields of six-membered cyclic ethers (VIII; R′ = CH_3, R″ = H) does not exceed 11%



(a) n = 1, X = Y = CH_2; (b) n = 2, X = Y = CH_2;
(c) n = 1, X = O, Y = CH_2 or R—Y = C_6H_5; (d) n = 1, X = CH_2, Y = O;
(e) n = 2, X = O, Y = CH_2 or R—Y = C_6H_5; (f) n = 2, X = CH_2, Y = O

SCHEME 1

and the reaction times are considerably longer than those of the corresponding δ-unsubstituted alcohols (VI; R′ = R″ = H).[2] This difference in reactivity between the secondary δ-hydrogen atoms and secondary ε-hydrogen atoms, involved in 1,5- and 1,6-hydrogen transfer, respectively, is attributed[2,14] to different free energies of activation (steric and probability factors) for the corresponding transition states

[13] V. M. Mićović, R. I. Mamuzić, D. Jeremić and M. Lj. Mihailović, *Tetrahedron Letters* No. 29, 2091 (1963); *Tetrahedron* **20**, 2297 (1964).

[14] M. Lj. Mihailović, Ž. Čeković, Z. Maksimović, D. Jeremić, Lj. Lorenc and R. I. Mamuzić, *Tetrahedron* **21**, 2799 (1965), and Refs therein.

(Scheme 1, XIIa and XIIb),[15] through which the conversion of alkoxy radicals (XIa and XIb) to the hydroxyalkyl carbon radicals (XIIIa and XIIIb) is presumed to take place.[14,16]

RESULTS AND DISCUSSION

In the light of these results, the action of lead tetra-acetate on acyclic 1,2- (IXc), 1,3- (IXe), 1,4- (IXd) and 1,5-hydroxy-ethers (IXf) has been studied, with a view to investigating the effect of the ether function on intramolecular 1,5- and 1,6-cyclization, i.e. on the formation of five-membered and six-membered ring compounds. All the oxidations were carried out in refluxing benzene, with one molar equivalent of lead tetra-acetate and in the presence of anhydrous calcium carbonate. The products were identified by comparison with authentic compounds, synthesized by independent routes.

If the mechanism shown on Scheme 1 is operative for hydroxy-ethers (IX, c–f),[17] then, in comparison to aliphatic alcohols (IX, a and b), homolytic intramolecular hydrogen transfer from the methylene carbon directly attached to the ether oxygen to the "electrophilic" hydroxyl oxygen in the alkoxy radical (XI, c–f), to give the carbon radical (XIII, c–f), should be somewhat retarded, due to the negative inductive effect of the ether oxygen; on the other hand, however, the same effect should facilitate the one-electron oxidation step (XIII → XIV)[14,18] and, in addition, stabilization by resonance of the carbon radical (XIII, c–f) and particularly of the corresponding carbonium ion (XIV, c–f) should also be enhanced. These competitive electronic factors, together with steric and probability requirements of the transition state (XII, c–f), will control the ease of the overall 1,5- and/or 1,6-cyclization process.

In the case of 1,2-hydroxy-ethers (IXc), such as 2-pentyloxyethanol (XVIa), 2-propoxy-1-propanol (XVIb) and 2-benzyloxyethanol (XVIc), in which the δ-methylene group (with respect to the hydroxyl group) is attached to the ether oxygen, the reaction with lead tetra-acetate affords the corresponding 2-alkyl- and 2-phenyl-1,3-dioxolanes (XVII) in 50–53% yield.[19] 2-Pentyloxyethanol (XVIa) gives, in addition, a small amount (ca. 1%) of n-propyl-1,4-dioxan (XVIII).

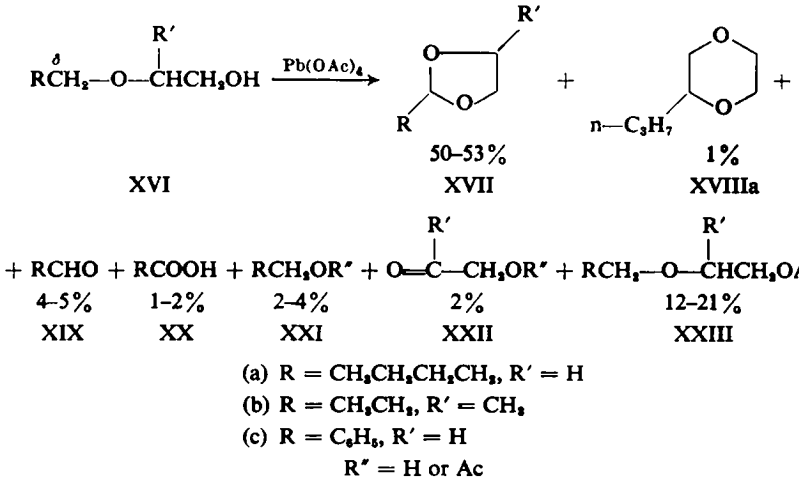
[15] A cyclic six-membered transition state (XIIa)(1,5-hydrogen transfer), leading to tetrahydrofurans (XVa), being more favourable than a seven-membered cyclic structure (XVb)(1,6-hydrogen abstraction), necessary for tetrahydropyran (XVb) formation.[14]

[16] See K. Heusler and J. Kalvoda, *Angew. Chem.* **76**, 518 (1964); *Ibid.* (International Ed.) **3**, 525 (1964), and Refs therein.

[17] Since lead tetra-acetate is expected to react more easily with the hydroxyl oxygen than with a methylene carbon atom, the formation of the carbon radicals (XIII, c–f) from hydroxy-ethers (IX, c–f) most probably takes place as illustrated on Scheme 1,[16] i.e. in the same way as from aliphatic alcohols (IX, a and b),[8,14] *via* the complex alkoxy lead triacetate (X, c–f) and alkoxy radical (XI, c–f), with subsequent hydrogen shift from carbon to oxygen (XI → XIII), and not by direct attack of the reagent on the δ- and ε-carbon atom (adjacent to the ether oxygen). This is substantiated by the fact that the lead tetra-acetate oxidation of ethers, which involves direct attack on the α-carbon atom, is a slow reaction,[4–6,8,9,11,12] while the oxidation of hydroxy-ethers (IX, c–f) proceeds at a relatively fast rate (see below and Experimental).

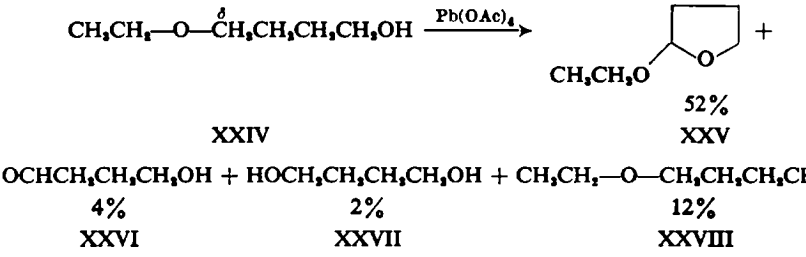
[18] Brought about by lead tetra-acetate or trivalent lead species, such as $Pb(OAc)_3$.[14]

[19] Intramolecular five-membered ring acetal and ketal formation involving substitution on the carbon adjacent to the ether oxygen, was observed when cyclic 1,4- and 1,2-hydroxy-ethers, in which one or both reacting centres are *geometrically fixed*, were subjected to lead tetra-acetate oxidation; P. F. Beal and J. E. Pike, *Chem. & Ind.* 1505 (1960); U. Scheidegger, K. Schaffner and O. Jeger, *Helv. Chim. Acta* **45**, 400 (1962).



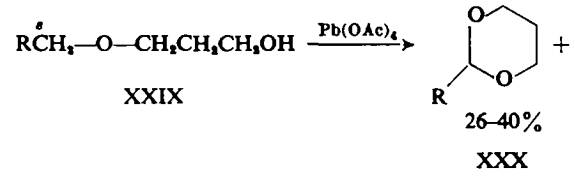
(a) R = $CH_3CH_2CH_2CH_2$, R′ = H
(b) R = CH_3CH_2, R′ = CH_3
(c) R = C_6H_5, R′ = H
R″ = H or Ac

A similar behaviour may be observed with 1,4-hydroxy-ethers (Scheme 1, IXd), 4-ethoxy-1-butanol (XXIV), under similar experimental conditions, being converted in 52% yield to 2-ethoxytetrahydrofuran (XXV).[19] All these results are similar to those obtained[14] with simple aliphatic alcohols and indicate that the *yields* of five-membered cyclic products (XVII and XXV, respectively; see also XVc and XVd in Scheme 1), the formation of which proceeds *via* 1,5-hydrogen transfer (XI → XIII), are not appreciably affected by the presence of the ether function. That the ether oxygen in hydroxy-ethers (XVI and XXIV) has, nevertheless, an activating influence on the adjacent methylene groups, one of which being in the δ-position to the hydroxyl group participates in 1,5-ring closure, follows from the fact that the lead tetraacetate oxidations of these alkoxy-alkanols are about twice as *fast* as those of the corresponding unbranched primary aliphatic alcohols (VI, R′ = R″ = H).[14]



However, in the case of 1,3-hydroxy-ethers (Scheme 1, IXe), such as 3-n-butoxy-1-propanol (XXIXa) and 3-benzyloxy-1-propanol (XXIXb), which can undergo only homolytic 1,6-hydrogen transfer (XIe → XIIIe) to give six-membered heterocycles (XVe), the presence of the ether oxygen adjacent to the ε-methylene group (with respect to the hydroxyl group) has a considerable activating influence on the ease of formation of 2-substituted 1,3-dioxans (XXX). Thus, 3-n-butoxy-1-propanol (XXIXa) affords 2-n-propyl-1,3-dioxan (XXXa) in 26–30% yield, and 3-benzyloxy-1-propanol (XXIXb) gives the corresponding 2-phenyl-1,3-dioxan (XXXb) in 40% yield. These yields are appreciably higher than the yield (11%) of six-membered

cyclic ethers (tetrahydropyran derivatives VIII) obtained upon lead tetra-acetate oxidation of 4,4-dimethyl-1-hexanol (VI; R = R′ = CH_3, R″ = H),[2] and, moreover, the time required for completion of the reaction is about 10–20 times shorter than in the case of the aliphatic alcohol. This difference in reactivity is best explained by the fact that in 1,3-hydroxy-ethers (XXIX; see also Scheme 1, IXe) the electron-attracting ether oxygen adjacent to the ε-methylene carbon facilitates the oxidation of



XXIX

26–40%

XXX

+ RCHO + RCOOH + RCH_2OAc + RCH_2—O—$CH_2CH_2CH_2OAc$

2–7% 1–2% 2–5% 13–20%

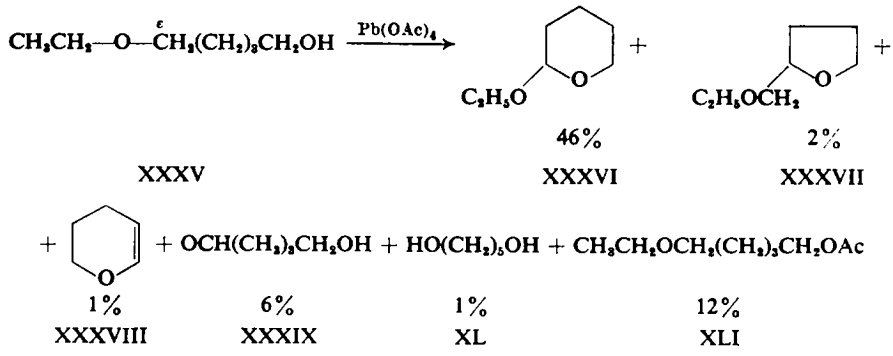
XXXI XXXII XXXIII XXXIV

(a) R = $CH_2CH_2CH_2$; (b) R = C_6H_4

the ε-carbon radical (Scheme 1, XIIIe) to the corresponding carbon cation (XIVe) and stabilizes (by resonance) both of these intermediate species (see discussion above). When, in addition, the ε-methylene carbon is also attached to a phenyl group, as in 3-benzyloxy-1-propanol (XXIXb), these polar and stabilization effects are still more pronounced (compare the yields of XXXa and XXXb), since the phenyl group has a large radical and cation stabilizing ability, and, like the ether function, shows a negative inductive effect.

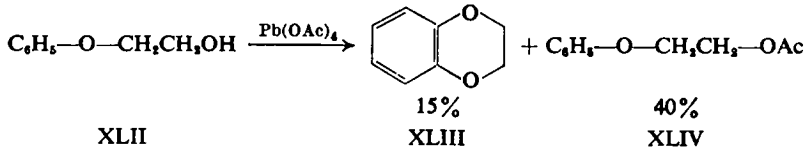
The activating influence of the ether oxygen on the adjacent ε-methylene group is particularly important in the case of a 1,5-hydroxy-ether (Scheme 1, IXf), such as 5-ethoxy-1-pentanol (XXXV), which reacts rapidly with lead tetra-acetate to give the corresponding six-membered cyclization product, 2-ethoxytetrahydropyran (XXXVI), in 46% yield, whereas the isomeric five-membered cyclic diether, 2-(ethoxymethyl)-tetrahydrofuran (XXXVII), is isolated in only 2% yield. Here, the above mentioned electronic effects of the ether function, which favour 1,6-hydrogen abstraction from the ε-methylene carbon, outweigh the steric and probability factors in the transition state (Scheme 1, XIIf), these two latter factors, as shown in the case of alcohols with non-activated δ- and ε-methylene groups (IX, a and b), favouring 1,5-hydrogen transfer from the δ-methylene carbon (XIa → XIIIa; six-membered transition state XIIa, leading to tetrahydrofurans XVa) rather than 1,6-hydrogen abstraction from the ε-methylene carbon (XIb → XIIIb; seven-membered transition state XIIb, leading to tetrahydropyrans XVb).[2,14]

Since the hydroxy-ethers studied (IXc–IXf in Scheme 1, or XVI, XXIV, XXIX and XXXV) are more reactive towards lead tetra-acetate than the corresponding aliphatic alcohols (shorter reaction times, similar or better yields of cyclization products), it may be concluded that the electron-attracting inductive effect of the ether oxygen does not play an important role in retarding intramolecular 1,5- and 1,6-hydrogen transfer from the methylene group (adjacent to the ether oxygen) to the electron-deficient ("electrophilic") hydroxyl oxygen (XI → XIII, c–f) in the alkoxy radical (XI, c–f) (a possibility envisaged in the discussion above), i.e. that this factor is



negligible in comparison to the ease of the one-electron oxidation step (XIII → XIV, c–f) and stabilization of the intermediate species (XIII, c–f) and (XIV, c–f).

Lead tetra-acetate reacts more slowly with 2-phenoxyethanol (XLII), the only cyclization product, isolated in 15% yield, being 1,4-benzodioxan (XLIII).



The formation of this cyclic diether can be best rationalized as a radical intramolecular *o*-alkoxylation (Scheme 2), proceeding *via* a σ-complex-type intermediate or transition state (XLV).[20–22]

The acetates of the starting alcohols (XXIII, XXVIII, XXXIV, XLI, XLIV) were obtained in all the lead tetra-acetate oxidations of hydroxy-ethers, in yields ranging from 12 to 40%. The formation of these compounds was discussed previously.[2,14,25]

Aldehydes, RCHO (XIX, XXXI), and ω-hydroxy-aldehydes, $OCH(CH_2)_nCH_2OH$ (XXVI, XXXIX), which are isolated in small yield (2–7%) upon lead tetra-acetate oxidation of the hydroxy-ethers (XVI, XXIX) and (XXIV, XXXV), respectively, represent hydrolysis products either of the corresponding cyclic acetals (XVII, XXX,

[20] Similarly to free-radical intramolecular *o*-acylation. cf. W. H. Urry, D. J. Trecker and H. D. Hartzler, *J. Org. Chem.* **29**, 1663 (1964).

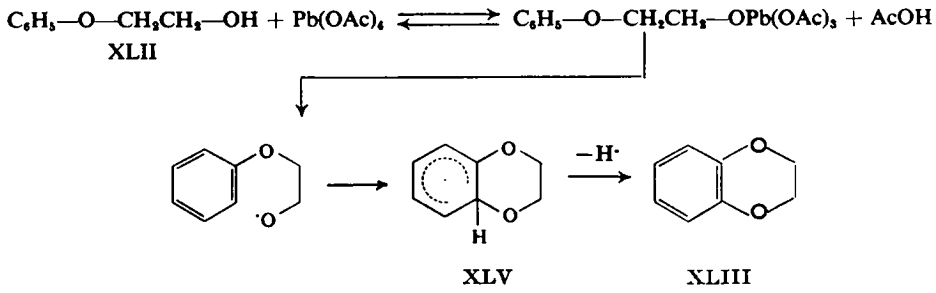
[21] Step XLV → XLIII might take place through an intermediate cationic species corresponding to XLV.

[22] The mechanism postulated in Scheme 1 and involving homolytic hydrogen transfer from carbon to oxygen does not appear to be likely in this case, since, as demonstrated recently, 2-phenylethanol, $C_6H_5CH_2CH_2OH$, upon oxidation with lead tetra-acetate, does not yield 2,3-dihydrobenzofuran (1,5-cyclization),[23] whereas 3-phenyl-1-propanol, $C_6H_5CH_2CH_2CH_2OH$, is converted, in part, to the corresponding 3,4-dihydro-2H-1-benzopyran (chroman) (1,6-ring closure).[24] If the sequence in Scheme 1 were operative for these oxidations, 2-phenylethanol would be expected to cyclize at least as readily as 3-phenyl-1-propanol, since tetrahydrofuran formation (XVa), involving a cyclic six-membered transition state (XIIa), is preferred to tetrahydropyran formation (XVb), which requires a seven-membered cyclic transition state (XIIb).[2,14]

[23] S. Moon and J. M. Lodge, *J. Org. Chem.* **29**, 3453 (1964).

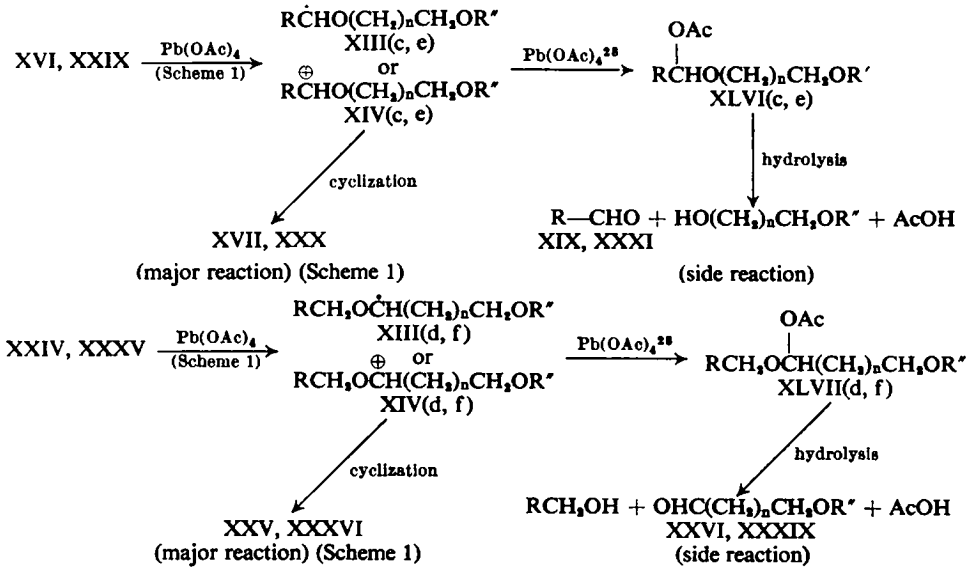
[24] To be published.

[25] M. Lj. Mihailović, Z. Maksimović, D. Jeremić, Ž. Čeković, A. Milovanović and Lj. Lorenc, *Tetrahedron* **21**, 1395 (1965).



Scheme 2

XXV and XXXVI) or of the open-chain acylals (Scheme 3, XLVI and XLVII), hydrolysis occurring during the oxidation reaction or/and in the course of the working-up procedure. These α-acetoxylated hydroxy-ethers (acylals) or their acetates (Scheme 3, XLVI and XVLII, R″ = H or Ac), which were actually not isolated,[26] would most probably be formed by acetoxylation of the corresponding carbon radicals (Scheme 3, XIII, c–f; see also Scheme 1) or carbonium ions (Scheme 3, XIV, c–f; see also Scheme 1).[27]



(c) n = 1; (d) and (e) n = 2; (f) n = 3
R″ = H or Ac

Scheme 3

[26] As already mentioned above, α-acetoxy derivatives and their hydrolysis products were obtained when alkyl, benzyl and cyclic ethers were subjected to the action of lead tetra-acetate.[4–9,18] The mechanism of this reaction was discussed by several authors.[4,5,7,9]

[27] If acetoxylation involves carbon radicals or cations with free hydroxyl groups (Scheme 3, XIII and XIV, c–f, R″ = H), this side reaction would represent an additional way of stabilization of the intermediate species (XIII and XIV), the other, major reaction being the cyclization process (discussed above).

[28] Or other species present in the reaction mixture which can act as acetoxylating agents ($\dot{Pb}(OAc)_3$, $\dot{AcO}$, $Pb(OAc)_3^{\ominus}$, $AcO^{\ominus}$, etc.).

2,3-Dihydro-4H-pyran (XXXVIII), detected in a small amount (about 1%) among the reaction products obtained from 5-ethoxy-1-pentanol (XXXV), is probably generated from the cyclic hemiacetal form[29] of 5-hydroxypentanal[30] (XXXIX) or its acetate (2-acetoxytetrahydropyran)[31] in the course of the isolation procedure (working up[30] or distillation[31]), rather than during the oxidation reaction itself, since it has been reported that dihydropyran (XXXVIII) is readily oxidized by lead tetra-acetate in benzene solution to give various acetoxylated dihydropyran and tetrahydrofuran derivatives.[32]

Attack of lead tetra-acetate (or other tetravalent and trivalent lead containing species present in the reaction mixture) on the activated carbon in position 2 of the 2-substituted cyclic diethers (XVII, XXV, XXX, XXXVI), or further attack by the same reagent of the α-acetoxy-ethers (acylals) (XLVI and XLVII in Scheme 3) would afford the corresponding 2-acetoxylated and α,α-diacetoxylated derivatives, respectively; these products would then undergo facile hydrolysis (probably during the working up procedure) to carboxylic acids.[33] The isolation of benzoic acid (XXc and XXXIIb), n-valeric acid (XXa) and n-butyric acid (XXXIIa), upon lead tetra-acetate oxidation of the corresponding hydroxy-ethers (XVIc, XXIXb, XVIa and XXIXa, respectively), in yields of 1–2%, confirms such a subsequent mode of action of the tetravalent lead compound.[34]

That a methylene group adjacent to the ether oxygen, but not able to participate in 1,5- or 1,6-cyclization since it is not in the δ- or ε-position to the hydroxyl group, may also be attacked to a minor extent by lead tetra-acetate to give the corresponding carbon radical (Scheme 4, XLVIII and XLIX),[35] follows from the fact that in most oxidations of

[29] C. D. Hurd, Jr., and W. H. Saunders, *J. Amer. Chem. Soc.* **74**, 5324 (1952); J. Colonge and P. Corbet, *Bull. Soc. Chim. Fr.* 283 (1960).

[30] Traces of acid are sufficient to effect conversion of 5-hydroxypentanal (XXXIX), in its cyclic form, to 2,3-dihydro-4H-pyran (XXXVIII); see R. Paul, *Bull. Soc. Chim. Fr.* [5] **1**, 971 (1934).

[31] 2-Acyloxy-tetrahydropyrans and 2-acyloxy-tetrahydrofurans easily decompose on heating (at 80–100°) to 2,3-dihydro-4H-pyran (XXXVIII) and 2,3-dihydrofuran, respectively; G. Sosnovsky, *Tetrahedron* **13**, 241 (1961). For the formation of 2-acetoxytetrahydropyran from 5-hydroxypentanal (XXXIX) see J. G. M. Brenner and D. G. Jones, Brit. 606, 764 (1948); *Chem. Abstr.* **43**, 1442 (1949); U.S. 2,504,797 (1950); *Chem. Abstr.* **44**, 6689 (1950); I. Á. Gerecs and M. Windholz, *Acta Chim. Acad. Sci. Hung.* **14**, 333 (1958); C. D. Hurd and T. Iwashige, *J. Org. Chem.* **24**, 1321 (1959).

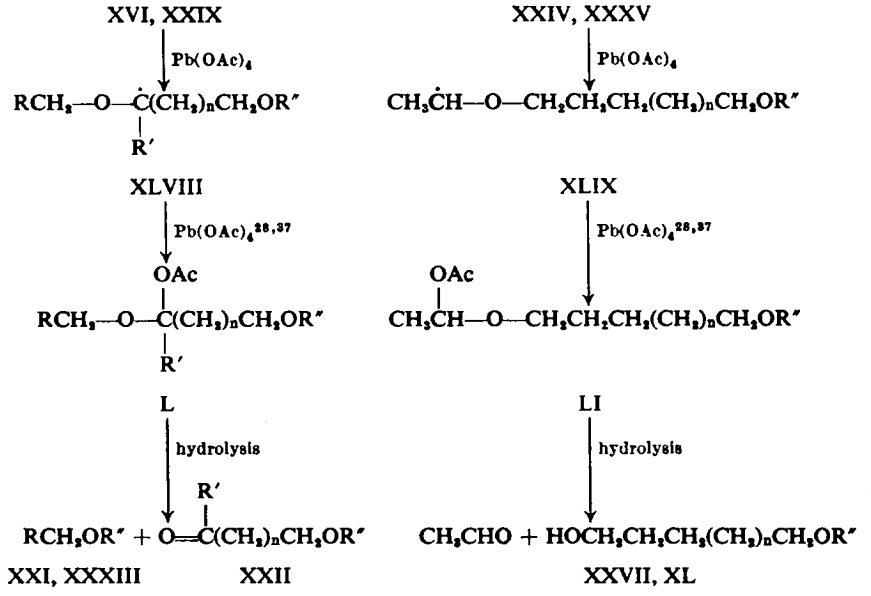
[32] C. D. Hurd and O. E. Edwards, *J. Org. Chem.* **19**, 1319 (1954),

[33] α,α-Diacetoxy-ethers and their hydrolysis products (among them carboxylic acids) were isolated in the lead tetra-acetate oxidation of n-dibutyl ether and dibenzyl ether.[5]

[34] Another possibility for the formation of carboxylic acids (XX and XXXII) would consist in the lead tetra-acetate catalyzed autooxidation of the corresponding aldehydes (XIX, XXXI).[14,35] However, since these aldehydes are themselves formed in low yields and since their oxidation in the presence of lead tetra-acetate proceeds only slowly,[35] it is believed that the acids (XX and XXXII) are generated, in major part, by hydrolysis of the 2-acetoxylated cyclic acetals or α,α-diacetoxylated ether-alcohols, as described above.

[35] These carbon radicals (Scheme 4, XLVIII and XLIX, R′ = H) might arise either by direct attack of lead tetra-acetate on the carbon adjacent to the ether oxygen, as in the case of simple ethers,[4–9,13] or, less probably, by way of the complex lead alkoxides, alkoxy radicals and hydrogen transfer from carbon to oxygen, according to a sequence of the type shown in Scheme 1. This latter mechanism would involve 1,3-, 1,4-, 1,7- or 1,8-hydrogen abstractions in the intermediate alkoxy radicals (corresponding to the starting hydroxy-ethers XVI, XXIX, XXIV and XXXV), with unfavourable transition states.[14] Cyclization products derived from such carbon radicals were not detected; their absence, however, does not provide evidence for distinguishing between direct attack on carbon

hydroxy-ethers, alcohols or their acetates[36] (XXI, XXVII, XXXIII, XL; see also Scheme 4) and carbonyl compounds (XXII), corresponding to hydrolysis products of the primarily formed α-acetoxylated hydroxy-ethers or their acetates (Scheme 4, L and LI), are isolated in yields ranging from 1 to 6%.



n = 0 or 1; R′ = H or CH_3; R″ = H or Ac

SCHEME 4

The formation of formaldehyde (Scheme 5, LIII) in the course of the lead tetra-acetate oxidation of 2-propoxy-1-propanol (Scheme 5, XVIb) and the detection fo acetaldehyde (LV) upon acidification of the reaction mixture suggest that this hydroxy-ether undergoes, to a certain extent (in at least 5% yield[37a]), fragmentation between the carbinol carbon atom and the adjacent tertiary carbon atom. The rate of the lead tetra-acetate fragmentation process is mainly dependent on the stability of the primarily formed carbon radicals.[14,16] Since the carbon radical (LII), derived from 2-propoxy-1-propanol (XVIb), and the corresponding carbon cation (LIV) are secondary and resonance stabilized by the adjacent oxygen atom, it is understandable that in this particular case the fragmentation reaction, brought about by lead tetra-acetate, occurs to a detectable extent, while with other unbranched primary hydroxy-ethers (and unbranched primary aliphatic alcohols[14]), which would afford primary

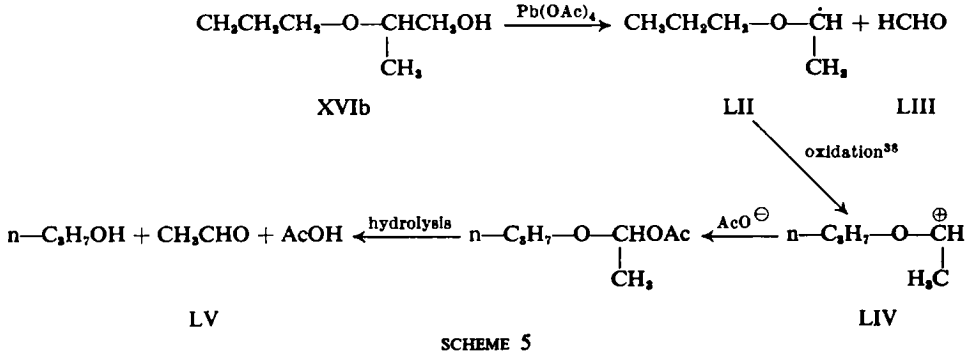
and the multistep mechanism involving hydrogen transfer, since both mechanisms would afford the same carbon radicals (Scheme 4, XLVIII and XLIX, R″ = H). Naturally, if the hydroxyl group of the starting ether-alcohols is first converted to an acetate group (in the course of the reaction), the formation of carbon radicals (Scheme 4, XLVIII and XLIX, R″ = Ac) can only proceed by direct attack of lead tetra-acetate on the carbon atom attached to the ether oxygen.

[36] These acetates arise by subsequent reaction of alcohols with lead tetra-acetate (or other lead containing species) or acetic acid (present in the reaction mixture).[14,25]

[37] Step XLVIII → L and XLIX → LI might take place *via* the carbon cations corresponding to the carbon radicals XLVIII and XLIX (see Scheme 1 and Scheme 3).

[37a] Since acetaldehyde (LV) was isolated in that amount (see Experimental).

carbon radicals (R—O—$\dot{C}H_2$ or R—$\dot{C}H_2$), this process is not observed.



SCHEME 5

Aldehydes corresponding to the starting alcohols are not isolated upon lead tetra-acetate oxidation of hydroxy-ethers, but their presence, in low yield (about 0·5–2%),[14] is inferred from IR spectra of the fractions boiling higher than the cyclic diethers obtained.

The lead tetra-acetate oxidation of acyclic hydroxy-ethers may therefore provide, in some cases, a convenient and useful method for the preparation of five-membered and six-membered cyclic acetals (and ketals) or their hydrolysis products (particularly the sometimes difficultly available and unstable hydroxycarbonyl compounds of type XXVI and XXXIX).

EXPERIMENTAL[39]

B.ps and m.ps are uncorrected. Analytical and preparative gas chromatography, and fractional distillations were carried out as reported earlier.[14,25] IR spectra were registered on a Perkin–Elmer Infracord, Model 137.

The perparation of lead tetra-acetate, drying of the reagents and benzene, and the general procedure for the lead tetra-acetate oxidations were described previously,[14] with the remark that the aqueous solutions were always *continuously* extracted with ether.

Immediately before use all the starting hydroxy-ethers were dried and fractionated. Their purity was always checked by means of gas chromatography.

The reaction products, obtained by fractional distillation or/and gas chromatographic separation, were identified by comparison of their physical properties (b.ps, refractive indices, gas-chromatographic retention times, IR spectra, m.ps of solid derivatives) with those of authentic compounds, synthesized by independent routes.

Carbonyl compounds and cyclic acetals were characterized (and if necessary quantitatively determined) by conversion to the corresponding 2,4-dinitrophenylhydrzaones.[40]

2-Pentyloxyethanol (XVIa)

(a) *Preparation.* This hydroxy-ether, b.p. 187–188° at 760 mm, n_D^{20} 1·4234 (lit.[41] b.p. 187–188° at 753 mm, n_D^{20} 1·4239), was prepared according to Cooper and Partridge.[41]

(b) *Synthesis of reaction products—2-n-Butyl-1,3-dioxolane* (XVIIa). Ethylene glycol (31 g, 0·5 mole), freshly distilled n-valeraldehyde (27 g, 0·31 mole) and 12 g Amberlite IR-120 (acid form) in

[38] By lead tetra-acetate, $Pb(OAc)_4$ or other lead containing species.

[39] We thank Mrs. R. Tasovac and Miss R. Dimitrijević, from the Microanalytical Laboratory of our Department, for the elemental microanalyses they carried out.

[40] Houben-Weyl, *Methoden der organischen Chemie* (Edited by E. Müller) 4th Edition; Vol. II, p. 457. Georg Thieme Verlag, Stuttgart (1953).

[41] F. C. Cooper and M. W. Partridge, *J. Chem. Soc.* 459 (1950), and Refs therein.

100 ml benzene were treated as described by Astle *et al.* (method C),[43] to give 30 g (74%) of XVIIa, b.p. 162–163° at 760 mm, n_D^{22} 1·4209 (lit.[43] b.p. 53–55° at 34 mm, n_D^{20} 1·4211). (Found: C, 64·4; H, 10·8. Calc. for $C_7H_{14}O_2$: C, 64·6; H, 10·8%.) With 2,4-dinitrophenylhydrazine in acid solution[40] it gives the 2,4-dinitrophenylhydrazone of n-valeraldehyde, m.p. 106–107°.[44]

n-Propyl-1,4-dioxan (XVIIIa). This cyclic diether, b.p. 157–159° at 760 mm, n_D^{20} 1·4301 (lit.[45] b.p. 155·6–157·1° at 746 mm, n_D^{20} 1·4298). (Found: C, 64·3; H, 10·9. Calc. for $C_7H_{14}O_2$: C, 64·6; H, 10·8%), was prepared from n-propylmagnesium bromide and monochloro-1,4-dioxan[46] in 30% yield.[45]

2-Pentyloxyethanol acetate (XXIIIa). Compound XVIa (6·5 g, 0·05 mole), 20 ml glacial acetic acid and 1 g *p*-toluenesulphonic acid were heated under reflux for 3 hr. Distillation of the reaction mixture under red. press. afforded 7·9 g (90·8%) *2-pentyloxyethanol acetate* (XXIIIa), b.p. 115–117° at 38 mm, n_D^{21} 1·4181. (Found: C, 61·8; H, 10·4. $C_9H_{18}O_3$ requires: C, 62·0; H, 10·4%.)

(c) *Oxidation.* Compound XVIa (13·2 g, 0·1 mole) in 130 ml of dry benzene was oxidized with 46·5 g $Pb(OAc)_4$ (0·1 mole + 5% excess), in the presence of 10·5 g anh. $CaCO_3$ (0·1 mole + 5% excess). The reaction was completed after refluxing for 30 min.

Fractional distillation of the neutral benzene–ether extract afforded 4 fractions. The first fraction (0·6 g), b.p. 97–104°, after purification by gas chromatography, gave 0·39 g (4·5%) of XIXa, 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 106–107°.[44] Preparative gas chromatography of the second fraction (0·75 g), b.p. 142–153°, afforded XXIa (R″ = Ac), n_D^{20} 1·4030,[47] in 4% yield (0·52 g). The third fraction (7·06 g, 54·3%), b.p. 159–165°, consisted of XVIIa, n_D^{20} 1·4214 (yield 53·4%), and traces (0·9%) of XVIIIa; both diethers were identical to the corresponding synthetic products (see above). The fourth fraction, b.p. 115–122° at 38 mm, was XXIIIa (3·7 g, 20·7%), $n_D^{21.5}$ 1·4182.

From the $NaHCO_3$ washings, upon acidification, extraction with ether, drying of the ether layer and evaporation of solvent and acetic acid, there was obtained 0·12 g (1·2%) of XXa, *p*-bromophenacyl ester, m.p. and mixed m.p. 75°.[44]

2-Propoxy-1-propanol (XVIb)

(a) *Preparation.* This alcohol was synthesized from α-propoxypropionic acid, through the corresponding ethyl ester and reduction with LAH. α-Propoxypropionic acid was prepared by reaction of 1-propanol and sodium with α-chloropropionic acid, according to the procedure described for the synthesis of ethoxyacetic acid.[48] The acid was obtained in 79·6% yield, b.p. 105° at 15 mm, n_D^{22} 1·4180 (lit. b.p. 105° at 17 mm,[49] 132° at 26 mm[50]). (Found: C, 54·2; H, 9·2. Calc. for $C_6H_{12}O_3$: C, 54·5; H, 9·1%.) *Ethyl α-propoxypropionate* was prepared from the acid and EtOH, in the presence of HCl, as reported for ethyl ethoxyacetate;[48] yield 68%, b.p. 68·5° at 20 mm and 80° at 31 mm, n_D^{22} 1·4050. (Found: C, 59·8; H, 10·1. $C_8H_{16}O_3$ requires: C, 60·0; H, 10·1%.) This ester (24·6 g, 0·154 mole) in 65 ml anh. ether was reduced with 6 g LAH in 150–200 ml anh. ether, in the usual way. Fractional distillation afforded 14·8 g (81·5%) of XVIb, b.p. 66° at 26 mm, 80° at 50 mm or 150·5° at 760 mm, n_D^{24} 1·4140 (lit.[51] b.p. 150·5–151° at 730 mm). (Found: C, 60·8; H, 11·9. Calc. for $C_6H_{14}O_2$: C, 61·0; H, 11·9%.)

(b) *Synthesis of reaction products. 2-Ethyl-4-methyl-1,3-dioxolane* (XVIIb). This cyclic acetal, b.p. 117·5° at 760 mm, n_D^{21} 1·4043 (lit. b.p. 114–117°,[52] 117·5°,[53] n_D^{20} 1·4048[53]), was prepared in 50%

[43] M. J. Astle, J. A. Zaslowsky and P. G. Lafyatis, *Ind. Eng. Chem.* **46**, 787 (1954).

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[44] R. L. Shriner, R. C. Fuson and D. Y. Curtin, *The Systematic Identification of Organic Compounds* 5th Edition. J. Wiley, New York (1964).

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[48] C. R. Noller and J. J. Gordon, *Org. Syntheses* **Coll Vol. 2**, 260 (1948).

[49] Z. Rodewald and E. Plazek, *Rocz. Chem.* **15**, 81 (1935); *Chem. Abstr.* **29**, 7281 (1935).

[50] B. Tchoubar and M. Z. Welvart, *Bull. Soc. Chim. Fr.* 959 (1948).

[51] H. L. Cox, W. L. Nelson and L. H. Cretcher, *J. Amer. Chem. Soc.* **49**, 1080 (1927).

[52] E. Augdahl and O. Hassel, *Acta Chem. Scand.* **9**, 172 (1955).

[53] A. Noshay and C. Price, *J. Org. Chem.* **23**, 647 (1958).

yield from 1,2-propanediol, propionaldehyde and Amberlite IR-120 (acid form), by the method of Astle *et al.* (procedure C).[43] With 2,4-dinitrophenylhydrazine in acid solution[40] it gives the 2,4-dinitrophenylhydrazone of propionaldehyde, m.p. and mixed m.p. 154–155°.[44]

2-Propoxy-1-propanol acetate (XXIIIb). Compound XVIb (5·9 g, 0·05 mole) and 20 ml glacial AcOH were esterified as described above for 2-pentyloxyethanol acetate, to give 7·2 g (90%) *2-propoxy-1-propanol acetate* (XXIIIb), b.p. 80° at 20 mm, n_D^{25} 1·4030. (Found: C, 59·8; H, 10·1. $C_8H_{16}O_3$ requires: C, 60·0; H, 10·1%.)

Acetoxy-2-propanone (XXIIb, R″ = Ac). This compound, b.p. 74–75·5° at 18 mm, n_D^{20} 1·4152, was prepared by lead tetra-acetate oxidation of acetone in benzene.[25] Its 2,4-dinitrophenylhydrazone melted at 115°.[25]

(c) *Oxidation.* The reaction between 7·08 g (0·06 mole) XVIb and 27·9 g (0·06 mole + 5% excess) $Pb(OAc)_4$ in 100 ml dry benzene, and in the presence of 6·3 g (0·06 mole + 5% excess) $CaCO_3$, was completed in 30 min. Formaldehyde (LIII), which was evolved during the oxidation, was detected by the colour reaction with chromotropic acid (1,8-dihydroxynaphthalene-3,6-disulphonic acid).[54]

Fractional distillation of the neutral benzene–ether extract gave the following products: In the low boiling ether and ether–benzene fractions, LV (5%) and XIXb (4·5%) were detected by gas-chromatographic separation and identified by comparison with respective reference compounds. The fraction boiling at 80–110° was further separated by gas chromatography to give 70 mg (about 2%) XXIb (R″ = H) and 0·52 g (7·5 %) XVIIb. The fraction boiling at 110–119° was redistilled and furnished a further 3·0 g (43%) of XVIIb, b.p. 112–118°, n_D^{21} 1·4040, 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. (with the derivative of propionaldehyde) 154–155°;[44] the total yield of XVIIb is therefore 50·5%. Gas chromatography of the fraction, b.p. 95–105° at 40 mm, afforded 0·15 g (2·2%) of XXIIb, (R″ = Ac), 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 114–115°,[25] and 1·39 g (14·4%) of XXIIIb, n_D^{25} 1·4038.

2-Benzyloxyethanol (XVIc)

(a) *Preparation.* This alcohol, b.p. 132–135° at 15 mm, n_D^{20} 1·5227 (lit. b.p. 138° at 15 mm,[55] 135° at 13 mm,[56] n_D^{20} 1·5217[56]), was obtained in 51·6% yield from ethylene glycol, benzyl chloride and solium.[55]

(b) *Synthesis of reaction products—2-Phenyl-1,3-dioxolane* (XVIIc). This cyclic acetal, b.p. 129° at 25 mm, n_D^{18} 1·5283 (lit. b.p. 129° at 25 mm,[57] 106–107° at 11 mm,[58] n_D^{18} 1·5285,[57] n_D^{20} 1·5270[58]), was prepared from benzaldehyde and ethylene glycol in the presence of Amberlite IR-120 (acid form), in 73% yield, according to Astle *et al.* (procedure C).[43] With 2,4-dinitrophenylhydrazine in acid solution[40] it gives the 2,4-dinitrophenylhydrazone of benzaldehyde, m.p. and mixed m.p. 236–237°.[44]

2-Benzyloxyethanol acetate (XXIIIc). Compound XVIc (7·6 g, 0·05 mole), 20 ml glacial AcOH and 1 g *p*-toluenesulphonic acid, treated as described above (see 2-pentyloxyethanol acetate), afforded 8 g (82·5%) of *2-benzyloxyethanol acetate* (XXIIIc), b.p. 140–142° at 15 mm, n_D^{25} 1·4968. (Found: C, 67·8; H, 7·4. $C_{11}H_{14}O_3$ requires: C, 68·0; H, 7·3%.)

(c) *Oxidation.* Compound XVIc (15·2 g, 0·1 mole) in 150 ml dry benzene was oxidized with 46·5 g (0·1 mole + 5% excess) $Pb(OAc)_4$, in the presence of 10·5 g (0·1 mole + 5% excess) anh. $CaCO_3$. The reaction was completed after refluxing for 30 min.

The neutral benzene–ether extract was subjected to fractional distillation. The first fraction (0·56 g, 5·3%), b.p. 75–82° at 25 mm, was XIXc, 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 236–237°.[44] The second fraction, b.p. 100–120° at 25 mm, was purified by gas chromatography to give 0·36 g (2·4%) of XXIc (R″ = Ac), n_D^{20} 1·5238.[47] The third fraction (8 g, 53·3%), b.p. 122–125° at 25 mm, consisted of XVIIc, n_D^{20} 1·5269, 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 236–237°.[44] The fourth fraction, b.p. 135–142° at 15 mm, was redistilled to give 2·33 g (12%) of XXIIIc, b.p. 139–142° at 15 mm, n_D^{25} 1·4970.

[54] J. Mitchell, Jr., in *Organic Analysis* Vol. I, pp. 287–288 (and Refs therein). Interscience, New York (1953).

[55] G. M. Bennett, *J. Chem. Soc.* **127**, 1277 (1925).

[56] E. L. Eliel, V. G. Badding and M. N. Rerick, *J. Amer. Chem. Soc.* **84**, 2371 (1962); see also J. D. Genzer, C. P. Huttrer and G. C. van Wessem, *Ibid.* **73**, 3159 (1951).

[57] P. Mastagli, Z. Zafiriadis and G. Lagrange, *C.R. Acad. Sci. Paris* **237**, 187 (1953).

[58] A. Rieche, E. Schmitz and E. Beyer, *Chem. Ber.* **91**, 1935 (1958).

From the $NaHCO_3$ washings, upon acidification, extraction with ether, drying of the ether layer and evaporation of the solvent and acetic acid, there was obtained 0·26 g (2·1%) of recrystallized XXc, m.p. and mixed m.p. 120–121°.[44]

4-Ethoxy-1-butanol (XXIV)

(a) *Preparation.* This alcohol, b.p. 180–181° at 756 mm, n_D^{20} 1·4250 (lit. b.p. 180–181,[59] 72° at 8 mm,[60] 76–80° at 14 mm,[61] n_D^{20} 1·4253,[59] 1·4229,[60] 1·4242[61]), was obtained from 1,4-butanediol, ethyl bromide and sodium in 56% yield, according to the procedure of Van Duzee and Adkins.[62]

(b) *Synthesis of reaction products—2-Ethoxytetrahydrofuran* (XXV). This cyclic acetal was prepared from tetrahydrofuran and ethanol, in the presence of t-butyl peroxide and CuCl (as catalyst), as reported by Lawesson and Berglund,[63] yield 30%, b.p. 125–126°, n_D^{20} 1·4147 (lit.[63] b.p. 125°, n_D^{20} 1·4149). (Found: C, 62·0; H, 10·6. Calc. for $C_6H_{12}O_2$: C, 62·0; H, 10·4%.) When treated with 2,4-dinitrophenylhydrazine in acid solution[40] it gives the 2,4-dinitrophenylhydrazone of XXVI, m.p. 116–118° (EtOH—H_2O) (lit. m.p. 118°,[64] 120–122°,[65] 118–120°[66]).

4-Ethoxy-1-butanol acetate (XXVIII). Compound XXIV (5·9 g, 0·05 mole) was esterified as described for 2-pentyloxyethanol acetate, to give 7·2 g (90%) of XXVIII, b.p. 102–104° at 50 mm, n_D^{20} 1·4142 (lit.[59] b.p. 192–193°, n_D^{20} 1·4161).

(c) *Oxidation.* Compound XXIV (11·8 g, 0·1 mole) was oxidized as described above. Lead tetra-acetate was completely consumed after 30 min of heating under reflux.

Upon evaporation of the solvents from the neutral benzene–ether extract, the residue was subjected to fractional distillation. The first fraction (7·7 g), b.p. 100–127°, was redistilled and gave 6 g (51·7%) of XXV, b.p. 123–127°, n_D^{20} 1·4150, 2,4-dinitrophenylhydrazone, m.p. 118° (see above). Gas chromatography of the second fraction (2·6 g), b.p. 94–102° at 48 mm, afforded 0·33 g (3·8%) of XXVI. (Found: C, 54·8; H, 9·0. Calc. for $C_4H_8O_2$: C, 54·5; H, 9·2%), 2,4-dinitrophenylhydrazone, m.p. 116–118°[64–66] (see above), and 1·98 g (12·4%) of XXVIII, identical with the synthetic ester. The third fraction, b.p. at 103–107° at 4 mm, consisted (IR spectrum) of XXVII (0·21 g, 2·3%) and gave a bis-α-naphthylurethan, m.p. 196–197°, which did not depress the m.p. of an authentic sample, m.p. 198–199°.[67]

3-Butoxy-1-propanol (XXIXa)

(a) *Preparation.* This alcohol, b.p. 83–87° at 15 mm, n_D^{20} 1·4249 (lit. b.p. 78–85° at 10 mm,[68] 81–85° at 13 mm,[62] n_D^{25} 1·4238[62]), was obtained in 64% yield by the procedure of Van Duzee and Adkins.[62]

(b) *Synthesis of reaction products—2-n-Propyl-1,3-dioxan* (XXXa). 1,3-Propanediol (7·6 g, 0·1 mole) and butyraldehyde (16 g, 0·2 mole) were treated with Amberlite IR-120 (acid form) by the method of Astle *et al.* (procedure C),[42] to give 6·5 g (50%) of XXXa, b.p. 78–80° at 70 mm, $n_D^{21.5}$ 1·4247 (lit.[69] b.p. 154–157°). (Found: C, 64·3; H, 11·1. Calc. for $C_7H_{14}O_2$: C, 64·6; H, 10·8%.) With 2,4-dinitrophenylhydrazine in acid solution[40] it gives the 2,4-dinitrophenylhydrazone of butyraldehyde, m.p. and mixed m.p. 122–123°.[44]

3-Butoxy-1-propanol acetate (XXXIVa). Compound XXIXa (6·6 g, 0·05 mole) was esterified as described for 2-pentyloxyethanol acetate, to afford 7·8 g (89·7%) of *3-butoxy-1-propanol acetate*

[59] A. Dewael, *Bull. Soc. Chim. Belges* **35**, 301 (1926).
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[61] P. M. Frearson and E. S. Stern, *J. Chem. Soc.* 3062 (1958).
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[63] S. O. Lawesson and C. Berglund, *Acta Chem. Scand.* **14**, 1854 (1960); *Arkiv Kemi* **17**, 465, 475 (1961).
[64] R. Paul and S. Tchelitcheff, *Bull. Soc. Chim. Fr.* 197 (1948).
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[68] C. D. Hurd and G. W. Fowler, *J. Amer. Chem. Soc.* **61**, 249 (1933).
[69] H. Hibbert and J. A. Timm, *J. Amer. Chem. Soc.* **46**, 1283 (1924).

(XXXIVa), b.p. 90–92° at 13 mm, $n_D^{21.5}$ 1·4161. (Found: C, 61·9; H, 10·5. $C_9H_{18}O_3$ requires: C, 62·0; H, 10·4%.)

(c) *Oxidation.* The oxidation of 13·2 g (0·1 mole) of XXIXa, performed as described above, was completed in 45 min.

The neutral benzene–ether extract was subjected to fractional distillation. From the benzene fraction (boiling up to 80°), XXXIa, 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 122–123°,[44] was isolated by gas chromatography in 6·9% yield (0·5 g). Redistillation of the second fraction (4·8 g), b.p. 70–100° at 100 mm, furnished 0·63 g (5·4%) of XXXIIIa, b.p. 120–125°, n_D^{20} 1·3945[47] (identical with an authentic sample[47]), and 3·4 g (26·2%) of XXXa, b.p. 153–157°, n_D^{20} 1·4252, 2,4-dinitrophenylhydrazone, m.p. 122°[44] (see above). The third fraction (4 g), b.p. 100–115° at 25 mm, afforded on redistillation 3·48 g (20%) of XXXIVa, b.p. 90–95° at 13 mm (identical with a synthetic product; see above).

From the $NaHCO_3$ washings, upon acidification and ether extraction (as described above), there was obtained 0·12 g (1·4%) of XXXIIa, characterized by conversion to its *p*-bromophenacyl ester, m.p. and mixed m.p. 62–63°.[44]

3-*Benzyloxy*-1-*propanol* (XXIXb)

(a) *Preparation.* This alcohol, b.p. 155° at 23 mm, n_D^{21} 1·5136 (lit. b.p. 142° at 10 mm,[70] 111° at 0·5 mm,[56] n_D^{20} 1·5152[56]), was obtained in 61% yield from 1,3-propanediol, benzyl chloride and sodium.[62]

(b) *Synthesis of reaction products—2-Phenyl*-1,3-*dioxan* (XXXb). This cyclic acetal, b.p. 98–100° at 4 mm, m.p. 50° (lit. b.p. 125° at 14 mm,[71] 98–99° at 4 mm,[72] m.p. 49–51°[71]), was prepared from benzaldehyde and 1,3-propanediol, in 69·5% yield, according to Astle *et al.* (method C).[43] With 2,4-dinitrophenylhydrazine in acid solution[40] it gives the 2,4-dinitrophenylhydrazone of benzaldehyde, m.p. and mixed m.p. 237°.[44]

3-*Benzyloxy*-1-*propanol acetate* (XXXIVb). Compound XXIXb (8·3 g, 0·05 mole) was esterified as described above (see 2-pentyloxyethanol acetate) to give 9·6 g (92·2%) of 3-*benzyloxy*-1-*propanol acetate* (XXXIVb), b.p. 121–123° at 4 mm, $n_D^{22.5}$ 1·4913. (Found: C, 69·1; H, 7·8. $C_{12}H_{16}O_3$ requires: C, 69·2; H, 7·7%.)

(c) *Oxidation.* The oxidation of 16·6 g (0·1 mole) of XXIXb, carried out as described above, was completed in 45 min.

By fractional distillation of the neutral benzene–ether extract and redistillation of the fractions there was obtained: XXXIb (0·21 g, 2%), b.p. 76–80° at 25 mm, 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 236–237°;[44] XXXIIIb (0·36 g, 2·4%), b.p. 110–112° at 25 mm (identical with an authentic sample);[47] XXXb (6·6 g, 40·2%), b.p. 97–103° at 4 mm, 2,4-dinitrophenylhydrazone, m.p. 236°[44] (see above); XXXIVb (2·77 g, 13·3%), b.p. 119–124° at 4 mm (identical with a synthetic product).

From the $NaHCO_3$ washings, by the usual procedure (see above), there was obtained 0·29 g (2·4%) of XXXIIb, m.p. and mixed m.p. 121–122°.[44]

5-*Ethoxy*-1-*pentanol* (XXXV)

(a) *Preparation.* This alcohol, b.p. 98° at 14 mm, n_D^{20} 1·4290 (lit. b.p. 89–91° at 9 mm,[60] 98° at 14 mm,[73] n_D^{20} 1·4291[60]), was obtained in 46·5% yield from 1,5-pentanediol, ethyl bromide and sodium, by the usual procedure.[62]

(b) *Synthesis of reaction—2-Ethoxytetrahydropyran* (XXXVI). This cyclic acetal was prepared from EtOH, 2-chlorotetrahydropyran (b.p. 44–47° at 15 mm[74]) and sodium, according to the procedure of Van Duzee and Adkins.[58] Yield 40%, b.p. 43–44° at 13 mm, n_D^{25} 1·4236 (lit. b.p. 44° at 13 mm,[75]

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46–47° at 20 mm,[76] n_D^{27} 1·4260,[75] n_D^{20} 1·4247,[78] n_D^{25} 1·4238[77]). (Found: C, 64·4; H, 10·8. Calc. for $C_7H_{14}O_2$: C, 64·6; H, 10·8%.) With 2,4-dinitrophenylhydrazine in acid solution[40] it gives the 2,4-dinitrophenylhydrazone of XXXIX, m.p. 107° (EtOAC) (lit. m.p. 107°,[75] 106·5–107°,[76] 109° [78]).

2-(*Ethoxymethyl*)*tetrahydrofuran* (XXXVII). This diether, b.p. 98–99° at 80 mm, n_D^{21} 1·4310 (lit.[79] b.p. 149–151°), was obtained in 69% yield from tetrahydrofurfuryl alcohol, ethyl bromide and sodium, according to the usual procedure.[68] (Found: C, 64·5; H, 10·9. Calc. for $C_7H_{14}O_2$: C, 64·4; H, 10·8%.)

5-*Ethoxy*-1-*pentanol acetate* (XLI). Compound XXXV (6·6 g, 0·05 mole) was esterified as described for 2-pentyloxyethanol acetate, to give 7·8 g (89·7%) of 5-*ethoxy*-1-*pentanol acetate* (XLI), b.p. 105° at 14 mm, n_D^{21} 1·4190. (Found: C, 62·2; H, 10·4. $C_9H_{18}O_3$ requires: C, 62·0; H, 10·4%.)

(c) *Oxidation.* Compound XXXV (9·92 g, 0·075 mole) was oxidized with 34·9 g (0·075 mole + 5% excess) $Pb(OAc)_4$ in 120 ml anh. benzene, in the presence of 10 g (0·1 mole) $CaCO_3$. The reaction lasted 30 min.

The neutral benzene–ether extract was subjected to fractional distillation. Gas chromatography and redistillation of the first fraction (5 g), b.p. 70–100° at 80 mm, afforded XXXVIII in about 1–2% yield (identical with a purified commercial product, b.p. 85–86° [44]);[80] XXXVI (4·5 g, 46·2%), b.p. 42–46° at 14 mm, n_D^{25} 1·4237, 2,4-dinitrophenylhydrazone, m.p. 107–108° (see above); XXXVII (2%). The fraction boiling in the range 60–95° at 8 mm (2·5 g) was redistilled and gave 0·43 g (5·6%) of XXXIX, b.p. 64–70° at 8 mm (identical with an authentic product, b.p. 64–67° at 10 mm[81]), 2,4-dinitrophenylhydrazone, m.p. 107–108° [75,76,78] (see above), and 1·6 g (12·3%) of XLI, b.p. 92–96° at 8 mm, n_D^{21} 1·4194 (see above). The last fraction (0·11 g, 1·4%), boiling above 94° at 1 mm, consisted mainly (IR spectrum) of XL and gave a bis-α-naphthylurethan, m.p. 146–148°, which did not depress the m.p. of the same derivative of authentic 1,5-pentanediol, m.p. 146–147°.[44]

2-*Phenoxyethanol* (XLII)

(a) *Preparation.* This alcohol, b.p. 164–166° at 80 mm, n_D^{20} 1·5343 (lit. b.p. 163–166° at 80 mm,[82] 118–121° at 12 mm,[83] n_D^{20} 1·5360[83]), was obtained from ethylene chlorohydrin and phenol, in 70% yield.[82]

(b) *Synthesis of reaction products.* 1,4-*Benzodioxan* (XLIII). This cyclic diether, b.p. 99–100° at 17 mm, n_D^{21} 1·5503 (lit. b.p. 101–102° at 18 mm,[84] 212–214° [85]), was prepared from catechol and ethylene bromide in 49% yield.[85]

2-*Phenoxyethanol acetate* (XLIV). Compound XLII (6·9 g, 0·05 mole) was esterified as described above (see 2-pentyloxyethanol acetate) to give 7·6 g (84·4%) of XLIV, b.p. 142° at 17 mm, $n_D^{19.5}$ 1·5095 (lit. b.p. 257·2°,[86] 252–256°,[87] n_D^{25} 1·5083,[86] n_D^{25} 1·5045[87]).

(c) *Oxidation.* Compound XLII (13·8 g, 0·1 mole) was oxidized as described above. The reaction was completed after 5·5 hr of heating under reflux.

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[80] This cyclic compound was also present (in traces) in the higher boiling fractions, which indicates that it was probably being formed during distillation, by decomposition of (not isolated) 2-acetoxy-tetrahydropyran.[81]

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Fractional distillation of the neutral benzene–ether extract afforded two major fractions. The first fraction (2·09 g, 15·4%), b.p. 98–105° at 17 mm, was XLIII, n_D^{21} 1·5508 (see above); the second fraction (7·9 g), b.p. 132–144° at 17 mm, upon redistillation furnished 7·25 g (40·3%) of XLIV, b.p. 140–143° at 17 mm, n_D^{20} 1·5100. The dark, partly resinified solid residue (2·4 g) was not investigated; it contained probably products acetoxylated in the benzene nucleus.[7,9,11,13]

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