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REACTIONS WITH LEAD TETRAACETATE—I

OXIDATION OF SATURATED ALIPHATIC ALCOHOLS PART 1[1]

V. M. Mićović, R. I. Mamuzić, D. Jeremić and M. Lj. Mihailović[2]
Department of Chemistry, Faculty of Sciences
and
Institute of Chemistry, Technology and Metallurgy, Belgrade, Yugoslavia

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Abstract—When oxidized with lead tetraacetate 1-heptanol and 1-octanol undergo cyclization to give as major products the corresponding 2-alkyltetrahydrofurans, accompanied by a small amount of the isomeric tetrahydropyran derivatives. Secondary aliphatic alcohols, under similar conditions, are converted to a mixture of *cis* and *trans* 2,5-dialkyltetrahydrofurans.

In 1933, Criegee *et al.*[3] reported that the first members of simple aliphatic alcohols (methanol, ethanol, 2-propanol)[4] were oxidized with lead tetraacetate, in the absence of solvent, to the corresponding carbonyl compounds. However, this reaction remained unnoticed until 1952, when Mićović and Mihailović[5] applied the lead tetracetate reaction (in benzene solution) for the preparation of the sensitive and at that time difficultly obtainable 2-, 3- and 4-pyridinecarboxaldehydes from the corresponding alcohols. Beginning from 1959 several papers appeared which showed that various steroid alcohols could react with lead tetraacetate in non-polar solvents to give tetrahydrofuran[6–8] and tetrahydropyran derivatives,[9,10] cyclization occurring when the position of and the distance between the reacting hydroxyl group and the σ- or ε-methyl, methylene or methine groups were favourable to ring closure. In these reactions the corresponding carbonyl compounds were obtained only as by-products, except in the case of 11β-hydroxysteroids, which were oxidized mainly to the oxo derivatives (the cyclic ethers being formed, if any, in low yields).[8,10]

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[1] Preliminary communication: V. M. Mićović, R. I. Mamuzić, D. Jeremić and M. Lj. Mihailović, *Tetrahedron Letters* No. 29, 2091 (1963).

[2] To whom enquiries should be made. Full address: Department of Chemistry, Faculty of Sciences, Post Box 550, Studentski trg 16, Belgrade, Yugoslavia.

[3] R. Criegee, L. Kraft and B. Rank, *Liebigs Ann.* **507**, 159 (1933).

[4] Results of detailed studies on the oxidation of alcohols of low molecular weight will be the subject of a forthcoming publication.

[5] V. M. Mićović and M. Lj. Mihailović, *Rec. Trav. Chim. Pays-Bas* **71**, 970 (1952).

[6] G. Cainelli, M. Lj. Mihailović, D. Arigoni and O. Jeger, *Helv. Chim. Acta* **42**, 1124 (1959); J. Kalvoda, G. Anner, D. Arigoni, K. Heusler, H. Immer, O. Jeger, M. Lj. Mihailović, K. Schaffner and A. Wettstein, *Helv. Chim. Acta* **44**, 186 (1961); G. Cainelli, B. Kamber, J. Keller, M. Lj. Mihailović, D. Arigoni and O. Jeger, *Helv. Chim. Acta* **44**, 518 (1961), and references therein. For the oxidation of an acyclic alcohol see C. F. Seidel, D. Felix, A. Eschenmoser, K. Biemann, E. Palluy and M. Stoll, *Helv. Chim. Acta* **44**, 598 (1961).

[7] A. Bowers, E. Denot, L. C. Ibanez, M. E. Cabezas and H. J. Ringold, *J. Org. Chem.* **27**, 1862 (1962).

[8] K. Heusler, J. Kalvoda, G. Anner and A. Wettstein, *Helv. Chim. Acta* **46**, 352 (1963), and subsequent papers.

[9] H. Immer, M. Lj. Mihailović, K. Schaffner, D. Arigoni and O. Jeger, *Experientia* **16**, 530 (1960); *Helv. Chim. Acta* **45**, 753 (1962).

[10] A. Bowers and E. Denot, *J. Amer. Chem. Soc.* **82**, 4956 (1960).

While in hydroxysteroids one or both of the reacting centers are geometrically fixed, this is not the case in acyclic alcohols. Because of free rotation, these alcohols can attain a large number of conformations, either favourable or unfavourable to the cyclization reaction. Moreover, some of the possible conformations could allow not only ring closure to five-membered or/and six-membered heterocycles, but the formation of lower and higher cyclic ethers as well.

For that reason in the present work the action of lead tetraacetate on saturated aliphatic alcohols with unbranched chains containing seven to nine carbon atoms was investigated. These alcohols, i.e. 1-heptanol, 1-octanol, 2-octanol and 5-nonanol, reacted more or less vigorously[11] with the tetravalent lead reagent, in boiling benzene, to give as major products pleasant smelling, volatile compounds, which did not contain carbonyl, hydroxyl or acetoxy groups, and which corresponded to the general formula $C_nH_{2n}O$. Since for one mole of alcohol at least one mole of lead tetraacetate was consumed in the course of the reaction, the lead reagent being converted to lead diacetate and acetic acid, it could be inferred that these oxidations also consisted in a formal dehydrogenation of the starting alcohol.

If one accepts Criegee's reaction course[12–14] of the lead tetraacetate oxidation of low molecular and aromatic alcohols,[3,5] phenols,[13,15] hydroquinones,[13,15] and glycols[3,12,14,15] to carbonyl compounds (without giving preference as to the actual mechanism—free radical or polar—of the reaction, this being irrelevant for the present discussion), the first step in the observed reaction of aliphatic alcohols would consist in the alcoholysis of the tetravalent lead compound with removal of the hydroxyl hydrogen. The second hydrogen atom, however, instead of being eliminated from the carbon atom bearing the hydroxyl group (as in the case of low molecular alcohols[3] and alcohols with aromatic character,[3,5,15] which are dehydrogenated to carbonyl compounds), would have to be removed from another carbon atom, belonging to a methylene (or methyl) group.

Dehydrogenation of this type can be inter- or intramolecular. In the first case one would expect open-chain ethers containing hydroxyl (acetate) or carbonyl groups (I).[16] However, there is no reason why such a reaction should stop after the etherification of two alcohol molecules and, by using an excess of lead tetraacetate, "polymerized" products could be formed,[17] with the further possibility of ring closure

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[11] With primary alcohols the reaction was exothermic and heating had to be discontinued for a while, whereas with secondary alcohols the oxidation was much less vigorous. With a 1:1 molar ratio of lead tetraacetate to alcohol the oxidation of primary alcohols was completed after about one hour, while secondary alcohols reacted more slowly, about three hours being needed for the complete consumption of the tetravalent lead reagent.

[12] R. Criegee, E. Höger, G. Huber, P. Kruck, F. Marktscheffel and H. Schellenberger, *Liebigs Ann.* **599**, 81, 99 (1956).

[13] R. Criegee, *Angew. Chem.* **70**, 173 (1958).

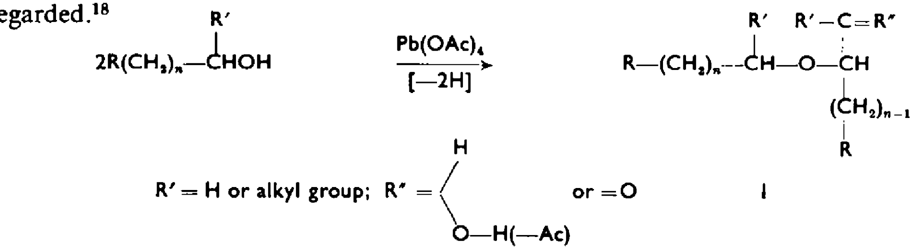
[14] J. P. Cordner and K. H. Pausacker, *J. Chem. Soc.* 102 (1953).

[15] R. Criegee in *Neuere Methoden der präparativen organischen Chemie*, pp. 21–38. Verlag Chemie, Berlin (1944).

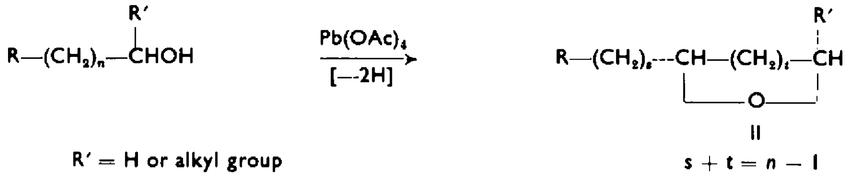
[16] A similar intermolecular substitution reaction involving a solvent molecule was observed when 3α-hydroxy-17β-acetoxy-5β-androstane was heated with lead tetraacetate in cyclohexane solution;[9] the yield of the open-chain ether, 3α-cyclohexyloxy-steroid, however, was low (about 4%), and other products were also formed.

[17] It is possible that such or similar products are present in the non-distillable viscous residue, which was obtained in all the studied cases, particularly when excess of lead tetraacetate was used.

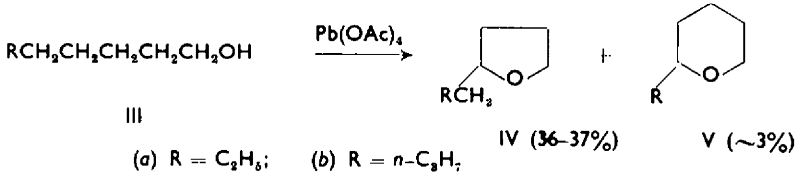
reactions. For reasons already mentioned (relatively low boiling points, absence of reactive functional groups), however, structures of type (I) for the major oxidation products of the investigated primary and secondary alcohols could be *a priori* disregarded.[18]



In the second case, intramolecular dehydrogenation, the lead tetraacetate oxidation would afford *cyclic ethers* (II), not containing other functional groups. Since such heterocyclic compounds corresponded in composition to the oxidation products of the investigated aliphatic alcohols, it was necessary to determine which cyclic ethers were obtained, i.e. the size of the oxide ring.



According to IR spectra, the major reaction products from 1-heptanol (IIIa) and 1-octanol (IIIb) were either tetrahydrofuran or tetrahydropyran derivatives.[19] By comparison with authentic samples (IR spectra, boiling points, refractive indices, retention times), synthesized by Raney nickel catalyzed hydrogenation of the corresponding substituted furans,[20,21] the obtained ethers proved to be 2-n-propyltetrahydrofuran (IVa) and 2-n-butyltetrahydrofuran (IVb), respectively. Their yields amounted approximately to 36–37%. In addition, by careful gas-chromatographic separation of the oxide fractions, small amounts of the isomeric 2-alkyltetrahydropyrans (V) were isolated, in yields not exceeding 3%. These compounds were identified by comparison of their retention times and IR spectra with those of authentic 2-ethyltetrahydropyran (V*a*) and 2-n-propyltetrahydropyran (V*b*).[21,22]



Secondary alcohols, 2-octanol (VIa) and 5-nonanol (VIb), after oxidation with

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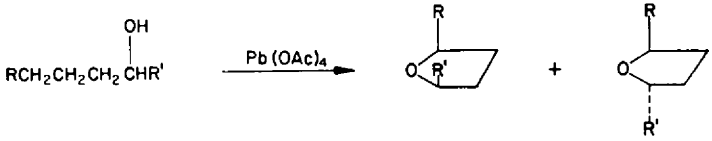
[18] Open-chain ethers corresponding to (I) are actually formed in small amounts, as observed in the case of the lead tetraacetate oxidation of low molecular aliphatic alcohols (to be published).

[19] In the reaction between lead tetraacetate and low molecular aliphatic alcohols, i.e. ethanol, 1-propanol, 2-propanol and 2-butanol, which can give only three- and/or four-membered cyclic ethers, the corresponding epoxides or trimethylene oxides were not formed (to be published).

[20] R. Paul, *Bull. Soc. Chim. Fr.* [5] **2**, 2227 (1935); *C.R. Acad. Sci., Paris* **200**, 1481 (1935); *Bull. Soc. Chim. Fr.* [5] **5**, 1053 (1938); cf. also *Bull. Soc. Chim. Fr.* 158 (1947).

[21] R. Paul, *C.R. Acad. Sci., Paris* **206**, 1028 (1938); *Bull. Soc. Chim. Fr.* [5] **6**, 331 (1939).

[22] R. Paul, *C.R. Acad. Sci., Paris* **198**, 1246 (1934); *Bull. Soc. Chim. Fr.* [5] **2**, 311 (1935).

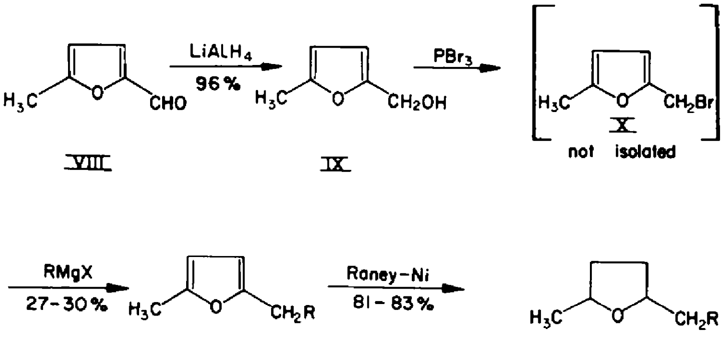


VI cis VII trans

(a) R = n-C_3H_7; R′ = CH_3 (b) R = CH_3 ; R′ = n-C_4H_9

lead tetraacetate, furnished also oxide fractions, which were separated by gas chromatography in two components. In both cases one of the isomeric cyclic ethers (the "A" stereoisomer, with lower boiling point and shorter retention time) proved to be identical with the 2,5-dialkyltetrahydrofuran prepared by Raney nickel hydrogenation of the corresponding furan derivative. The other cyclic ether (the "B" stereoisomer, with higher boiling point and longer retention time) in the oxide fraction was not the isomeric tetrahydropyran derivative,[23] but, on the basis of its IR spectrum, appeared to be the second geometrical isomer of the corresponding 2,5-dialkyltetrahydrofuran.[24] In the case of 2-octanol (VIa) the total yield of *cis* and *trans* 2-methyl-5-n-propyltetrahydrofuran (VIIa) amounted to 30%, the ratio of geometrical isomers (A:B) being 40:60. 5-Nonanol (VIb) afforded 20% of stereoisomeric 2-n-butyl-5-methyltetrahydrofurans (VIIb), the ratio of "A" to "B" isomer being 45:55. From these results it appears that cyclization of secondary aliphatic alcohols by means of lead tetraacetate is not stereoselective.

The hitherto unreported 2-methyl-5-n-propyltetrahydrofuran (VIIa) and 2-n-butyl-5-methyltetrahydrofuran (VIIb) were prepared from 5-methylfurfural (VIII), by the following sequence of reactions:



VIII IX X not isolated

XI VII

(a) $R=CH_3CH_2$ (b) $R=CH_3CH_2CH_2$

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[23] This was established by synthesizing the isomeric tetrahydropyrans, which could have been formed by the lead tetraacetate cyclization of 2-octanol (VIa) and 5-nonanol (VIb), and by comparing their physical properties with those of the isolated "B" cyclic ethers. 2-Ethyl-6-methyltetrahydropyran (possible product from 2-octanol) was prepared according to K. Alder, H. Offermanns and E. Rüden, *Ber. Dtsch. Chem. Ges.* **74B,** 905 (1941), and 2-n-butyltetrahydropyran (possible product from 5-nonanol) was obtained by the procedure described by R. Paul.[21,22]

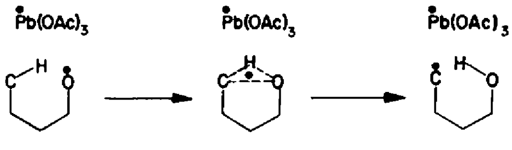
[24] The IR spectra of the "A" and "B" cyclic ethers are very similar. They differ only in details and both have characteristic absorption bands of the tetrahydrofuran ring and bands showing that the relative concentration of the methyl groups is greater than in monosubstituted cyclic ethers, thus pointing to the presence of disubstituted tetrahydrofurans. The small differences are attributed to the different geometry of the "A" and "B" compounds. Therefore, it appears that the cyclic ethers "B" are geometrical isomers of the 2,5-dialkyltetrahydrofurans "A".

It should be noted that according to gas chromatography the Raney nickel hydrogenation of 2-alkyl-5-methylfurans (XI) gave only one stereoisomeric form of the corresponding tetrahydrofurans (VII), which was identical to the configuration of the "A" cyclic ethers (with lower boiling points and shorter retention times) obtained from 2-octanol (VIa) and 5-nonanol (VIb), respectively. Since it is improbable that hydrogenation of the furan ring of the 2,5-dialkylfurans (XI) in the presence of Raney nickel would afford only the *trans* product, and since it was recently shown by synthesis[25] and thermodynamic treatment[26] that the lower-boiling 1,3-dimethylcyclopentane had the *cis*-configuration and the higher-boiling isomer the *trans*-configuration, then, by analogy, one could tentatively assign the *cis*-configuration to the 2,5-dialkyltetrahydrofurans ("A" cyclic ethers) with lower boiling point (*cis*-VIIa and *cis*-VIIb) and the *trans*-configuration to the 2,5-dialkyltetrahydrofurans ("B" cyclic ethers) with higher boiling point (*trans*-VIIa and *trans*-VIIb).

Other products of the oxidation of primary and secondary aliphatic alcohols were the corresponding carbonyl compounds, isolated in low yields (2–5%), the acetates of the starting alcohols, and high-boiling or partially resinified, unidentified material. In addition, a certain amount of starting alcohol was always recovered unchanged, even when an excess of lead tetraacetate was used.

By increasing the amount of oxidizing agent to 1·5 and 2 moles (per mole of alcohol), the time required for complete consumption of lead tetraacetate was considerably increased, but the yields of cyclic ethers were not noticeably improved, in spite of the fact that in these cases less starting alcohol was recovered after the reaction. Moreover, by increasing the quantity of oxidizing agent, the amount of high-boiling and polymerized products became larger. Such a behaviour indicates that lead tetraacetate, when in excess, does not react only with the starting alcohol, but also with the cyclic ethers formed during the reaction, thus causing a decrease in their yields.

From the results obtained it can be concluded that cyclization of monohydroxylic alcohols by means of lead tetraacetate is not limited to hydroxy compounds with geometrically fixed centers (as in the case of steroid alcohols), and that open-chain alcohols can also attain a conformation favourable to the formation of a transition state (XIII) in which a hydrogen atom is transferred from the δ- or ε-carbon atom (XII) to the hydroxyl oxygen radical (XIV).[27]



XII XIII XIV

Since cyclization of saturated aliphatic alcohols by means of lead tetraacetate

[25] S. F. Birch and R. A. Dean, *J. Chem. Soc.* 2477 (1953); *Liebigs Ann.* **585**, 234 (1954).

[26] J. N. Haresnape, *Chem. & Ind.* 1091 (1953).

[27] The mechanism of intramolecular lead tetraacetate radical reactions was discussed by K. Heusler and J. Kalvoda in a paper presented at the XIX International Congress of Pure and Applied Chemistry, London, July 10–17, 1963; K. Heusler and J. Kalvoda, *Angew. Chem.*, in press. See also C. Meystre, K. Heusler, J. Kalvoda, P. Wieland, G. Anner and A. Wettstein, *Experientia* **17**, 475 (1961); D. H. R. Barton, J. M. Beaton, L. E. Geller and M. M. Pechet, *J. Amer. Chem. Soc.* **82**, 2640 (1960).

provides a direct and useful route to 2-alkyltetrahydrofurans and 2,5-dialkyltetrahydrofurans, the application of this reaction to other aliphatic alcohols is being the subject of further investigations.

EXPERIMENTAL

Gas chromatography was carried out on a Perkin-Elmer instrument model 154-D, equipped with thermistor detectors. The columns (2 m × 4 mm and 4 m × 6 mm) consisted of polypropylene glycol adsorbed on Chromosorb and were operated at a temp of 80° with H_2 (100 ml/min) as carrier gas. IR spectra were recorded with a Perkin-Elmer IR spectrophotometer model 13-U. Fractional distillations were carried out through a spiral Jansen column (inner diameter of the spiral 0·8 cm, length of the spiral 3 m). B.ps and m.ps are uncorrected.

Starting Products

Lead tetraacetate[28,29] was dried *in vacuo* (P_2O_5 and KOH). Its purity was determined iodometrically.[30] 1-Heptanol, 1-octanol and 2-octanol were commercial products; 5-nonanol was prepared from n-butylmagnesium bromide and ethyl formate.[31] Before use, the alcohols were dried (K_2CO_3) and fractionated. Their purity was verified by means of gas chromatography. Thiophene-free benzene, dried over Na, was used as solvent.

Lead Tetraacetate Oxidations

General procedure. In a round-bottomed flask, fitted with a reflux condenser and sealed stirrer, were placed 500 ml benzene, 50 g starting alcohol and the calculated quantity (+10% excess) of lead tetraacetate (based on the pure product). The mixture was stirred and heated to boiling until a more or less vigorous reaction (depending upon the alcohol used) set in. Heating was interrupted as long as the mixture boiled for itself (5–7 min) and was resumed after the exothermic reaction had subsided. After the tetravalent lead had been completely consumed (negative starch-iodide test) and converted to lead diacetate, refluxing was stopped and the flask cooled to room temp.

The reaction mixture was treated with dry ether (120 ml) and allowed to stand for 1–2 hrs at 5°. The solution was decanted, the residue in the flask treated with 100 ml benzene and the mixture heated to reflux for 5 min (with stirring). After cooling to 10°, the mixture was filtered, the precipitate of lead diacetate returned to the flask and the extraction with benzene repeated. The combined filtrates were diluted with ether (200 ml) and washed successively with water, 10% Na_2CO_3 aq and water (until neutral). After drying (K_2CO_3), the ether and benzene were removed by fractional distillation and the liquid residue (yellow to brown) was subjected to steam distillation, until about 3 l. distillate had passed over. The small amount of viscous, oily liquid (partly resinified) remaining in the flask was not further investigated. The aqueous distillate was extracted with ether, the ethereal layer dried (Na_2SO_4) and, after evaporation of the ether, the residue fractionated under atm. press.

Two fractions were obtained, the first (lower-boiling) containing the cyclic ethers and the second (higher-boiling) containing the unreacted alcohol and its acetate. The dark-brown residue (high-boiling and probably polymerized products) was not further investigated. The first fraction was distilled through the fractionating column 2–3 times, until the product which passed over boiled in a relatively narrow temp range. For elementary microanalysis and gas chromatography the fraction thus purified was further distilled over KOH, Na and finally over $LiAlH_4$. The identification of the cyclic ethers in this fraction was carried out, after separation by means of gas chromatography, by recording the IR spectra of the components and comparing them with spectra of the corresponding products of known structure.

The second fraction was redistilled, and the unreacted alcohol identified by conversion to its phenylurethan. In some cases, after separation by gas chromatography, the alcohol and its acetate were identified by comparing their IR spectra with the spectra of authentic products.

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[28] J. C. Bailar, Jr., *Inorganic Syntheses* **1**, 47 (1939).

[29] The reagent without lead chloride was used in most reactions, although lead tetraacetate contaminated with the chloride[28] gave similar yields of reaction products.

[30] R. Criegee, *Ber. Dtsch. Chem. Ges.* **64**, 260 (1931); see also M. S. Kharasch, H. N. Friedlander and W. H. Urry, *J. Org. Chem.* **16**, 533 (1951).

[31] G. H. Coleman and D. Craig, *Org. Syntheses*, Coll. Vol. 2, 179 (1948).

In both fractions the carbonyl compound (corresponding to the starting alcohol) was quantitatively determined and characterized by conversion to the corresponding 2,4-dinitrophenylhydrazone.[32]

Primary aliphatic alcohols

1-*Heptanol* (IIIa). From 50 g (0·43 mole) of 1-heptanol and 230·5 g (0·43 mole + 10%) of 91% lead tetraacetate (molar ratio 1:1), after 60–75 min of heating and by working up the mixture as described above, there was obtained 19·8 g (40·3% yield) of cyclic ethers, b.p. 130–136° at 760 mm. (Found: C, 73·3; H, 12·1. Calc. for $C_7H_{14}O$: C, 73·6; H, 12·3%). This mixture consisted of 2-n-propyltetrahydrofuran (IVa) (37·1% yield), b.p. 132–133° at 760 mm,[33] n_D^{20} 1·4220,[34] and 2-ethyltetrahydropyran (Va) (3·2% yield), n_D^{20} 1·4266[35] (ratio of isomers 92:8).

The second fraction afforded on redistillation 9·8 g of products, b.p. 174–177°, containing unchanged 1-heptanol (IIIa) (phenylurethan, m.p. and mixed m.p. 64°[36]) and 1-heptylacetate. From both fractions 1-heptanal, in the form of its 2,4-dinitrophenylhydrazone (m.p. and mixed m.p. 107°[36]), was isolated in 2·2% yield. The residue (not investigated) amounted to 12 g.

1-*Octanol* (IIIb). (a) By using a molar ratio 1:1, 50 g (0·38 mole) of 1-octanol and 206·3 g (0·38 mole + 10% excess) of 91% lead tetraacetate, after heating for 75 min, furnished 19·4 g (39·4% yield) of cyclic ethers, b.p. 155–162° at 760 mm. (Found: C, 74·6; H, 12·4. Calc. for $C_8H_{16}O$: C, 74·9; H, 12·6%). This mixture, after separation by gas chromatography, gave 2-n-butyltetrahydrofuran (IVb) (36·6% yield), b.p. 159–160° at 760 mm,[33] n_D^{20} 1·4270,[37] and 2-n-propyltetrahydropyran (Vb) (2·8% yield), n_D^{20} 1·4316[38] (ratio of isomers 93:7).

From the second fraction, on redistillation, there was obtained 9·3 g of products, b.p. 192–196°, which contained unchanged 1-octanol (IIIb) (phenylurethan, m.p. and mixed m.p. 73–74°[36]) and 1-octyl acetate. From both fractions 1-octanol, in the form of its 2,4-dinitrophenylhydrazone (m.p. and mixed m.p. 105°[36]), was obtained in a 2% yield. The residue (not investigated) amounted to 8·4 g.

(b) The same reaction was repeated by using 1·5 mole of lead tetraacetate per mole of 1-octanol. The mixture had to be heated under reflux for 2 hr and 30 min. The yield of cyclic ethers, b.p. 156–161° at 760 mm, was 20·5 g (41·6% yield), and the fraction containing 1-octanol and 1-octyl acetate, b.p. 192–198°, amounted to 8·7 g, residue 9 g.

(c) With 2 moles of lead tetraacetate for one mole of 1-octanol the reaction lasted 5 hr and 20 min, and afforded 16·5 g (33·5% yield) of cyclic ethers, b.p. 155–162° at 760 mm, and 7·6 g alcohol + acetate, b.p. 192–196°, residue 12·2 g.

Secondary aliphatic alcohols

2-*Octanol* (VIa). (a) This alcohol (50 g, 0·38 mole) and 203·3 g (0·38 mole + 10%) of 92% lead tetraacetate (molar ratio 1:1) did not react as vigorously as the primary alcohols, and it was not necessary to interrupt heating of the reaction mixture; 3 hr-refluxing was needed to complete the reaction.

The first fraction, after 2 fractional distillations, gave 14·4 g (29·2% yield) of cyclic ethers, b.p. 140–146° at 768 mm, $n_D^{20.5}$ 1·4218. (Found: C, 74·6; H, 12·4. Calc. for $C_8H_{16}O$: C, 74·9; H,

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[32] E. Müller (Editor-in-chief), *Methoden der organischen Chemie* (Houben-Weyl) Vol. II (Fourth Edition), p. 457. Georg Thieme Verlag, Stuttgart (1953).

[33] B.p. micro-determination was carried out according to the modified (capillary) Emich method. See N. D. Cheronis, *Micro- and Semimicro Methods, Technique of Organic Chemistry* (A. Weissberger, Editor-in-chief) Vol. VI, pp. 190–192. Interscience, New York (1954).

[34] 2-n-Propyltetrahydrofuran, prepared by Raney Ni hydrogenation of 2-n-propylfuran,[20,21] had b.p. 131–132·5° at 748 mm, $n_D^{20.5}$ 1·4222.

[35] Authentic 2-ethyltetrahydropyran[21,22] had b.p. 126–127° at 752 mm, n_D^{20} 1·4268.

[36] *cf.* A. I. Vogel, *Practical Organic Chemistry* (Third Edition). Longmans Green, London (1961); R. L. Shriner, R. C. Fuson and D. Y. Curtin, *The Systematic Identification of Organic Compounds* (Fourth Edition). J. Wiley, New York (1957); T. Malkin and T. C. Tranter, *J. Chem. Soc.* 1178 (1951).

[37] 2-n-Butyltetrahydrofuran, prepared by Raney Ni hydrogenation of 2-n-butylfuran,[20,21] had b.p. 157·5–158° at 746 mm, $n_D^{20.5}$ 1·4266.

[38] Authentic 2-n-propyltetrahydropyran[21,22] had b.p. 151–152° at 756 mm, n_D^{20} 1·4310.

12·6%). This mixture of cyclic ethers was separated by gas chromatography into *2-methyl-5-n-propyltetrahydrofuran* "A" (presumably *cis*-VIIa), b.p. 141–142° at 768 mm,[34] $n_{\mathrm{D}}^{20\cdot5}$ 1·4200 (Found: C, 74·7; H, 12·5. $C_8H_{16}O$ requires: C, 74·9; H, 12·6%) (yield 11·7%) and *2-methyl-5-n-propyltetrahydrofuran* "B" (presumably *trans*-VIIa), b.p. 143–144° at 768 mm,[32] $n_{\mathrm{D}}^{20\cdot5}$ 1·4235 (yield 17·5%) (Found: C, 74·8; H, 12·6. $C_8H_{16}O$ requires: C, 74·9; H, 12·6%) (ratio of "A" to "B" stereoisomer 40:60).

Redistillation of the second fraction afforded 12·4 g of products, b.p. 175–181°, which consisted of unchanged 2-octanol (VIa) and 2-octyl acetate. From both fractions 2-octanone, in the form of its 2,4-dinitrophenylhydrazone (m.p. and mixed m.p. 59° [36,39]), was isolated in 3% yield. The residue (not investigated) amounted to 8·6 g.

(b) The same reaction with 1·5 mole of lead tetraacetate per mole of 2-octanol, after 5 hr-heating under reflux, afforded 15·9 g (32·3% yield) of cyclic ethers, b.p. 140–146° at 760 mm, and 8·5 g of a mixture, b.p. 175–181°, containing 2-octanol and the corresponding acetate, residue 10 g.

(c) When 2 moles of lead tetraacetate were used for one mole of alcohol, the reaction mixture had to be heated to boiling for 10 hr before the tetraacetate reagent was consumed. Redistillation of the two fractions gave 13·7 g (27·8%) of cyclic oxides, b.p. 140–144° at 760 mm, and 8·1 g 2-octanol and 2-octyl acetate, residue 14·3 g.

5-Nonanol (VIb). The reaction between this secondary alcohol (50 g, 0·347 mole) and 195·8 g (0·347 mole + 10%) 86·4% lead tetraacetate (molar ratio 1:1) was mild and it was not necessary to interrupt heating. The lead reagent reacted completely after 3 hrs of refluxing. Working up the mixture as described above furnished 10·1 g (20·5%) of cyclic ethers, b.p. 166–172° at 760 mm, $n_{\mathrm{D}}^{20\cdot5}$ 1·4260. (Found: C, 76·0; H, 12·7. Calc. for $C_9H_{18}O$: C, 76·0; H, 12·8%). This mixture of cyclic oxides was separated by gas chromatography into *2-n-butyl-5-methyltetrahydrofuran* "A" (presumably *cis*-VIIb) (yield 9·2%), b.p. 166–167° at 760 mm,[33] $n_{\mathrm{D}}^{20\cdot5}$ 1·4248 (Found: C, 76·1; H, 12·6. $C_9H_{18}O$ requires: C, 76·O; H, 12·8%) and *2-n-butyl-5-methyltetrahydrofuran* "B" (presumably *trans*-VIIb) (yield 11·3%), b.p. 169° at 760 mm,[33] $n_{\mathrm{D}}^{20\cdot5}$ 1·4281 (Found: C, 75·9; H, 12·8. $C_9H_{18}O$ requires: C, 76·0; H, 12·8%) (ratio of "A" to "B" stereoisomer 45:55).

The second fraction afforded upon redistillation 15·9 g of products, b.p. 192–198°, consisting of unchanged 5-nonanol (VIb) and the corresponding acetate. From both fractions 5-nonanone, in the form of its 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 41° [36], was isolated in 5% yield. The residue (not investigated) amounted to 8 g.

Synthesis of 2,5-dialkyltetrahydrofurans

2-Methyl-5-n-propyltetrahydrofuran "A" (VIIa; presumably the *cis*-form) and 2-n-butyl-5-methyltetrahydrofuran "A" (VIIb; presumably the *cis*-form) were prepared starting from 5-methylfurfural (VIII), which was obtained by degradation of saccharose.[40]

5-Methylfurfuryl alcohol (IX). 5-Methylfurfural (VIII; 140·8 g; 1·28 mole) in 140 ml anhydrous ether was added dropwise to a suspension of 13·3 g (0·35 mole) $LiAlH_4$ in 500 ml dry ether, in such a way as to maintain gentle reflux of the reaction mixture. After the addition was complete, stirring was continued for 15 min at room temp. The mixture was then cooled in ice and decomposed by dropwise addition of 50 ml water, followed by 2 N H_2SO_4 (about 700 ml was necessary to dissolve the inorganic precipitate). The ethereal layer was worked up in the usual manner and gave, upon distillation in vacuo, 137·9 g (96·2% yield) 5-methylfurfuryl alcohol (IX), b.p. 93–93·5° at 22 mm.[41] (Found: C, 64·1; H, 7·3. Calc. for $C_6H_8O_2$: C, 64·3; H, 7·2%).

5-Methylfurfuryl bromide (X) was obtained as described for furfuryl bromide,[20] from 40 g (0·357 mole) 5-methylfurfuryl alcohol (IX) and 35 g (0·129 mole) PBr_3. 5-Methylfurfuryl bromide was not isolated, but directly used, in ether solution, for the preparation of 2,5-dialkylfurans.

2-Methyl-5-n-propylfuran (XIa). This compound was synthesized by the procedure used for the preparation of 2-alkylfurans.[20] Mg (19·4 g; 0·8 gram-atom), C_2H_5Br (87·1 g; 0·8 mole) and 5-methylfurfuryl bromide (X), obtained from 80 g, i.e. 0·714 mole, of 5-methylfurfuryl alcohol, afforded

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[39] T. Shenton and J. C. Smith, *Chem. & Ind.* 1510 (1958).

[40] E. W. Scott and J. R. Johnson, *J. Amer. Chem. Soc.* **54**, 2553 (1932).

[41] This alcohol was previously synthesized by other routes. T. Reichstein and H. Zschokke, *Helv. Chim. Acta* **15**, 249 (1932); A. L. Mndzkoyan, V. G. Afrikyan, M. T. Grigoryan and E. A. Markaryan, *Dokl Akad. Nauk. Armyan. SSR* **25**, 277 (1957); *Chem. Abstr.* **52**, 12835 (1958).

31 g (35% yield, calculated on 5-methylfurfuryl alcohol) *2-methyl-5-n-propylfuran* (XIa), b.p. 64–69° at 60 mm.[42] (Found: C, 77·3; H, 9·7. Calc. for $C_8H_{12}O$: C, 77·4; H, 9·7%).

2-n-Butyl-5-methylfuran (XIb) was prepared analogously from 19·4 g (0·8 gram-atom) Mg, 98·3 g (0·8 mole) n-propyl bromide and 5-methylfurfuryl bromide (X) (obtained from 80 g of the corresponding alcohol). There was obtained 26·9 g (27·4% yield, calculated on 5-methylfurfuryl alcohol) 2-n-butyl-5-methylfuran (XIb), b.p. 82–85° at 48 mm.[42] (Found: C, 78·1; H, 10·3. Calc. for $C_9H_{14}O$: C, 78·2; H, 10·2%).

2-Methyl-5-n-propyltetrahydrofuran "A" (VIIa) was obtained by the hydrogenation of 2-methyl-5-n-propylfuran (XIa) (29·4 g; 0·24 mole), in the presence of ca. 5 g Raney Ni (W-2) (initial press.: 80–90 atm, temp: 105–115°) according to Paul's method of hydrogenation of 2-ethylfuran.[20] The resulting *2-methyl-5-n-propyltetrahydrofuran* "A" (VIIa, presumably the *cis*-form; 25·1 g; 82·7% yield), b.p. 140–142° at 760 mm, $n_D^{20.5}$ 1·4198, was purified by further distillation over K.[43] (Found: C, 75·2; H, 12·6; $C_8H_{16}O$ requires: C, 74·9; H, 12·6%). According to gas chromatography, the product was pure and appeared to consist of only one stereoisomer.

2-n-Butyl-5-methyltetrahydrofuran "A" (VIIb, presumably the *cis*-form) was synthesized in the same way as the lower homologue VIIa. 2-n-Butyl-5-methylfuran (XIb; 26·9 g; 0·20 mole) was hydrogenated in the presence of ca. 5 g Raney Ni (W-2) (initial press: 75–86 atm, temp: 105–115°) to afford upon fractional distillation, 22·5 g (81·3%) *2-n-butyl-5-methyltetrahydrofuran* "A" (VIIb), b.p. 164–165° at 748 mm, $n_D^{20.5}$ 1·4244, which was purified by a further distillation over K. (Found: C, 75·9; H, 12·8. $C_9H_{18}O$ requires: C, 76·0; H, 12·8%). According to gas chromatography, the product was pure and appeared to consist of only one stereoisomer.

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[42] M. Fétizon and P. Baranger, *Bull. Soc. Chim. Fr.* 1311 (1957) prepared 2-methyl-5-n-propylfuran and 2-n-butyl-5-methylfuran by the hydrazine hydrate reduction of the corresponding 2-acyl-5-methylfurans.

[43] After completion of this work, the preparation of 2-methyl-5-n-propyltetrahydrofuran (probably mixture of *cis* and *trans* stereoisomers), b.p. 140–142°, n_D^{20} 1·4200, by hydrogenolysis of 1-(2-furyl)-3-butanol, with intermediate formation and cyclization of the corresponding 1,4-alkanediol, was reported. N. I. Shuikin, I. F. Belskiĭ and R. A. Karakhanov, *Dokl Akad. Nauk SSSR* **127,** 815 (1959); I. F. Belskiĭ and N. I. Shuikin, *Doklady Akad. Nauk SSSR* **128,** 945 (1959); I. F. Belskiĭ, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* 142 (1962); N. I. Shuikin, B. V. Lopatin and B. L. Lebedev, *Zh. Anal. Khim.* **16,** 639 (1961) (b.p. 144–145°, n_D^{20} 1·4240). See also A. Kirmann and L. Wartski, *C.R. Acad. Sci., Paris* **250,** 3492 (1960).