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THE REACTION OF ALDEHYDES WITH 4-METHYL-4-PENTEN-2-OL AND α-TERPINEOL

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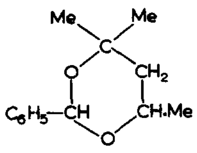
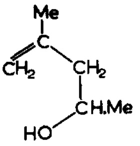
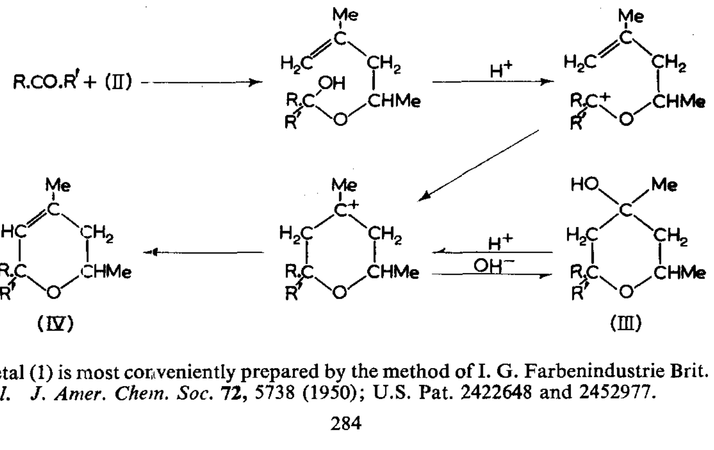
Abstract—The proton-catalysed interaction of aldehydes with 4-methyl-4-penten-2-ol affords a series of substituted tetrahydro-pyranols, which may be smoothly dehydrated to the corresponding dihydro-pyrans. The latter are converted by catalytic hydrogenation to tetrahydro-pyrans. α-Terpineol reacts analogously with, for example, benzaldehyde: the structure of the product so formed is discussed.

IN THE course of an attempted preparation of the virtually odourless cyclic acetal 4:4:6-trimethyl-2-phenyl-1:3-dioxan (I) by the action of hydrochloric acid on a mixture of benzaldehyde and 2-methyl-pentan-2:4-diol, under conditions rather more vigorous than those recommended in the literature,[1] a liquid by-product of similar volatility to that of the desired cyclic acetal was obtained. The by-product could not be effectively separated from the cyclic acetal by fractional distillation but it could be differentiated from it by gas chromatographic analysis and by virtue of its distinctive odour.


(I)


(II)

It was thought possible that an explanation of the formation of the odorous by-product might be found in the interaction of the primary dehydration product of 2-methyl-pentan-2:4-diol, viz: 4-methyl-4-penten-2-ol (II), with carbonyl compounds under the influence of acid catalysts. Substituted dehydro-pyrans are stated to result, according to the following reaction scheme:—[2]


(IV) (III)

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[1] The cyclic acetal (I) is most conveniently prepared by the method of I. G. Farbenindustrie Brit. Pat. 346115.
[2] Williams *et al.* *J. Amer. Chem. Soc.* **72**, 5738 (1950); U.S. Pat. 2422648 and 2452977.

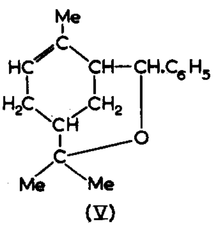
It was therefore assumed that in the original experiment 4-methyl-pentan-2:4-diol had to some extent decomposed under the influence of the anhydrous hydrochloric acid, affording (II) which had then reacted with the benzaldehyde. To confirm this hypothesis some of the reactions described by Williams *et al.*[2] were re-investigated and others were carried out with alternative aldehydes.

In contrast to the findings of Williams *et al.*, who did not report the isolation of 2:4-dimethyl-6-phenyl-tetrahydropyran-4-ol (III, $R = C_6H_5$, $R' = H$), it was found that when benzaldehyde was condensed with (II) at 10–15° in the presence of one mole of sulphuric acid most (60–75 per cent) of the aldehyde reacted to give initially this pyranol. By distillation at a lower pressure than was employed by the previous workers (0·5 mm instead of 5 mm) it was isolated in a substantially pure form. This product could then be smoothly dehydrated by distillation from potassium bisulphate to yield 2:4-dimethyl-6-phenyl-3:6-dihydro-2(H)-pyran (IV, $R = C_6H_5$, $R' = H$).

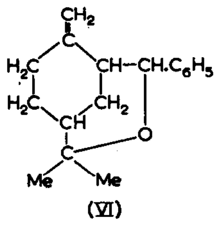
Other substituted pyranols and 2(H)-pyrans have been prepared analogously from anisaldehyde, cinnamaldehyde, piperonal, and heptaldehyde. The reaction product of (II) with citronellal afforded a mixture of four different products (gas chromatographic analysis) but these could not be effectively separated by distillation and were not further investigated. The possibilities of stereoisomerism which are latent in the pyranols were revealed in the case of the anisaldehyde reaction product (III, $R = p\text{-MeO}{\cdot}C_6H_4$, $R' = H$) by the isolation of two products having m.p. 126–127° and 84–86° respectively.

Catalytic hydrogenation of the 2(H)-pyrans proceeded smoothly, in the two cases investigated, to yield the corresponding tetrahydropyrans.

In view of the ease with which aldehydes were found to interact with (II) it was thought that α-terpineol might also react with aldehydes in a similar way, the structure of this compound favouring the steric requirements of the reaction. Interaction of benzaldehyde and α-terpineol under similar experimental conditions to those employed for (II) afforded a white solid, m.p. 64–65°. Analytical data suggested one of the structures (V) or (VI) by analogy with the reaction products of aldehydes with (II), but in this connection it is necessary to take into account the work of Lombard and Adam in this field.[3] These workers condensed benzaldehyde with *dl*-limonene under the influence of zinc chloride or sulphuric acid and obtained a compound, m.p. 62–63°. From *d*-limonene they obtained an analogous product, m.p. 93–95°. Repetition of the work of Lombard and Adam confirmed these results and a direct comparison of our compound, m.p. 64–65°, with theirs, m.p. 62–63°, became possible. Mixed melting point determinations and comparisons of infra-red spectra showed that they were identical.



(V)



(VI)

The French workers proposed three alternative formulae (all different from

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[3] R. Lombard and J. Adam *Bull. Soc. Chim. Fr.* 1216 (1954).

(V) and (VI)) for their products. These were deduced by analogy with similar structures obtained by condensing limonene with formaldehyde, and were not supported by chemical evidence. Formulae (V) and (VI), unlike those of Lombard and Adam, meet our postulate of semi-acetal formation as the first stage of the reaction some reservation is, however, necessary at this stage as to the position of the double bond.

EXPERIMENTAL

4-*Methyl-4-penten-2-ol* (II). 2-Methyl-2:4-pentandiol (1770 g, 15 moles) was refluxed with anhydrous copper sulphate (0·9 g) until the boiling point fell to 80°. Slow distillation gave a fraction boiling below 100°, which was discarded, followed by a fraction b.p. 100–135° from which, by the addition of salt, the unsaturated alcohol was separated and redistilled, b.p. 72°/100 mm, through a Vigreux column. Yield: 834 g, i.e. 59 per cent overall, allowing for the recovery of 95 g of the original diol.

2(H)-*Pyrans* (IV). The general procedure recommended by Williams *et al.*[2] was followed. The aldehyde was added to the reaction mixture either at 10–15° or at such a rate that the temperature remained just below 30° without any effect on the course of the reaction. The reaction mixtures were allowed to stand at atmospheric temperatures for 36–48 hr in order to secure maximum yields of 2(H)-pyrans. At this point, after dilution of the reaction mixture with an equal volume of benzene, washing with 5 per cent aqueous sodium carbonate and water, and evaporation of the solvent and unchanged 4-methyl-4-penten-2-ol, the residue was submitted to fractional distillation *in vauco*. When it was desired to isolate the pyranol (III) distillation was carried out at 0·1–1 mm: otherwise 0·5–1 per cent of potassium bisulphate was added at this stage and the distillation carried out at such a pressure that the 2(H)-pyran distilled at ca. 150°. Physical and analytical data for the compounds thus obtained are shown in Table 1:

TABLE 1. COMPOUNDS OF GENERAL FORMULA (IV), (R′ = H)

R	B.p. (°/mm)	Formula	Required %		Found %	
			C	H	C	H
C_6H_5-	78·5/0·7	$C_{13}H_{16}O$	82·92	8·58	83·21	8·58
p-$MeOC_6H_4-$	98/0·05	$C_{14}H_{18}O_2$	77·00	8·30	77·19	8·56
$C_6H_5CH{:}CH-$	96/0·18	$C_{15}H_{18}O$	84·07	8·47	83·84	8·55
3:4-$CH_2O_2C_6H_3-$	102/0·15	$C_{14}H_{16}O_3$	72·39	6·94	72·36	6·85
n-$C_6H_{13}-$	116–117/16·5	$C_{13}H_{24}O$	79·53	12·32	78·18	12·09

In general it was not found easy to separate the 2(H)-pyrans completely from their associated precursors, the pyranols (III). This applied particularly to the 2(H)-pyran derived from heptaldehyde (IV, R = C_6H_{13}–, R′ = H). The presence of a weak hydroxyl band in the infra-red spectrum of this product, even after repeated fractionation, explained the slightly low per cent carbon figure found by analysis.

2:4-*Dimethyl-6-phenyl-3:6-dihydro-2*(H)-*pyran* (IV, R = C_6H_5, R′ = H). (a) Benzaldehyde (318 g, 3 moles) and 4-methyl-4-penten-2-ol (267 g, 3 moles) were interacted according to the above general method. After removing unchanged reactants a residue (458 g) remained, and this was distilled in portions. Thus a 47 g portion on distillation over potassium hydrogen sulphate (0·5 g) at 20 mm pressure afforded 38 g of dehydrated product. Redistillation afforded an analytically pure product, b.p. 72°/0·2 mm. Dehydration of larger batches proved impracticable due to the formation of malodorous by-products.

(b) Benzaldehyde (106 g, 1 mole), 4-methyl-4-penten-2-ol (100 g, 1·12 moles) and Amberlite IR-120 resin (30 g) were stirred for 12 hr at 60°. The resin was separated by filtration and the filtrate was distilled over potassium hydrogen sulphate (2 g), yielding, after fractionation 49 g (67 per cent, after allowing for recovery of unchanged reactants) of the required product.

Pyranols (III). The pyranols were isolated from the distillation residues (see notes under "2(H)-pyrans" above) by distillation, without a dehydrating agent, at a sufficiently low pressure. Yields varied from 60–75 per cent, and details of the pyranols studied are set out in Table 2:

TABLE 2. COMPOUNDS OF GENERAL FORMULA (III), R′ = H

R	B.p. (°/mm)	M.p.(°)	Formula	Required %		Found %	
				C	H	C	H
C_6H_5–	114/0·7	30	$C_{13}H_{18}O_2$	75·69	8·80	75·17	8·71
p-$MeOC_6H_4$–(a)	155–160/2	124–125	$C_{14}H_{20}O_3$	71·15	8·53	71·97	9·08
p-$MeOC_6H_4$–(b)	155–160/2	84–85	$C_{14}H_{20}O_3$	71·15	8·53	71·82	9·03

Isomers (a) and (b) were separated by fractional crystallization from light petroleum (b.p. 40–60°), the former being the less soluble. Analytical figures indicated that traces of the dehydration products were present in both of them.

Tetrahydro-pyrans. The appropriate dihydro-pyran (IV) (100 g) was dissolved in ethanol (100 ml) and hydrogenated at normal pressures in the presence of Raney nickel catalyst freshly prepared from 20 g of alloy. Details of the compounds obtained are given in Table 3.

TABLE 3. TETRAHYDRO-PYRANS DERIVED FROM 2(H)-PYRANS (IV)

R	B.p. (°/mm)	Formula	Required %		Found %	
			C	H	C	H
C_6H_5–	56/0·1	$C_{13}H_{18}O$	82·06	9·54	82·38	9·53
p-$MeOC_6H_4$–	89/0·1	$C_{14}H_{20}O_2$	76·32	9·15	76·11	9·29

Reaction product of α-terpineol and benzaldehyde. α-Terpineol (154 g, 1 mole) containing sulphuric acid (1 g) was gradually added, with stirring, to benzaldehyde (106 g, 1 mole) at room temperature, The mixture was then heated to 120° for 3 hr. After cooling, it was diluted with benzene (200 ml), and washed first with dilute sodium carbonate solution and then with water. After evaporation of the solvent, distillation *in vacuo* afforded a product (110 g, b.p. 117–125°/0·3 mm) which solidified on cooling. After recrystallization from methanol it had m.p. 64–65° (Found: C, 83·69; H, 9·15. $C_{17}H_{22}O$ requires C, 84·28; H, 9·15 per cent).

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