286. *αβ-Unsaturated Aldehydes and Related Compounds. Part III.* The Addition of Alcohols to the Dimers of Acraldehyde and α-Methylacraldehyde.*†

By R. H. Hall.

Acid-catalysed reaction of the cyclic dimer of acraldehyde with methanol or ethanol gives the corresponding 6-alkoxy-2-dialkoxymethyltetrahydropyran in good yield. Application of the method to the cyclic dimer of α-methylacraldehyde results, however, in a mixture which contains the 7-alkoxy-1 : 4-dimethyl-6 : 8-dioxa*bicyclo*[3 : 2 : 1]octane, the 6-alkoxy-2-dialkoxymethyltetrahydropyran, and, in most instances, the 6-alkoxy-2-formyltetrahydro-2 : 5-dimethylpyran, the alkoxy-groups in each case being derived from the alcohol employed.

The acid-catalysed addition of alcohols to dihydropyrans to give 2-alkoxytetrahydropyrans is well known (cf. Paul, *Bull. Soc. chim.*, 1934, **1**, 973; Woods and Kramer, *J. Amer. Chem. Soc.*, 1947, **69**, 2246); it has indeed been used as a method for protecting alcohol groups since the alcohol can readily be recovered by acid hydrolysis of the adduct (Parham and Anderson, *ibid.*, 1948, **70**, 4187). This paper describes the application of the addition reaction to the cyclic dimers of acraldehyde and α-methylacraldehyde, 2-formyl-3 : 4-

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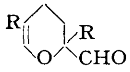
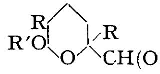
dihydropyran (I; R = H) and 2-formyl-3 : 4-dihydro-2 : 5-dimethylpyran (I; R = Me), respectively.

From the reaction of acraldehyde dimer (I; R = H) with methanol or ethanol in the presence of anhydrous hydrogen chloride at temperatures of 0° to atmospheric, the corresponding 6-alkoxy-2-dialkoxymethyltetrahydropyrans (II; R = H, R′ = Me or Et) were obtained in good yields. When the dimer of α-methylacraldehyde (I; R = Me) was subjected to reaction with a large excess of methanol or ethanol, however, the products were more complex: at room temperature methanol gave a poor yield of 2-dimethoxymethyltetrahydro-6-methoxy-2 : 5-dimethylpyran (II; R = R′ = Me), considerable amounts of lower-boiling compounds being also obtained; these were shown to contain 7-methoxy-1 : 4-dimethyl-6 : 8-dioxa*bicyclo*[3 : 2 : 1]octane (III; R = R′ = Me) and, in addition, in the majority of cases, 2-formyltetrahydro-6-methoxy-2 : 5-dimethylpyran (IV; R = R′ = Me), which could not be separated from the bicyclic compound by distillation. Precise conditions for avoiding the formation of the formyl compound could not be found, the presence or absence of this material in the products appearing to be fortuitous.


(I)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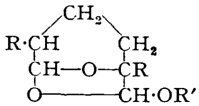
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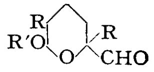
(IV)

The structure of (III; R = R′ = Me) was established by elementary analysis, lack of reaction with semicarbazide acetate in neutral solution, and infra-red spectroscopic analysis (discussed below) which confirmed the absence of functional groups other than ether groups. The only formula compatible with all these is that shown. While this work was in progress Stoner and McNulty (*J. Amer. Chem. Soc.*, 1950, **72**, 1531) reported the preparation of such a compound by the treatment of α-methylacraldehyde dimer with methanol in the presence of calcium chloride as catalyst and somewhat later Whetstone (U.S.P. 2,511,891) described similar work in which hydrogen chloride was used as catalyst; in the latter investigation the amount of methanol employed was restricted to about 2 moles per mole of dimer. Certain of the physical constants recorded by these authors for their products did not agree very closely, however, with those of the material obtained in the present work. These inconsistencies were tentatively ascribed to the stereochemistry of this bicyclic polyether; several stereoisomers were obviously possible and these may have been interconverted, at least partly, on attempted fractionation. In partial confirmation it was found that material made by Whetstone's method (*loc. cit.*) had a refractive index significantly different from that obtained in the earlier work reported here; nevertheless, the two compounds had very similar infra-red absorption spectra (see below). The products were obviously of the same type, but not identical.

2-Formyltetrahydro-6-methoxy-2 : 5-dimethylpyran (IV; R = R′ = Me) was characterised as its semicarbazone but could not be obtained pure; regeneration from the semicarbazone was not attempted in view of the known instability of 2-alkoxytetrahydropyrans towards acids (Parham and Anderson, *loc. cit.*). The structure assigned to the formyl compound was based on analysis of the semicarbazone which showed that the parent carbonyl compound was derived from one mol. of 2-formyl-3 : 4-dihydro-2 : 5-dimethylpyran (I; R = Me) and one mol. of methanol. The formyl compound was probably an intermediate in the formation of 2-dimethoxymethyltetrahydro-6-methoxy-2 : 5-dimethylpyran (II; R = R′ = Me); the other likely intermediate, namely, the dimethyl acetal of 2-formyl-3 : 4-dihydro-2 : 5-dimethylpyran, was not detected in the reaction products.

Replacement of methanol by ethanol in the reaction with 2-formyl-3 : 4-dihydro-2 : 5-dimethylpyran (I; R = Me) gave similar results although the yield of 2-diethoxymethyl-6-ethoxytetrahydro-2 : 5-dimethylpyran (II; R = Me, R′ = Et) was extremely poor. 7-Ethoxy-1 : 4-dimethyl-6 : 8-dioxa*bicyclo*[3 : 2 : 1]octane (III; R = Me, R′ = Et) and 6-ethoxy-2-formyltetrahydro-2 : 5-dimethylpyran (IV; R = Me, R′ = Et) were both present in the lower-boiling products; the former was isolated in pure condition in some experiments and on one occasion in two, apparently stereoisomeric, forms. 6-Ethoxy-2-formyltetrahydro-2 : 5-dimethylpyran (IV; R = Me, R′ = Et) was characterised as its semicarbazone but, as in the case of the corresponding 6-methoxy-compound (IV; R = R′ = Me), was not obtained pure.

In order to prepare reasonable quantities of 2-diethoxymethyl-6-ethoxytetrahydro-2 : 5-dimethylpyran (II; R = Me, R′ = Et), the crude product from the low-temperature reaction of 2-formyl-3 : 4-dihydro-2 : 5-dimethylpyran (I; R = Me) with ethanol containing hydrogen chloride was mixed with methylene dichloride and submitted to azeotropic distillation to remove water. Neutralisation of the anhydrous material, followed by fractionation, afforded a 37% yield of the pure compound (II; R = Me, R′ = Et).

The infra-red absorption spectra of all compounds of type (III) obtained as above did not contain any bands due to carbonyl or hydroxyl groups. A very intense band near 1100 cm.$^{-1}$ was present in each case; this, in the absence of carbonyl and hydroxyl groups, was good evidence for the presence of ether linkages. The spectra also had strong bands in the region 920—980 cm.$^{-1}$ which, by analogy with the spectra of paraldehyde, dioxan, tetrahydropyran, etc., suggested that at least one ether group was part of a saturated ring system.

EXPERIMENTAL

2-*Formyl*-3 : 4-*dihydropyran* (I; R = H).—Acraldehyde dimer was prepared from freshly distilled acraldehyde by the method of Sherlin, Berlin, Serebrennikova, and Rabinovich (*J. Gen. Chem., U.S.S.R.*, 1938, **8**, 22; cf. Alder and Rüden, *Ber.*, 1941, **74**, 920). The pure material had b. p. 40°/10·5 mm., 47·5°/15 mm., n_D^{20} 1·463 (Sherlin *et al.*, *loc. cit.*, give b. p. 40—40·5°/10 mm., 44°/13 mm., n_D^{20} 1·4660), and changed during a few days to a transparent resin; it was therefore used immediately it had been distilled. The semicarbazone had m. p. 119—120° (Sherlin *et al.*, *loc. cit.*, give m. p. 123°), and the dimedone *derivative* (from aqueous ethanol) m. p. 143—144° (Found: C, 70·15; H, 8·25. $C_{22}H_{30}O_5$ requires C, 70·55; H, 8·05%). A portion, hydrogenated in ethanol over Raney nickel until two mols. had been absorbed, furnished tetrahydro-2-hydroxymethylpyran, b. p. 73—74·5°/11 mm., 181—182°/760 mm., n_D^{17} 1·4583 (Soc. des Usines Chimiques Rhone-Poulenc, B.P. 595,379, give b. p. 184—186°, $n_D^{24·5}$ 1·4565; Helberger, Ulubay, and Civelekoglu, *Annalen*, 1949, **561**, 215, give b. p. 70—72°/12 mm.); this gave a 3 : 5-*dinitrobenzoate*, which separated from 95% ethanol in needles, m. p. 84—85° (Found: C, 50·3; H, 4·75; N, 8·7. $C_{13}H_{14}O_7N_2$ requires C, 50·3; H, 4·55; N, 9·05%), and a *hydrogen* 3-*nitrophthalate*, m. p. 163—164° (Found: C, 54·5; H, 4·85; N, 4·95. $C_{14}H_{15}O_7N$ requires C, 54·35; H, 4·9; N, 4·55%), from ethanol.

2-*Formyl*-3 : 4-*dihydro*-2 : 5-*dimethylpyran* (I; R = Me).—The dimer of α-methylacraldehyde was prepared by refluxing the parent aldehyde at atmospheric pressure for several days, recovering unchanged monomer by distillation at atmospheric pressure, and distilling the residual dimer *in vacuo* (cf. Stoner and McNulty, *loc. cit.*). Pure 2-formyl-3 : 4-dihydro-2 : 5-dimethylpyran had b. p. 58°/13 mm., n_D^{20} 1·4533 (Schulz and Wagner, *Angew. Chem.*, 1950, **62**, 105, give b. p. 55—56°/12 mm.; Stoner and McNulty, *loc. cit.*, give n_D^{20} 1·454; Shell Development Co., U.S.P. 2,479,283, gives n_D^{20} 1·4537). Its semicarbazone had m. p. 175—176° (Rohm and Haas Co., U.S.P. 2,473,497, and Shell Development Co., *loc. cit.*, give m. p. 174—177° and 177°, respectively).

Reaction of Acraldehyde Dimer with Ethanol.—A solution of anhydrous hydrogen chloride (1·25 g.) in absolute ethanol (50 ml.) was added slowly to a stirred, cooled solution of (I; R = H) (47 g.) in absolute ethanol (200 ml.) at 0—4°. The resultant mixture was stirred and kept at 0° for 1 hr., then allowed to warm gradually to room temperature and kept for 40 hr.

The product was made just alkaline to litmus by the cautious addition of ethanolic sodium ethoxide solution below 3°, and then a slight excess of glacial acetic acid was added. The filtered mixture was evaporated *in vacuo* and the crude product distilled without a column. Subsequent fractionation of the distillate (81·0 g.), b. p. 80—130°/11 mm., afforded pure 2-*diethoxymethyl*-6-*ethoxytetrahydropyran* (62·6 g., 63%), b. p. 114—117°/9 mm., n_D^{20} 1·4330 (Found: C, 61·95; H, 10·25. $C_{12}H_{24}O_4$ requires C, 62·05; H, 10·4%).

Reaction of Acraldehyde Dimer with Methanol.—A solution of anhydrous hydrogen chloride (1·42 g.) in methanol (50 ml.) was added during 30 min. to a stirred, cooled solution of (I; R = H) (59 g.) in methanol (236 ml.) at 0—4°. The resultant mixture was stirred below 4° for a further 30 min. and then kept at room temperature for some hr. Isolation of the product as described above afforded pure 2-*dimethoxymethyltetrahydro*-6-*methoxypyran* (71·5 g., 71%), b. p. 93—96°/10 mm., n_D^{20} 1·4369 (Found : C, 57·15; H, 9·45. $C_9H_{18}O_4$ requires C, 56·8; H, 9·55%).

Reaction of α-Methylacraldehyde Dimer with Methanol.—(*a*) Addition of (I; R = Me) (53 g.) to methanol (60 ml.) resulted in the spontaneous evolution of heat. The cooled solution was added dropwise, below 4°, to a stirred solution of anhydrous hydrogen chloride (0·236 g.) in methanol (170 ml.), and the mixture kept in ice for some hr. and then at room temperature for several days. The product was made alkaline to litmus by means of methanolic sodium methoxide, a slight excess of acetic acid added, and the mixture distilled *in vacuo*. After removal of methanol, material (65·1 g.) was collected (boiling range 75—120°/9—10 mm.), which on subsequent fractionation afforded the following main fractions : (i) b. p. 80—82°/10 mm. (14·55 g.), n_D^{20} 1·4500 (Found : C, 63·1, 63·05; H, 9·2, 9·3. Calc. for $C_9H_{16}O_3$: C, 62·75; H, 9·35%), and (ii) 2-*dimethoxymethyltetrahydro*-6-*methoxy*-2 : 5-*dimethylpyran* (26·05 g.), b. p. 101—102°/10 mm., n_D^{20} 1·4399, d_4^{20} 1·0063 (Found : C, 60·25, 60·3; H, 10·1, 10·3%; $[R]_D^{20}$ 57·16. $C_{11}H_{22}O_4$ requires C, 60·5; H, 10·15%; $[R]_D^{20}$ 57·37).

Fraction (i) was probably 7-methoxy-1 : 4-dimethyl-6 : 8-dioxa*bicyclo*[3 : 2 : 1]octane (see p. 1399). Stoner and McNulty (*loc. cit.*) give b. p. 125°/100 mm., n_D^{20} 1·445, and Whetstone (*loc. cit.*) gives b. p. 66—66·5°/9·5 mm. for this compound.

Most experiments, under the same or slightly different conditions, gave low-boiling fractions, *e.g.*, b. p. 82·5—83·5°/12 mm., n_D^{20} 1·4417, which contained, in addition to the bicyclic compound, an isomeric carbonyl compound [Found (for the fraction) : C, 63·5, 62·6; H, 9·55, 9·3. $C_9H_{16}O_3$ requires C, 62·75; H, 9·35%]. A *semicarbazone*, prepared from such a fraction in neutral solution, had m. p. 211° (from ethyl acetate) (Found : C, 52·65; H, 8·15; N, 18·3. $C_{10}H_{19}O_3N_3$ requires C, 52·4; H, 8·35; N, 18·3%). The carbonyl compound was thus 2-*formyltetrahydro*-6-*methoxy*-2 : 5-*dimethylpyran*.

(*b*) (cf. Whetstone, *loc. cit.*) Methanolic hydrogen chloride (1·2 ml.; 0·5N) was added below 40° to a stirred, cooled, solution of (I; R = Me) (56 g.) in methanol (32 ml.). The resultant mixture was kept at 39—40° for 1 hr., cooled, neutralised with calcium carbonate (1 g.), stirred for ½ hr., filtered, and finally fractionated. A fraction (11·55 g.), b. p. 70°/12 mm. (Whetstone, *loc. cit.*, gives b. p. 66—66·5°/9·5 mm.), n_D^{20} 1·4414 (Found : C, 62·95; H, 9·6. Calc. for $C_9H_{16}O_3$: C, 62·75; H, 9·35%), was obtained which appeared to be a stereoisomer of the 7-methoxy-1 : 4-dimethyl-6 : 8-dioxa*bicyclo*[3 : 2 : 1]octane obtained as in (*a*).

Reaction of α-Methylacraldehyde Dimer with Ethanol.—(*a*) Addition of (I; R = Me) (70 g.) to ethanol (70 ml.) resulted in the spontaneous evolution of heat. The cooled mixture was added, below 3°, to a stirred solution of anhydrous hydrogen chloride (0·314 g.) in ethanol (205 ml.) which had previously been cooled below 2° and the resultant solution was kept at room temperature for several hr. Ethanolic sodium ethoxide was added cautiously to the mixture until it was just alkaline to litmus. A slight excess of acetic acid was then introduced and the solvent evaporated *in vacuo*. The crude product was filtered to remove inorganic salts, then distilled, and the distillate (61·7 g.), b. p. 75—110°/9·5 mm., fractionated, giving three main fractions : (i) b. p. 75·5—79°/10 mm. (17·0 g.), n_D^{20} 1·4380 (Found : C, 64·1, 64·25; H, 9·95, 9·65. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·75%); (ii) b. p. 87·5—89°/10 mm. (28·0 g.), n_D^{20} 1·4469 (Found: C, 64·35; H, 9·7%); and (iii) b. p. 119·5—121°/10 mm. (10·75 g.), n_D^{20} 1·4345—1·4388, probably slightly impure 2-diethoxymethyl-6-ethoxytetrahydro-2 : 5-dimethylpyran [see (*b*) below].

By infra-red analysis, fractions (i) and (ii) were shown to be very similar but not identical. Their spectra (see above for details) indicated the absence of carbonyl and hydroxyl groups but strong absorption due to ether groups, probably both in and out of a ring, was observed in each case. The compounds are probably stereoisomers of 7-*ethoxy*-1 : 4-*dimethyl*-6 : 8-*dioxa*bicyclo-[3 : 2 : 1]*octane*.

Most experiments, under the same or slightly different conditions, gave low-boiling fractions, *e.g.*, b. p. 90—90·5°/13 mm., n_D^{20} 1·4390, which contained, in addition to the bicyclic compound, an isomeric carbonyl compound [Found (for fraction) : C, 64·45; H, 9·55. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·75%). A *semicarbazone*, prepared in neutral solution, formed needles, m. p. 223—224°, from aqueous ethanol (Found : C, 54·25; H, 8·6; N, 17·3. $C_{11}H_{21}O_3N_3$ requires C, 54·3; H, 8·7; N, 17·25%). Hence the carbonyl compound was most probably 6-*ethoxy*-2-*formyltetrahydro*-2 : 5-*dimethylpyran*.

(*b*) A solution of (I; R = Me) (70 g.) in ethanol (85 ml.) was added below 20° to ethanol (203 ml.) containing anhydrous hydrogen chloride (1·44 g.) which was cooled in ice. Methylene dichloride (250 ml.) was then introduced and the mixture distilled through a 3-ft. Vigreux column fitted with a phase-separating still-head which decanted the upper layer in the distillate continuously and returned the lower layer to the column as reflux.

After 44 hr.' heating, the product was cooled, made just alkaline to litmus with ethanolic sodium ethoxide, and then just neutral with acetic acid. After removal of solvents the product was distilled *in vacuo*. Subsequent fractionation of the distillate afforded pure 2-*diethoxymethyl*-6-*ethoxytetrahydro*-2 : 5-*dimethylpyran* (48·5 g., 37%), b. p. 125—125·5°/12 mm., n_D^{20} 1·4332 (Found : C, 65·05; H, 10·7. $C_{14}H_{28}O_4$ requires C, 64·6; H, 10·85%).

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