

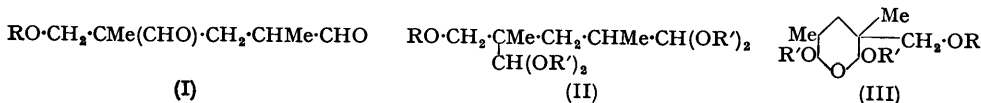
*$\alpha\beta$ -Unsaturated Aldehydes and Related Compounds. Part VI.**
Pyran Derivatives from α -Methylacraldehyde.†

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Treatment of 2-alkoxymethyl-2:4-dimethylpentanedials with aliphatic alcohols in the presence of acids gave 2:6-dialkoxy-3-alkoxymethyltetrahydro-3:5-dimethylpyrans. The use of an activated clay as catalyst led to a 2-alkoxy-3-alkoxymethyl-3:4-dihydro-3:5-dimethylpyran, a probable intermediate in the production of the corresponding 2:6-dialkoxytetrahydro-compound.

THE dialdehydes (I) derived from α -methylacraldehyde and aliphatic alcohols (Bewley, Hall, Howe, Lacey, and the Distillers Co., Ltd., B.P. 706,176) polymerised readily at room temperature. An attempt was therefore made to convert them into stable acetals by treating them with alcohols in the presence of acid catalysts. The compounds obtained, in high yields, were not the diacetals (II), however, but were derived from one mol. of the dialdehyde and two mols. of the alcohol with the elimination of one mol. of water. As they contained no aldehyde or hydroxyl groups and no ethylenic unsaturation they were formulated as 2:6-dialkoxy-3-alkoxymethyltetrahydro-3:5-dimethylpyrans (III).



They were very stable compounds and, unlike 2:6-diethoxytetrahydropyran (Hall and Howe, *J.*, 1951, 2480), could not be induced to react with alcohols to give the diacetals (II). Attempts to regenerate the original dialdehydes by acid hydrolysis resulted in a slow reaction leading to gross decomposition; any α -methylacraldehyde set free was presumably hydrated as hydroxyaldehydes in the strongly acid medium since none was recovered from the hydrolysate.

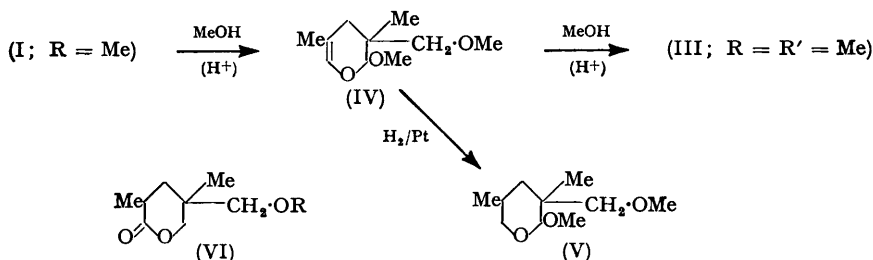
When the reaction between the dialdehyde (I; R = Me) and methanol was catalysed by an activated clay, the product was lower-boiling than the compound (III; R = R' = Me) and was derived from one mol. each of dialdehyde and alcohol with elimination of one mol. of water. It was unsaturated, absorbed one mol. of hydrogen on catalytic hydrogenation, did not contain any aldehyde or hydroxyl groups, and on treatment with methanolic hydrogen chloride readily yielded the pyran (III; R = R' = Me). It was therefore formulated as 3:4-dihydro-2-methoxy-3-methoxymethyl-3:5-dimethylpyran (IV) and its hydrogenation product as tetrahydro-2-methoxy-3-methoxymethyl-3:5-dimethylpyran (V).

The dihydropyran (IV) represents an interesting intermediate stage to the 2:6-

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† B.P. Appl. 19,145/50 describes part of this work.

dimethoxy-compound (III; R = R' = Me), the mild catalyst used evidently not being sufficiently acidic to function as catalyst for the addition of a second mol. of methanol.



The dialdehydes (I; R = Me or Et) used required careful purification to free them from the close-boiling isomeric δ -lactones (VI) with which they were usually contaminated in the crude state and into which they readily passed on treatment with alkaline reagents (cf. Smith and the Shell Development Co., U.S.P. 2,526,702; de Jong and the Shell Development Co., U.S.P. 2,576,901).

EXPERIMENTAL

2-Alkoxyethyl-2 : 4-dimethylpentanedials.—2-Methoxymethyl- and 2-ethoxymethyl-2 : 4-dimethylpentanedial were prepared from α -methylacraldehyde by the method of Bewley *et al.* (*loc. cit.*). The methoxy-compound had b. p. 110°/12 mm., n_D^{20} 1.4457 (Found : C, 62.6; H, 9.5. Calc. for C₉H₁₆O₃ : C, 62.75; H, 9.35%); its *bis*-2 : 4-dinitrophenylhydrazone separated from ethyl acetate in yellow flocks, m. p. 207° (Found : C, 47.35; H, 4.4; N, 21.6. C₂₁H₂₄O₉N₈ requires C, 47.35; H, 4.55; N, 21.05%). The 2-ethoxymethyl compound had b. p. 117—119°/11 mm., n_D^{20} 1.4424 (Found : C, 64.05, 64.2; H, 9.45, 9.6. Calc. for C₁₀H₁₈O₃ : C, 64.5; H, 9.75%); its *bis*-2 : 4-dinitrophenylhydrazone separated from ethyl acetate in yellowish-orange flocks, m. p. 169—170° (Found : C, 48.05; H, 4.65; N, 20.5. C₂₂H₂₆O₉N₈ requires C, 48.35; H, 4.8; N, 20.5%).

Both dialdehydes polymerised readily at room temperature. The freshly-distilled 2-methoxymethyl compound was shown by infra-red analysis to contain not more than 1—2% of the isomeric δ -lactone. [An authentic specimen of the latter was prepared from the dialdehyde, essentially by the method of Smith and the Shell Development Co. (*loc. cit.*); it had a characteristic infra-red absorption peak at 1741 cm.⁻¹ (carbonyl group in a saturated δ -lactone ring).]

Reaction of the Dialdehydes with Aliphatic Alcohols.—The general method was as follows : A solution of the dialdehyde in the appropriate alcohol was mixed cautiously, at or below room temperature, with a mixture of the acid catalyst and the alcohol, and the resultant mixture was kept (or stirred in the case of a solid catalyst) either at or above room temperature for some hours. In certain cases when the mixture was refluxed some benzene was added in order to entrain the water of reaction, the still being fitted with a phase-separating still-head which enabled the aqueous phase in the distillate to be decanted continuously while the oil phase was returned to the column. The quantities of reagents employed, etc., are summarised in Table 1.

In every case where a soluble catalyst was employed the final reaction product was made slightly alkaline by the addition of a slight excess of suitable base, *e.g.*, the appropriate sodium alkoxide dissolved in the corresponding alcohol, or a salt such as sodium acetate. Where a solid, insoluble, catalyst had been employed (*e.g.*, fuller's earth) the reaction product was merely filtered. In experiment 5 (Table 1) the reaction mixture was finally evaporated *in vacuo* to remove most of the methanol, and the product was isolated with ether. In all cases the final product was fractionated carefully to recover the cyclic ether. The physical constants and analytical results for these ethers are summarised in Table 2.

Treatment of 3 : 4-Dihydro-2-methoxy-3-methoxymethyl-3 : 5-dimethylpyran with Methanol.—A solution of the dihydropyran (18.6 g.) in methanol (30 ml.) was stirred and cooled (in ice) while methanolic hydrogen chloride (10 ml.; 2.08% w/v) was added dropwise. The mixture was kept at room temperature for some days, made alkaline with sodium methoxide (from 0.2 g. of sodium) dissolved in methanol (*ca.* 5 ml.), and fractionated to give tetrahydro-2 : 6-dimethoxy-3-methoxymethyl-3 : 5-dimethylpyran (15.95 g.; 73% yield), b. p. 100—102°/9 mm., n_D^{20} 1.4398, identical with that obtained above (see Table 2).

TABLE 1. Reaction of 2-alkoxymethyl-2 : 4-dimethylpentanedials
[RO·CH₂·CMe(CHO)·CH₂·CHMe·CHO] with alcohols (R'OH).

No.	Dialdehyde		Alcohol		Catalyst		Temp.		Product *		Notes
	R	g.	R'	g.	Nature	g.	Initial	Final	Wt., g.	Yield, %	
1	Me	129	Me	480	HCl	3·0	0°	ca. 15°	141·5	87	A
2	"	43·0	"	160	T.S.A.†	2	ca. 15	"	41·2	75	—
3	"	57·0	"	106	F.E.‡	16	"	30	27·8	45	B
4	"	43·0	"	80	"	24	"	reflux	34·3	73	B
5	"	57·4	"	213	CaCl ₂	55·5	"	ca. 15	0	0	C
6	"	86·0	Et	460	HCl	2·9	0	"	102·3	83	—
7	"	86·0	"	541	"	2·9	<4	reflux	119·2	97	D (250)
8	"	129·2	"	688	H ₂ SO ₄	4·4	<10	"	155·1	84	D (200)
9	"	43·0	Pr ^l	300	"	3·7	ca. 15	ca. 15	45·5	66	—
10	"	43·0	"	300	"	3·7	"	reflux	29·7	43	D (200)
11	"	43·0	Bu ⁿ	185	"	1·85	"	"	40	53·1	70
12	"	43·0	C ₆ H ₁₃ Et-2	195	"	1·85	"	"	55	0	—
13	"	43·0	"	195	"	1·85	"	120—140	19·1	18	D (20)
14	"	28·7	"	130	F.E.‡	13·0	"	120	24·2	35	—
15	Et	74·0	Me	128	HCl	0·17	<0	ca. 15	76·0	82	—
16	"	93·0	Et	232	"	0·25	"	reflux	110·0	85	D (200)

* Unless otherwise specified the products were 2 : 6-dialkoxy-3-alkoxymethyltetrahydro-3 : 5-dimethylpyrans (see Table 2 for constants, etc.).

† Toluene-*p*-sulphonic acid.

‡ Fuller's earth (Fullers' Earth Union Ltd., No. 237).

Notes : A. Product gave negative tests for unsaturation (bromine in carbon tetrachloride, aqueous permanganate), active hydrogen (Zerewitinoff), and aldehyde function (Schiff's reagent and Tollens's reagent), and its infra-red absorption spectrum contained no bands due to hydroxyl, carbonyl, or aldehyde groups. B. Product was 3 : 4-dihydro-2-methoxy-3-methoxymethyl-3 : 5-dimethylpyran, b. p. 78—79°/9 mm., n_D^{20} 1·4488 (Found : C, 64·9, 64·9; H, 9·9, 10·0. C₁₀H₁₈O₃ requires C, 64·5; H, 9·75%). It gave positive tests for unsaturation (bromine in carbon tetrachloride, aqueous permanganate), negative tests for active hydrogen (Zerewitinoff) and aldehyde function (Schiff's reagent and Tollens's reagent), and absorbed 1·0 mol. of hydrogen on catalytic hydrogenation in glacial acetic acid over Adams's catalyst at room temperature and pressure (see below). Its infra-red absorption spectrum indicated that it contained no hydroxyl groups and that a carbonyl or aldehyde group was very doubtful; a peak at 1681 cm.⁻¹ was tentatively assigned to an $\alpha\beta$ -unsaturated ether group. C. Unchanged material (47·35 g.) recovered. D. Benzene (vol. in ml. given in parentheses) added before refluxing began in order to entrain water of reaction.

TABLE 2. Substituted tetrahydro-3 : 5-dimethylpyrans.

Substituents	B. p./mm.	n_D^{20}	d_4^{20}	Formula	Found, %		Reqd., %		[R] _D ²⁰	
					C	H	C	H	Found	Calc.
2 : 6-Dimethoxy-3-methoxymethyl-	102°/10	1·4400	1·0053	C ₁₁ H ₂₂ O ₄ ^a	60·9	10·2	60·5	10·15	57·22	57·37
2 : 6-Diethoxy-3-methoxymethyl-	116°/11	1·4359	0·9655	C ₁₃ H ₂₆ O ₄ ^b	63·35	10·65	63·4	10·65	66·61	66·70
3-Methoxymethyl-	122—124°/	1·4335	—	C ₁₅ H ₃₀ O ₄	63·5	10·55	66·0	11·0	65·65	11·05
2 : 6-diisopropoxy-*	11·5	1·4357	*		66·0	11·15	65·6	11·15	—	—
2 : 6-Di-n-butoxy-3-methoxymethyl-	154°/9	1·4412	—	C ₁₇ H ₃₄ O ₄	67·65	11·25	67·5	11·35	—	—
2 : 6-Di-2'-ethyl-hexyloxy-3-methoxymethyl-	214—215°/15	1·4505	—	C ₂₅ H ₅₀ O ₄	72·9	11·8	72·4	12·15	—	—
3-Ethoxymethyl-2 : 6-dimethoxy-	109°/10	1·4387	0·9872	C ₁₃ H ₂₄ O ₄ ^c	62·4	10·55	62·05	10·4	61·86	61·99
2 : 6-Diethoxy-3-ethoxymethyl-	121°/10	1·4345	0·9509	C ₁₄ H ₂₈ O ₄ ^d	64·5	10·7	64·6	10·85	71·22	71·38
					64·7	10·8				

* Attempts to purify this further by stirring it with aqueous 2*N*-sodium hydroxide at 80—100° for 2 hr., or by boiling it with isopropanol containing anhydrous hydrogen chloride whilst removing any water present as the water-isopropanol azeotrope, were unavailing, the recovered material in each case showing the same spread of refractive index. The analytical results given are for fractions at the extremes of the refractive-index range. The infra-red absorption spectra of the fractions were very similar and were consistent with the view that stereoisomers were present.

^a Found : *M*, 212. Requires *M*, 218. ^b Found : *M*, 235. Requires *M*, 246. ^c Found : *M*, 226. Requires *M*, 232. ^d Found : *M*, 256. Requires *M*, 260.

Hydrogenation of 3 : 4-Dihydro-2-methoxy-3-methoxymethyl-3 : 5-dimethylpyran.—The dihydropyran (15·0 g.), dissolved in glacial acetic acid (50 ml.), was hydrogenated at atmospheric pressure and temperature over Adams's platinum oxide catalyst (0·6 g.). 1·0 mol. of hydrogen was rapidly absorbed; hydrogenation then almost ceased. Isolation of the product by filtration followed by distillation afforded tetrahydro-2-methoxy-3-methoxymethyl-3 : 5-dimethylpyran (11·0 g.; 72%), b. p. 86—87°/10 mm., n_D^{20} 1·4398 (Found : C, 64·1, 64·05; H, 10·75, 10·9. C₁₀H₂₀O₃ requires C, 63·8; H, 10·7%).

Hydrolysis of Tetrahydro-2 : 6-dimethoxy-3-methoxymethyl-3 : 5-dimethylpyran.—A mixture of the tetrahydropyran (50 g.), methanol (75 ml.), and aqueous 5N-hydrochloric acid (100 ml.) was refluxed for 5 hr., and then cooled, and the product isolated with ether. The ether extract was washed in turn with water, aqueous sodium hydrogen carbonate solution, and then water, and finally dried (Na_2SO_4). Fractionation of the solution afforded unchanged material (31.65 g.; 63%), but no 2-methoxymethyl-2 : 4-dimethylpentanedial or α -methylacraldehyde was obtained.

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