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Studies on Intermediates Involved in the Syntheses of Pentaerythritol and Related Alcohols. III.* Syntheses of α-Hydroxymethyl-substituted Aldehydes

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Methods for the preparation of the α-hydroxymethyl-substituted aldehydes postulated as intermediates in the production of the polyalcohols pentaerythritol, trimethylolethane, and trimethylolpropane are reported. These syntheses involve as their key steps the $LiAlH_4$-reduction of the corresponding acetal esters. The acetals obtained are stable substances, from which the free aldehydes can be generated rather free from by-products in dilute aqueous solution. On attempted concentration, however, those aldehydes, which have α-hydrogens, tend to loose water under formation of unsaturated aldehydes. All the aldehydes have been characterized as 2,4-dinitrophenylhydrazones and as acetals but only two of them as free aldehydes.

Three mass produced polyalcohols, namely 2,2-bis(hydroxymethyl)-1,3-propanediol (pentaerythritol, VI), 2-hydroxymethyl-2-methyl-1,3-propanediol (trimethylolethane, TME, X) and 2-ethyl-2-hydroxymethyl-1,3-propanediol (trimethylolpropane, TMP, XIV) are prepared *via* crossed aldol condensations with formaldehyde (I) followed by crossed Cannizzaro reactions with this aldehyde. The postulated reaction sequences involve as intermediates the hydroxyaldehydes 3-hydroxypropanal (monomethylolacetaldehyde, hydracrolein, III), 3-hydroxy-2-hydroxymethylpropanal (dimethylolacetaldehyde, IV), 3-hydroxy-2,2-bis(hydroxymethyl)-propanal (trimethylolacetaldehyde, V), 3-hydroxy-2-methylpropanal (monomethylolpropionaldehyde, VII), 3-hydroxy-2-hydroxymethyl-2-methylpropanal (dimethylolpropionaldehyde, IX), 2-ethyl-3-hydroxypropanal (monomethylolbutyraldehyde, XII), and 2-ethyl-3-hydroxy-2-hydroxymethylpropanal (dimethylolbutyraldehyde, XIII) as shown in Scheme 1.

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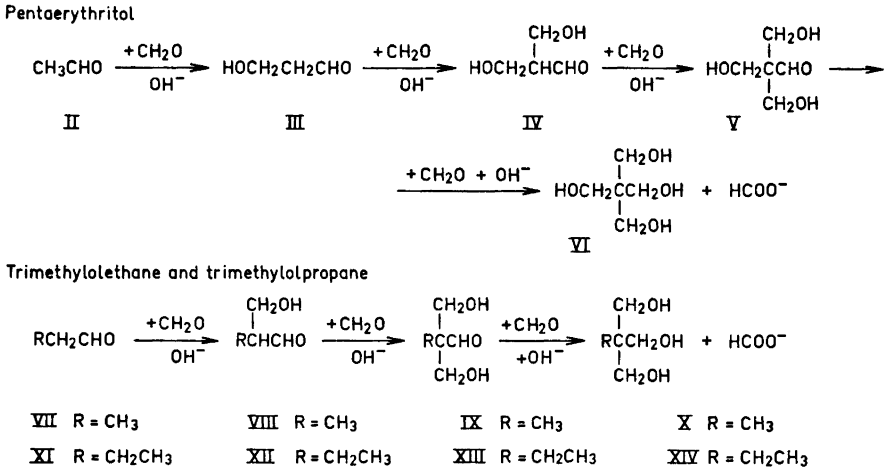
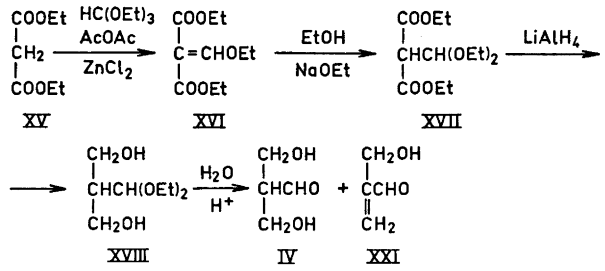


Scheme 1.

Of these hydroxyaldehydes III,[1] V,[2] IX,[3] and XIII [4] have been obtained in a more or less pure state by means of direct condensation of I with acetaldehyde (II), propionaldehyde (VII), and butyraldehyde (XI), respectively. Compound III has also been obtained by acid-catalyzed hydration of 2-propenal.[5] In all these cases the reaction mixtures are difficult to work up, and our attempts to repeat these condensations failed to give pure products. The procedures for the preparation of IX[3] and XIII [4] call for the use of stoichiometric amounts of I with K_2CO_3 as the condensing agent. Thin layer chromatography of the products obtained indicated the formation in both cases of at least three compounds, neither of which was identical with those obtained by the procedures described below. The use of an excess of I to avoid formation of the less hydroxymethyl-substituted aldehydes IV, VIII, and XII gives products, which are difficult to free completely from I. Armour *et al.*[2] successfully used a chromatographic method to perform this task in the case of V, but we did not succeed in repeating this separation.

In connection with work on the detailed kinetics and mechanism of the pentaerythritol synthesis, methods for the preparation of V and the previously unknown IV were sought for. It was found that both substances could be obtained *via* extensions of the synthesis of diethyl diethoxymethylmalonate (XVII) described by Fuson *et al.*[6] as outlined in Schemes 2 and 4. The same general synthetic route has been used for the syntheses of IX and XIII (Scheme 5) and of VIII and XII (Scheme 6). In addition, further extensions of the same general principle have made accessible the aldehydes III (Scheme 8) and the previously unknown dehydration product of IV, 2-hydroxymethyl-2-propenal (XXI, Scheme 3).

The first step in the synthesis of IV is a modification [7] of the original procedure of Claisen [8] for the synthesis of XVI. The mechanism is not known with certainty, but the reaction is thought to involve XVII as an intermediate.[7]



Scheme 2.

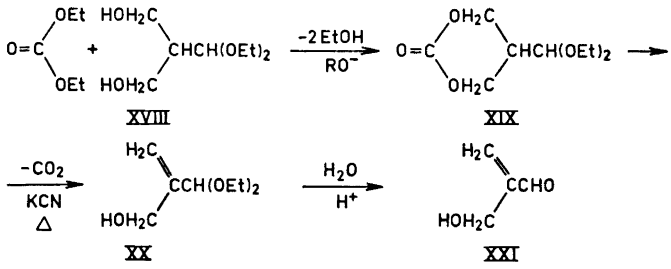
Work by Post and Erickson [9] indicated that the reagent actually effecting the diethoxymethylation is acetoxydiethoxymethane (XXII). This compound is formed in a reaction between the orthoformate and acetic anhydride. A probable route to the proposed intermediate XVII then seems to involve electrophilic attack by the diethoxymethyl cation on the double bond of the enol of the malonate ester. The function of the zinc chloride probably is to catalyze the enolization of the diethyl malonate and to effect fission of XXII by complexing with the acetoxyl group. The catalyst is not necessary for the reaction to occur, but it does improve the yield. The analogous condensations with XXVI and XXIX (Scheme 5) show that only one active hydrogen is needed for the reaction to occur, but the lower yields obtained in these cases indicate steric hindrance. In these cases the acetyl-substituted malonic esters, which could be formed in analogous reactions with acetic anhydride, were identified as minor by-products by means of vapour phase chromatography in combination with mass spectrometry.

The intermediate ester XVII (Scheme 2) then undergoes acid-catalyzed elimination of ethanol giving XVI. As the next step in the synthetic sequence shows, the ester XVII actually is the more stable one at lower temperatures, but the high temperature used and the continuous removal of ethanol as ethyl acetate from the reaction mixture force the elimination to completion. Base-catalyzed addition of ethanol to XVI then gives XVII, which on reduction with $LiAlH_4$ provides the diethyl acetal of IV (XVIII) in excellent yield and purity.

The hydrolysis of this acetal turned out to be complicated, since it was found, that IV very easily undergoes dehydration, especially in the presence of bases. Thus, the slightest excess of base, remaining after neutralization of an acid hydrolysis reaction mixture, is likely to cause extensive dehydration of IV giving XXI. This latter aldehyde then can react further in different ways, which is the subject of a separate study. It was found, however, that brief passage of XVIII through an H^+-saturated cation exchanger with water as eluent gives IV in a rather pure state in aqueous solution.

For a study of the equilibrium between IV and its dehydration product XXI[10] a way to prepare this latter aldehyde was needed. Base-catalyzed dehydration of IV did not give a sufficiently pure product. Instead the utilization of a reaction observed by Searles *et al.*[11] in connection with work on the

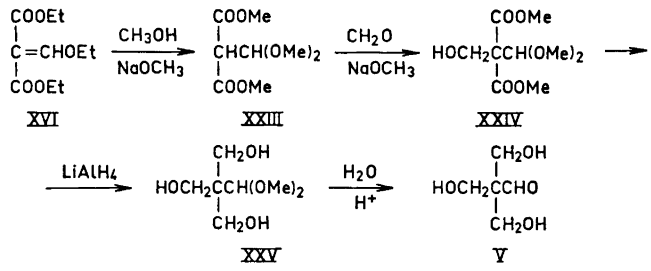
synthesis of oxetanes led to a convenient route for the preparation of XXI. These authors found that on pyrolysis, in the presence of alkaline catalysts, of 2-oxo-1,3-dioxanes, those carrying a 5-hydrogen gave as main products allylic alcohols instead of oxetanes. When this method was applied to the 2-oxo-1,3-dioxane XIX, the allyl alcohol XX was obtained in about 55 % yield, based on XVIII, and mild acid hydrolysis of XX, preferably brought about by means of brief passage through an acid ion exchanger, gave XXI (Scheme 3).



Scheme 3.

Attempts were made to synthesize trimethylolacetaldehyde (V) with trimethyl methanetricarboxylate as starting material. The expected product from the first step, trimethyl diethoxymethylmethanetricarboxylate, was only formed in a very low yield, however, irrespective of whether the condensation with triethyl orthoformate was brought about with zinc chloride or other Lewis acids as catalysts or *via* the sodium or ethoxymagnesium derivative of trimethyl methanetricarboxylate in Grignard-type reactions.

Other possible routes were therefore examined. Base-catalyzed reaction of XVI with methanol gave XXIII. This ester, on base-catalyzed reaction with formaldehyde, gave the crystalline hydroxymethyl-substituted ester XXIV (Scheme 4; *cf.* Böhme and Teltz [12]).

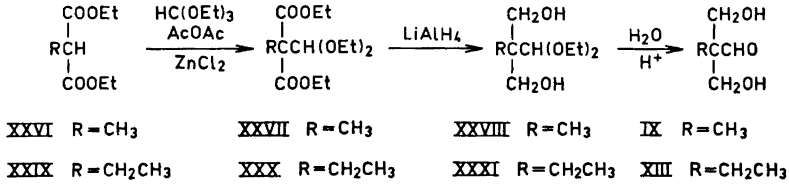


Scheme 4.

Substitution of methoxy groups for the ethoxy groups was found suitable since XXIV was found to be crystallizable and therefore more easily purified than the corresponding liquid ethyl ester.

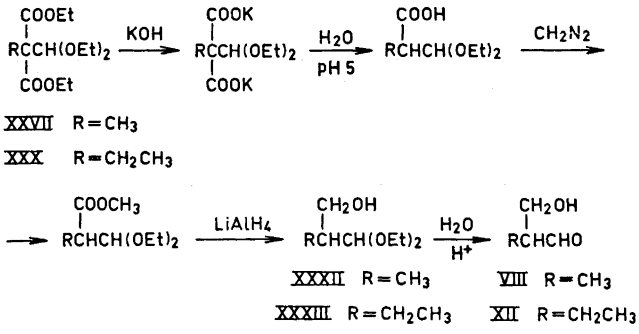
Reduction of XXIV with $LiAlH_4$ gave XXV, but only in an impure state and in a low yield (about 5 %) when the mixture was worked up in the manner used for XVIII. This method involved destruction of unreacted $LiAlH_4$ with a moderate excess of water, followed by hydrolysis of the salts by treatment with carbon dioxide. Other conventional methods were equally unsatisfactory, apparently because of formation during the reduction of difficultly hydrolyzable complex aluminium salts. Destruction of excess $LiAlH_4$ with aqueous KOH followed by precipitation of the aluminium as phosphate gave a somewhat more satisfactory result, even if the yields varied from 25 to 65 % in different runs. The resulting dimethyl acetal XXV then could be purified by crystallization.

The hydroxyaldehydes IX and XIII were prepared in the same manner as IV. Condensation of the appropriate alkyl-substituted malonic esters with triethyl orthoformate gave the esters XXVII and XXX in moderate yields and the remaining steps were straightforward (Scheme 5).



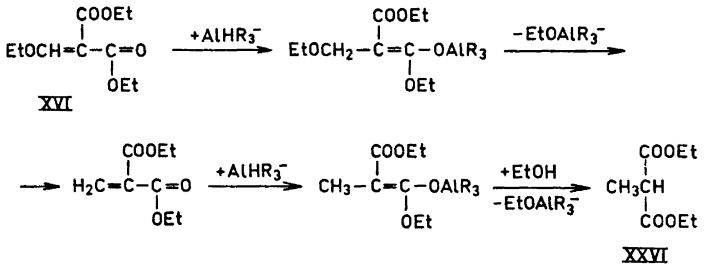
Scheme 5.

The corresponding monohydroxymethyl-substituted aldehydes VIII and XII were obtained starting from the esters XXVII and XXX, respectively. The esters were saponified and with remarkable ease decarboxylated to the corresponding monobasic acids. Esterification with diazomethane without isolation of the acids was followed by reduction to give the acetals of VIII (XXXII) and of XII (XXXIII), respectively (Scheme 6).



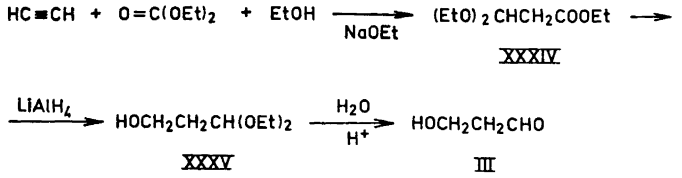
Scheme 6.

The decarboxylation was complicated by subsequent partial elimination of ethanol resulting in formation of the corresponding β-ethoxy α,β-unsaturated acids. On the other hand no significant hydrolysis of the acetal groups was observed. The acetals XXXII and XXXIII were obtained in a rather pure state, although the esters to be reduced were contaminated with the corresponding unsaturated esters. These latter probably are converted into products with completely reduced enol ether groups, in analogy with what was found on reduction of XVI (Scheme 7). This compound gave XXVI as the only isolated product in 25 % yield.



Scheme 7.

The analogous preparation of aldehyde III involved reduction of the ester acetal XXXIV, prepared by the method of Croxall and Schneider,[13] to the corresponding acetal XXXV (Scheme 8).



Scheme 8.

The product (XXXV) showed a tendency to form polymeric acetals of the probable type $H(-OCH_2CH_2CH(OEt)-)_n-OEt$ by elimination of ethanol, possibly catalyzed by acid impurities. The distilled product proved to be stable.

Thus it has been found possible to prepare all of the intermediate hydroxymethyl-substituted aldehydes sought for *via* reduction of the corresponding ester acetals. The acetals obtained are stable substances, from which the free aldehydes can be generated by hydrolysis. All of the aldehydes were characterized as 2,4-dinitrophenylhydrazones. The majority of the aldehydes, carrying α-hydrogens, were found to dehydrate so easily that they only could be obtained slightly contaminated with their dehydration products in dilute aqueous

solution. These solutions were sufficiently pure, however, to allow kinetic investigations of some of the reactions, which these aldehydes can undergo in alkaline solutions. These investigations will be reported in forthcoming publications.

EXPERIMENTAL

The organic chemicals used were of the purest grades commercially available (most of them obtained from Fluka AG) and were used without further purification. The purity of starting materials and products were generally tested by vapour phase chromatography on a Perkin-Elmer 800 instrument. IR-spectra were recorded on a Beckman IR-9 instrument and NMR-spectra on a Varian A-60 instrument. Elemental analyses were performed at the Microanalytical Laboratory at the Institute of Physical Chemistry, University of Vienna. Melting and boiling points are uncorrected.

Diethyl ethoxymethylenemalonate (*XVI*) was prepared by the method reported in *Org. Syn.*[7] B.p.$_{1.2}$ 122–123°C. Yield 55 to 60 %. IR-spectrum with strong, slightly split carbonyl peak at 1733 and 1715 cm^{-1} and strong conjugated C=C peak at 1638 cm^{-1}.

Diethyl diethoxymethylmalonate (*XVII*) was prepared by the method of Fuson *et al.*[6] B.p.$_{1.2}$ 111–112°. Yield 80 to 85 %. IR-spectrum with strong, split carbonyl peak at 1740 and 1758 cm^{-1}.

3-Hydroxy-2-hydroxymethylpropanal diethyl acetal (*XVIII*). To a slurry of 57 g of $LiAlH_4$ (1.5 mol) in 1 l of ether kept under a slow stream of N_2 a solution of 131 g of XVII (0.5 mol) was added dropwise at a rate sufficient to keep the ether refluxing. After the first vigorous reaction had subsided the reaction mixture was heated under reflux overnight. The excess $LiAlH_4$ was destroyed by careful addition of 250 ml of water and then carbon dioxide was bubbled through the slurry for 2 h to hydrolyze the salts. The slurry was filtered and the salts washed repeatedly with ether and ethanol. The collected filtrates were freed from solvents by evaporation and the residual oil distilled under high vacuum in a "Kugelrohr". Yield 76.8 g (86 %) of b.p.$_{0.04}$ 120–140°. (Found: C 53.91; H 10.36. Calc. for $C_8H_{18}O_4$: C 53.91; H 10.17.) The IR-spectrum, which bears a strong resemblance to those of the other hydroxyaldehyde acetals, is given in Fig. 1.

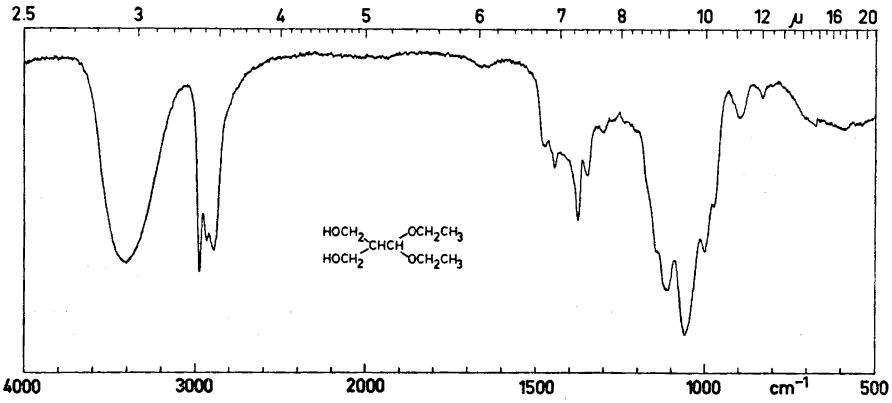


Fig. 1. IR-spectrum of 3-hydroxy-2-hydroxymethylpropanal diethyl acetal.

3-Hydroxy-2-hydroxymethylpropanal (*IV*). A solution of 0.5 g of XVIII in 10 ml of water was passed through a carefully washed, H^+-saturated ion exchange column, 80 × 1 cm, with water as eluent. The eluent was evaporated under reduced pressure and the residual oil dried over P_2O_5 under vacuum. The oil, which was soluble in water, gave

a correct analysis. (Found: C 46.02; H 7.87. Calc. for $C_4H_8O_3$: C 46.15; H 7.75.) However, this may be incidental, since the experience with the other hydroxyaldehydes was, that the extent of drying was decisive for the results obtained. Incomplete drying of course gave too low carbon contents, while extended drying gave too high carbon contents, probably because of dehydration or acetal formation with consequent loss of water. The IR-spectrum had no carbonyl peak, which indicates extensive formation of hemiacetals.

2,4-Dinitrophenylhydrazone of IV. To a solution of 840 mg of 2,4-dinitrophenylhydrazine (DNPH) in 20 ml of diethyleneglycol dimethyl ether (diglym) and 3 ml of acetic acid 810 mg of XVIII was added (*cf.* method of Shine [14]). After addition of 10 ml of water the solution was kept at 30° for 40 h. The yellow crystals formed were recrystallized twice from water – diglym 1 : 4 and dried over P_2O_5. M.p. 149 – 151°. (Found: C 42.35; H 4.15; N 19.77. Calc. for $C_{10}H_{12}N_4O_6$: C 42.26; H 4.26; N 19.71.) Generally it was found, that when the dinitrophenylhydrazones of the hydroxyaldehydes were recrystallized, the presence of solvents with six-membered ring molecules like benzene, cyclohexane and dioxane had to be avoided, since these solvents crystallized together with the aldehyde derivatives as evidenced by NMR-spectra and elemental analyses.

2-Hydroxymethyl-2-propenal diethyl acetal (XX). A mixture of 30 g of XVIII, 29.8 g of diethyl carbonate and 0.1 g of Na was kept at 50° in a flask, equipped with column and condenser, until all the metal had reacted and was then heated to boiling. The ethanol formed was distilled off and the residue was taken up in an equal volume of benzene, washed with 5 ml of brine and then dried over Na_2SO_4. 5-Diethoxymethyl-3-oxo-1,3-dioxane (XIX) could be obtained by distillation of this solution, but since a considerable amount of the carbonic ester formed seems to be present in oligomeric or polymeric form, a higher yield of XX is obtained in the following step if the crude product from the first step is used. After evaporation of the benzene an oil (33.8 g) was obtained, which was mixed with 6.5 g of KCN and gradually heated to 200° in a small flask, equipped with column and condenser. The acetal XX distilled off, carried by a slow stream of N_2. The crude distillate, which contained, among other impurities, a small amount of diethyl carbonate, was purified by vacuum distillation. Yield 15.4 g (57 %) of b.p.$_7$ 88°. (Found: C 59.67; H 10.20. Calc. for $C_8H_{16}O_3$: C 59.97; H 10.07.)

2-Hydroxymethyl-2-propenal (XXI). Hydrolysis of 3.6 g of XVIII in 10 ml of 0.05 M H_2SO_4 for 2 h gave a mixture which was carefully neutralized to pH 7.0 (measured with a pH-meter) with saturated aqueous $Ba(OH)_2$. The resulting solution was chromatographed on a silica gel column with acetone as eluent. The hydrolysis product IV lost water during the passage through the column and the fractions containing XXI were collected and evaporated. About 1 g of a colorless liquid, which gave an NMR-spectrum consistent with a monomeric structure but showing also the presence of a small amount of acetone as impurity, was obtained. When kept for a few hours, even at low temperature, the compound polymerized to give a clear resin, which gave an almost correct analysis. (Found: C 55.15; H 7.07; O 37.58. Calc. for $(C_4H_6O_2)_n$: C 55.81; H 7.03; O 37.17.) Dilute aqueous solutions of XXI were obtained by acid hydrolysis of XX. The carbon dioxide in the air was sufficient to cause complete hydrolysis over a week in a solution which was kept at room temperature. In kinetic runs the formation of XXI in solutions of XX in 10^{-4} M H_2SO_4 was followed by measuring the UV-absorbance maximum of the hydrolysis product (213.5 nm). The pseudo first order rate constant at 25.00° was obtained from a plot of $\log(\alpha_\infty - \alpha_t)$ against time. After dividing by the hydronium ion concentration, the second order rate constant 22.2 l sec^{-1} mol^{-1} was obtained. The absorbancy of XXI at 213.5 nm was determined to $10\,130 \pm 160$ l mol^{-1} cm^{-1}.

2,4-Dinitrophenylhydrazone of XXI. A solution of 2 g of XX in 15 ml of water was added to a solution of 5.1 g of DNPH in 80 ml of 65 % phosphoric acid. The crystals obtained after 30 min were filtered off and washed with water. Preparative thin layer chromatography on silica gel with $CH_3NO_2 - CH_3OH$ 20 : 1 as eluent gave red crystals of m.p. 181 – 183°. (Found: C 44.95; H 3.72; N 21.09. Calc. for $C_{10}H_{10}N_4O_5$: C 45.12; H 3.79; N 21.05.) This compound was obtained in the same manner from XVIII, but the crude product in this case contained a considerably larger proportion of the DNPH-derivative of IV.

Dimethyl dimethoxymethylmalonate (XXIII). To 500 ml of methanol 54 g of XVI and 1 g of Na were added. After stirring for 2 h at 50° the solution was neutralized with glacial acetic acid. The solvent was evaporated and the residue taken up in $CHCl_3$ and washed twice with water. After drying over Na_2SO_4 the solvent was evaporated and the

residual oil examined by VPC and NMR. The product was a mixture of about 75 % of XXIII and 25 % of compounds with one remaining ethoxy group. The treatment was repeated twice, after which the proportion of XXIII was over 98 % and the yield 45.8 g (89 %).

Dimethyl dimethoxymethylhydroxymethylmalonate (*XXIV*). A mixture of 175 g of ester XXIII, 34 g of dry paraformaldehyde (99 % CH_2O) and 10 g of K_2CO_3 in 600 ml of DMSO was stirred for 48 h at room temperature and then taken up in water. Repeated extraction with $CHCl_3$ gave a solution of XXIV, which was washed several times with water to remove the DMSO. After drying over $CaSO_4$ and evaporation of the solvent an oil (139 g; yield 70 %) was obtained, which slowly crystallized. Recrystallization from diisopropyl ether gave white crystals of m.p. 45 – 47°. (Found: C 45.76; H 6.74. Calc. for $C_9H_{16}O_7$: C 45.76; H 6.83.) NMR-spectrum (in $CDCl_3$) showed peaks at 2.93 – 3.15 ppm (triplet; CH_2OH), 3.60 ppm ($CH(OCH_3)_2$), 3.76 ppm ($COOCH_3$), 4.12 – 4.23 ppm (doublet; CH_2OH) and 4.98 ppm ($CH(OR)_2$).

2,2-Bis(hydroxymethyl)-3-hydroxypropanal dimethyl acetal (*XXV*). An ether solution of 11.8 g of XXIV was added dropwise to 4.75 g of $LiAlH_4$ in 1 l of ether. After reflux overnight excess $LiAlH_4$ was destroyed by careful addition of 20 g of KOH in 500 ml of water. After further addition of 14.8 g of K_2HPO_4 and 11.6 g of KH_2PO_4 in 50 ml of water, the resultant slurry was stirred for 2 h on a water bath at 50° whereafter most of the ether had distilled off. The mixture was neutralized with acetic acid, filtered and the filtrate evaporated to dryness under reduced pressure. The residue was extracted five times with acetone and the combined extracts on evaporation gave 5.5 g of an oil, which slowly crystallized (crude yield 62 %). Recrystallization from acetone – benzene 5 : 1 gave white crystals of m.p. 109 – 110°. (Found: C 46.70; H 8.90. Calc. for $C_7H_{16}O_5$: C 46.66; H 8.95.) NMR-spectrum showed singlets at (ppm upfield from the OH-peak) 0.00 ppm (OH), 0.21 ($CH(OCH_3)_2$), 1.03 (CH_2OH) and 1.13 ($CH(OCH_3)_2$) in D_2O.

2,2-Bis(hydroxymethyl)-3-hydroxypropanal (*V*). A solution of 1 g of XXV in 25 ml of 0.05 M H_2SO_4 was stirred at room temperature for 2 h and was then carefully neutralized to pH 7.0 with aqueous $Ba(OH)_2$. The resulting solution was filtered and evaporated under reduced pressure. The residual oil was crystallized from benzene – methanol 1 : 1. Recrystallization gave 410 mg of colorless crystals of m.p. 138 – 139° (lit.[2] 132 – 134°). (Found: C 44.54; H 7.53. Calc. for $C_5H_{10}O_4$: C 44.77; H 7.51.) Spectral data were in agreement with those reported [2] and showed that the free aldehyde is present only to a minor extent in D_2O-solution and not at all in the crystalline state.

2,4-Dinitrophenylhydrazone of V. A solution of 1 g of XXV in 25 ml of methanol – water 1 : 1 was added to 25 ml of a 0.25 M solution of DNPH in 85 % phosphoric acid – methanol 3 : 2. After 1 h the crystals obtained were filtered off and washed with methanol – water 1 : 1. Recrystallization from water gave yellow needles of m.p. 194 – 195° (lit.[2] 198 – 199°). (Found: C 42.04; H 4.50; N 17.92. Calc. for $C_{11}H_{14}N_4O_7$: C 42.04; H 4.49; N 17.83.)

Diethyl diethoxymethylmethylmalonate (*XXVII*). This compound was prepared in analogy with XVI from 1000 g of XXVI as starting material. Yield 472 g (30 %) of b.p.$_{0.03}$ 84°. (Found: C 56.35; H 8.82. Calc. for $C_{13}H_{24}O_6$: C 56.51; H 8.75.) About 60 % of the starting material was recovered unchanged.

3-Hydroxy-2-hydroxymethyl-2-methylpropanal diethyl acetal (*XXVIII*). The reduction of the ester XXVII was carried out in the same way as the reduction of XVII. Yield 86.2 g from 134.8 g of XXVII (92 %). (Found: C 56.31; H 10.69. Calc. for $C_9H_{20}O_4$: C 56.23; H 10.49.)

3-Hydroxy-2-hydroxymethyl-2-methylpropanal (*IX*) was prepared in the same way as V and was crystallized from benzene – methanol. The colorless crystals of m.p. 107 – 109° were obtained first after several weeks standing. (Found: C 50.77; H 8.48. Calc. for $C_5H_{10}O_3$: C 50.83; H 8.53.) The spectral properties were similar to those of V.

2,4-Dinitrophenylhydrazone of IX. This derivative was prepared in the same way as that of IV. Yellow crystals of m.p. 167 – 168°. (Found: C 44.40; H 4.83; N 18.77. Calc. for $C_{11}H_{14}N_4O_6$: C 44.30; H 4.73; N 18.78.) The IR-spectrum, which is representative for those of all of the DNPH-derivatives, is shown in Fig. 2.

Diethyl diethoxymethylethylmalonate (*XXX*). The preparation was analogous with that of XVI. Yield 238 g from 1000 g of XXIX (15 %). B.p.$_{0.03}$ 106°. (Found: C 58.17; H 9.09. Calc. for $C_{14}H_{26}O_6$: C 57.91; H 9.03.) More than 75 % of the starting material was recovered unchanged. NMR-spectrum is shown in Fig. 3.

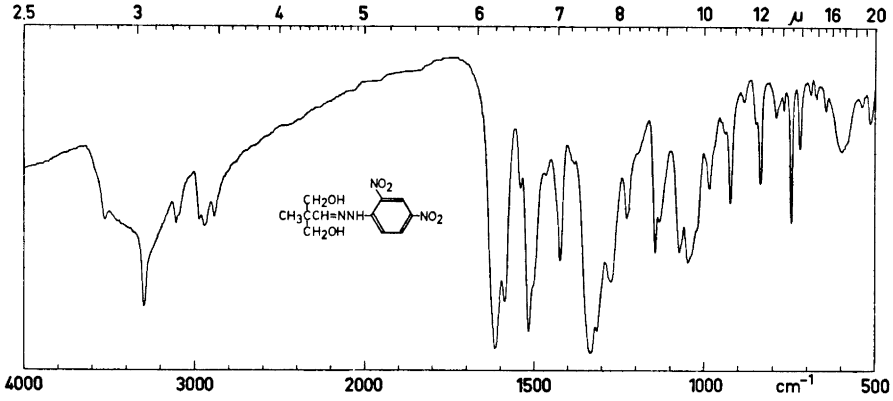


Fig. 2. IR-spectrum of 3-hydroxy-2-hydroxymethyl-2-methylpropanal 2,4-dinitrophenylhydrazone.

2-Ethyl-3-hydroxy-2-hydroxymethylpropanal diethyl acetal (*XXXI*). The reduction of XXX was carried out in the same way as that of XVII. Yield 60.5 g from 104 g of XXX (82 %). (Found: C 58.37; H 10.92. Calc. for $C_{10}H_{22}O_4$: C 58.23; H 10.75.) Attempts to obtain crystalline aldehyde XIII in the same way as V was obtained from XXV have failed so far.

2,4-Dinitrophenylhydrazone of XIII. This derivative was prepared in the same way as that of IV. Yellow crystals of m.p. 151 – 152° (lit.[4] 146 – 148°). (Found: C 46.25; H 5.16; N 17.94. Calc. for $C_{12}H_{16}N_4O_6$: C 46.15; H 5.16; N 17.94.)

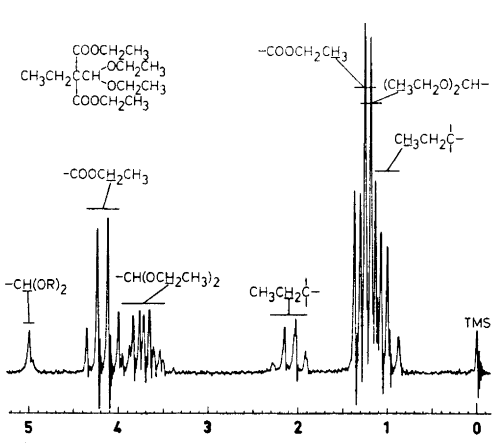


Fig. 3. NMR-spectrum of diethyl diethoxymethylethylmalonate.

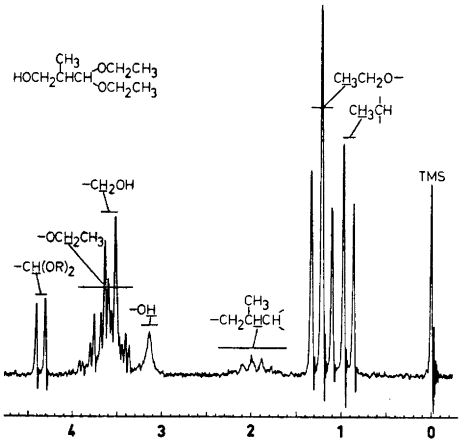


Fig. 4. NMR-spectrum of 3-hydroxy-2-methylpropanal diethyl acetal.

3-Hydroxy-2-methylpropanal diethyl acetal (*XXXII*). A stirred solution of 55.2 g of XXVII (0.2 mol) and 33.6 g of KOH (0.6 mol) in 1000 ml of 70 % ethanol was refluxed overnight. The bulk of the ethanol was then evaporated and replaced by water. Acidification to pH 5.0 with phosphoric acid caused evolution of CO_2 at room temperature. During

3 h N_2 was bubbled through the solution, which was then repeatedly extracted with $CHCl_3$. The combined extracts were washed once with a small amount of water and then dried over $CaSO_4$. Diazomethane in ether was added until the yellow colour of the reagent no longer vanished. Evaporation of the resulting solution gave 30.8 g of an oil, which was shown by VPC and NMR to contain about 90 % of methyl 3,3-diethoxy-2-methylpropionate. Reduction of this oil in the manner used for XVII gave 22.1 g of redistilled XXXII. Yield based on XXVII 68 %. (Found: C 59.43; H 11.37. Calc. for $C_8H_{18}O_3$: C 59.23; H 11.18.) NMR-spectrum is shown in Fig. 4.

2,4-Dinitrophenylhydrazone of VIII. This derivative was prepared in the same way as that of IV. Yellow crystals of m.p. 165–167°. (Found: C 44.71; H 4.51; N 20.99. Calc. for $C_{10}H_{12}N_4O_5$: C 44.78; H 4.51; N 20.89.) NMR-spectrum is shown in Fig. 5.

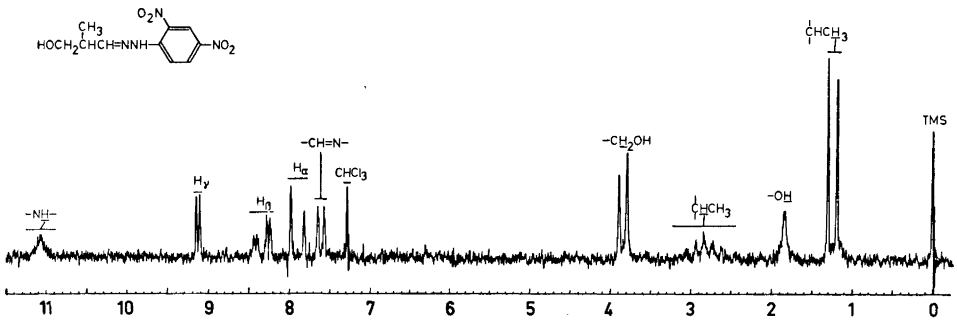


Fig. 5. NMR-spectrum of 3-hydroxy-2-methylpropanal 2,4-dinitrophenylhydrazone.

2-Ethyl-3-hydroxypropanal diethyl acetal (XXXIII). This compound was prepared in the manner used for XXXII from 25 g of XXX. Yield 10.8 g (71 %). (Found: C 61.18; H 11.28. Calc. for $C_9H_{20}O_3$: C 61.33; H 11.44.)

2,4-Dinitrophenylhydrazone of XII. This derivative was prepared in the same way as that of IV. Yellow crystals of m.p. 114–116°. (Found: C 46.73; H 4.98; N 19.56. Calc. for $C_{11}H_{14}N_4O_5$: C 46.81; H 5.00; N 19.85.)

Reduction of XVI. A solution of 54 g of the ester in 200 ml of ether was added to a solution of 10 g of $LiAlH_4$ in 800 ml of ether at room temperature. After 18 h stirring the mixture was worked up in a manner analogous to that used in the reduction of XVII. An oil was obtained (16.2 g), which on distillation gave 11.1 g of a compound identified by VPC and NMR as the ester XXVI. Yield 25 %.

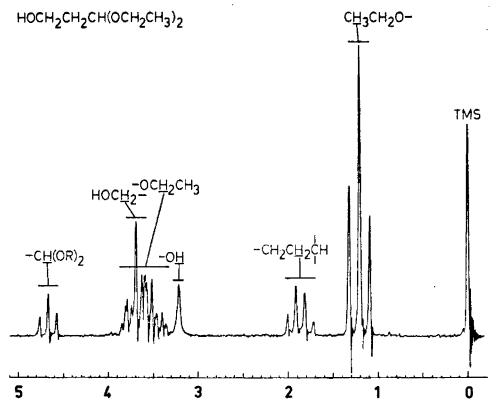


Fig. 6. NMR-spectrum of 3-hydroxypropanal diethyl acetal.

Ethyl 3,3-diethoxypropionate (XXXIV). This ester was prepared from acetylene and diethyl carbonate with sodium methoxide as condensing agent.[13] The crude mixture of XXXIV and the corresponding unsaturated ester, ethyl 3-ethoxy-2-propenoate, obtained was treated with sodium ethoxide in ethanol at 40°. After equilibration the mixture contained about 90 % of XXXIV as compared with about 50 % before this treatment. Pure XXXIV of $b.p._{0.6}$ 53° was obtained by distillation under vacuum.

3-Hydroxypropanal diethyl acetal (XXXV) was prepared by reduction of XXXIV (86.8 g) with 17.4 g of $LiAlH_4$ in 2 l of ether. The reaction mixture was worked up in analogy with the preparation of XVIII from XVII. Yield 61.0 g (90 %) of $b.p._{10}$ 90–92°. (Found: C 56.57; H 10.67. Calc. for $C_7H_{16}O_3$: C 56.73; H 10.88.) The compound has been reported earlier but not characterized.[15] NMR-spectrum is shown in Fig. 6. A preparation of crude acetal lost ethanol on standing under formation of a viscous, polymeric acetal, as indicated by NMR-spectrum of the residue after removal of distillable material. The monomeric acetal could be recovered, however, by treatment of the viscous polymer with ethanol, containing p-TsOH as catalyst, followed by careful neutralization and distillation.

2,4-Dinitrophenylhydrazone of III. This derivative was prepared in the same way as that of IV. Yellow crystals of m.p. 137–138°. (Found: C 42.26; H 3.94; N 21.94. Calc. for $C_9H_{10}N_4O_5$: C 42.53; H 3.97; N 22.04.)

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