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CHEMICAL AND SPECTROSCOPIC PROPERTIES OF 2-FORMYL-1,4-BENZODIOXANE AND 3-KETO-3,4-DIHYDRO-2H-1,5-BENZODIOXEPIN

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Abstract—2-Formyl-1,4-benzodioxane has been synthesized by an unambiguous route and proved different from the isomeric carbonyl compound, $C_9H_8O_3$, previously isolated in the course of alkaline permanganate oxidation of a 2-hydroxymethyl-1,4-benzodioxane preparation. On the basis of N.M.R. spectrum, the structure of 3-keto-3,4-dihydro-2H-1,5-benzodioxepin has been established for the isomeric $C_9H_8O_3$ compound. Evidence is given that the benzodioxepin originated by oxidation of 3-hydroxy-3,4-dihydro-2H-1,5-benzodioxepin originally present as impurity in the 2-hydroxy methyl-1,4-benzodioxane preparation. Chemical and spectroscopic properties of the two isomeric compounds are discussed.

2-HYDROXYMETHYL-1,4-BENZODIOXANE (I) can be oxidized with alkaline permanganate to give 1,4-benzodioxane-2-carboxylic acid (II) in moderate yield.[1] During oxidation of I, prepared from pyrocathechine and 1,3-dichloro-2-hydroxy-propane,[2] a small yield of a crystalline compound, $C_9H_8O_3$, was isolated.

This compound reveals in the I.R. spectrum (Fig. 3) a strong band in the carbonyl region at 1748 cm^{-1}, which suggests the presence of an aldehyde function.[3] The presence of the 1,4-benzodioxane ring-system is supported by the two bands at 1585 and 1493 cm^{-1}, which are characteristic of the C=C stretching vibrations of a disubstituted benzene ring carrying a di-ether function (Table 1).[4] The strong band at 1259 cm^{-1}, is associated with a =C—O—R grouping of an aryl ether.[5] However, in the region between 1000–800 cm^{-1} (where normally benzodioxane derivatives show at least three bands)[6] only two bands were observed.

A crystalline phenyl-hydrazone, 4-nitro-phenyl-hydrazone, 2,4-dinitro-phenyl-hydrazone and semicarbazone may be obtained from the carbonyl compound $C_9H_8O_3$. It reacts with methyl magnesium iodide to give a crystalline methyl carbinol $C_{10}H_{12}O_3$, reduces immediately both Fehling's and Tollen's reagents and gives a qualitative positive test, when treated with 5,5-dimethyl-cyclohexane-1,3-dione (methone), although a pure methone derivative could not be isolated. It is well known that aldehydes can be obtained by alkaline permanganate oxidation of primary alcohols.[7]

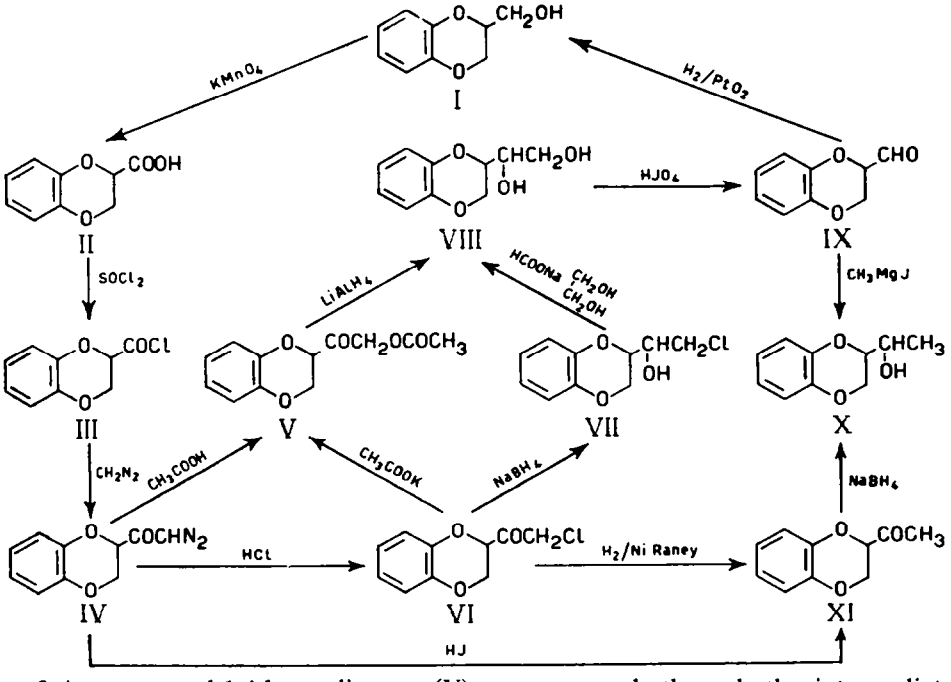
[1] J. Koo, S. Avakian and G. J. Martin, *J. Amer. Chem. Soc.* **77**, 5375 (1955).
[2] E. Fourneau, *J. Pharm. Chim.* 7, 98 (1910) prepared the same alcohol by condensation of pyrocathechine and epichlorohydrine. P. Maderni has briefly described the condensation with 1,3-dichloro-2-hydroxy-propane. Thèse à la Faculté des Sciences de l'Université de Paris: Contribution à l'étude des Sympathicolytiques de Synthèse, Paris (1934).
[3] L. J. Bellamy, *The Infra-red Spectra of Complex Molecules* p. 114. Methuen, London (1956).
[4] L. J. Bellamy, *The Infra-red Spectra of Complex Molecules* p. 60. Methuen, London (1956).
[5] L. J. Bellamy, *The Infra-red Spectra of Complex Molecules* p. 100. Methuen, London (1956).
[6] G. B. Marini-Bettolo, R. Landi Vittory and L. Paoloni, *Gazz. Chim. Ital.* **86**, 1336 (1956). See also Table 1.
[7] Houben-Weyl, *Methoden der Organischen Chemie* Vol. VII; p. 180. Thieme Verlag, Stuttgart (1954).

Therefore on the basis of the above chemical and spectroscopical findings, structure (IX) seems likely for the carbonyl compound $C_9H_8O_3$.

There are two facts, however, that require explanation: (a) the I.R. spectrum of this carbonyl compound does not show in the finger print region the general features expected of a benzodioxane derivative[6] and (b) catalytic hydrogenation does not give the expected 2-hydroxymethyl-1,4-benzodioxane, but a phenolic substance as yet unidentified.

As the 1,4-benzodioxane ring-system is known to be stable towards catalytic hydrogenation,[8] it seemed very unlikely that the presence of a —CHO group in position 2 would induce a facile cleavage of the phenoxy group. In fact, phenoxyacetaldehyde (structurally related to aldehyde (IX) by having a —CHO group α to the phenoxy group) does not undergo the catalytic hydrogenolysis of the ethereal linkage.[9] Consequently, the isolation of a phenol, by catalytic hydrogenation of the carbonyl compound $C_9H_8O_3$, is considered a definitive argument against the assignment of structure (IX).

As at this time, there was no indication that alcohol (I) contained an impurity, an unambiguous synthesis of the aldehyde (IX) was considered necessary. Its synthesis through the direct condensation of pyrocathechine and 1,2-dibromo-propionaldehyde diethyl acetal failed, as well as some other classical routes such as the Sommelet reaction, also in its modifications, and the Krönke reaction. Finally the aldehyde (IX) was synthesized by the reaction sequence illustrated in Chart I.



2-Acetoxyacetyl-1,4-benzodioxane (V) was prepared, through the intermediate diazo-keto (IV), by reacting the known acid chloride (III)[1] with diazomethane and

[8] C. Milani, R. Landi Vittory and G. B. Marini-Bettolo, *Rend. Ist. Sup. Sanità* XXII, 207 (1959); G. B. Marini-Bettolo, R. Landi Vittory, M. A. Jorio, F. Bovet-Nitti and O. Orsingher, *Ibid.* XXIII, 1110 (1960).

[9] K. W. Rosemund and F. Zetzschen, *Chem. Ber.* 56, 1481 (1923).

subsequent treatment with acetic acid. The same keto-ester (V) was then obtained more conveniently by reaction of the known 2-chloroacetyl-1,4-benzodioxane (VI)[10] with potassium acetate.

Lithium-aluminium hydride reduction of the keto-ester (V) gave 2(1′,2′-dihydroxy)-ethyl-1,4-benzodioxane (VIII) in moderate yield; the same diol was prepared in better yield by reacting the known chlorohydrin (VII)[10] with sodium formate in the presence of ethylene glycol.[11]

Finally, periodic acid oxidation of diol (VIII) gave the desired 2-formyl-1,4-benzodioxane (IX), the total yield starting from III being about 60 per cent.

The aldehyde thus prepared, is different from the carbonyl compound which had tentatively been assigned structure (IX). It is an oil having a pungent odour and the functional derivatives differ from those obtained from the isomeric compound. Its I.R. spectrum (Fig. 1) shows a band at 1742 cm^{-1} characteristic of the —CHO group, two bands at 1597 and 1493 cm^{-1} associated with the C=C stretching vibrations of the benzene ring carrying the ether function, a band at 1258 cm^{-1} due to the =C—O—R stretching vibrations, and three bands at 950, 927 and 849 cm^{-1} associated with the particular structure of the 1,4-benzodioxane ring-system.

Further proof that this is the aldehyde (IX) was obtained from the identity of the derived methyl carbinol and the one prepared by sodium borohydride reduction of 2-acetyl-1,4-benzodioxane (XI). The latter compound was obtained by either halogenolysis of the chloro-ketone (VI),[12] or by hydroiodic acid treatment of the diazo-ketone (IV).

The final proof that this compound is 2-formyl-1,4-benzodioxane was provided by its catalytic reduction to 2-hydroxymethyl-1,4-benzodioxane (I), all the products represented in Chart I being thus correlated with the starting material.

2-Formyl-1,4-benzodioxane shows interesting chemical and spectroscopic properties. At room temperature after a few days, the relatively mobile liquid becomes an oil of increasing viscosity. Then its I.R. spectrum shows that the band due to the aldehyde group is less intense, than in the spectrum recorded immediately after distillation. Also, the N.M.R. spectrum recorded after a few days standing (Fig. 2), shows that the peak due to the aldehyde hydrogen (0·25 p.p.m.)[13] has an area corresponding only to 0·4 H. This signifies that at the moment the N.M.R. spectrum was recorded, structure (IX) contributed only about 40 per cent. This is in agreement with the decrease in intensity of the aldehyde band observed in the I.R. spectrum. However, the area of the peak due to the four aromatic hydrogens (3·12 p.p.m.)[14] corresponds well to the expected value of 4 H. The quadruplet (5·42–5·70 p.p.m.) due to the resonance of the hydrogen attached to the —CHO group and of the methylene hydrogens, also shows an area in good agreement with the expected value of 3 H.

All these spectroscopic findings can be explained in terms of a partial polymerization of 2-formyl-1,4-benzodioxane, possibly giving a cyclic trimer similar to that of paraldehyde.

[10] V. Rosnati and F. De Marchi, *Gazz. chim. ital.* **61**, 605 (1961).
[11] B. T. Brooks and I. W. Humphrey, *J. Industr. Eng. Chem.* **9**, 750 (1917); Y. M. Beasley, V. Petrow, O. Stephenson and A. M. Wild, *J. Pharm. and Pharmacol.* **11**, 36 (1959); V. Petrow, O. Stephenson and A. M. Wild, *Ibid.* **12**, 45 (1960).
[12] V. Rosnati, D. Misiti and F. De Marchi, *Gazz. chim. ital.* In press.
[13] L. M. Jackman, *Applications of N.M.R. Spectroscopy in Organic Chemistry* p. 62. Pergamon Press, London (1959).
[14] P. L. Corio and B. P. Dailey, *J. Amer. Chem. Soc.* **78**, 3043 (1956).

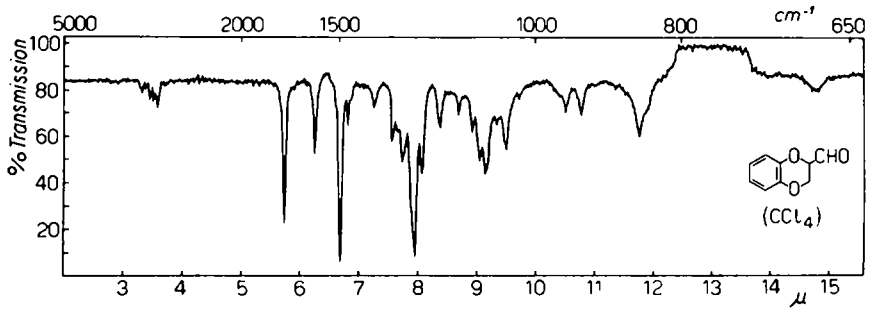


FIG. 1.

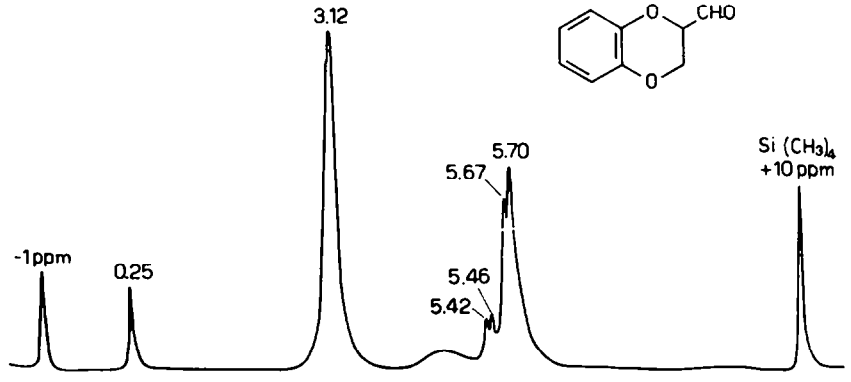


FIG. 2.

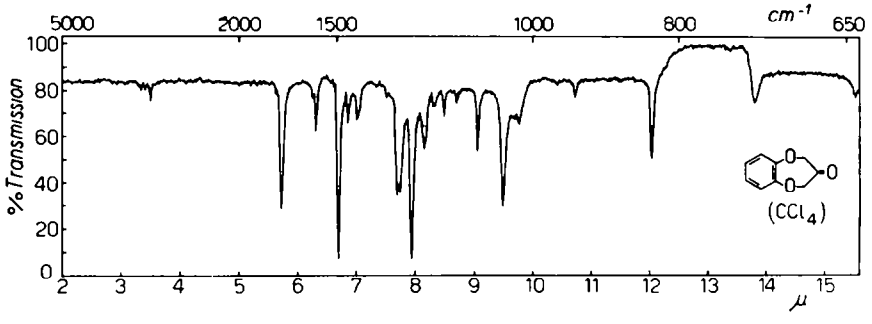


FIG. 3.

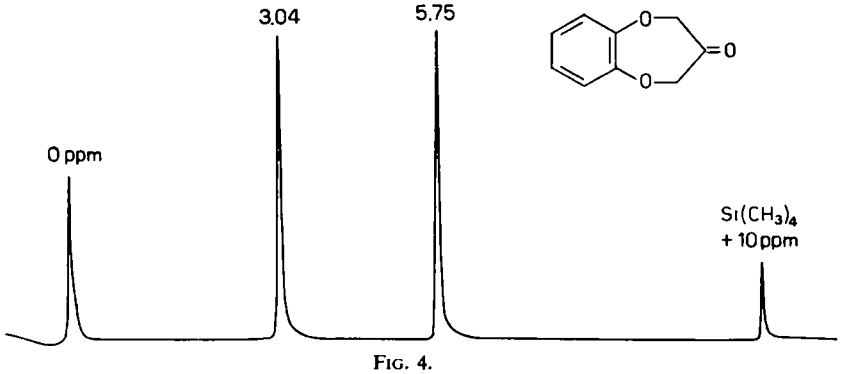
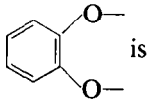


FIG. 4.

By heating, however, depolymerization occurs, since redistillation of the viscous oil gives a product which shows the same boiling point, mobility and I.R. spectrum of the original aldehyde (IX).

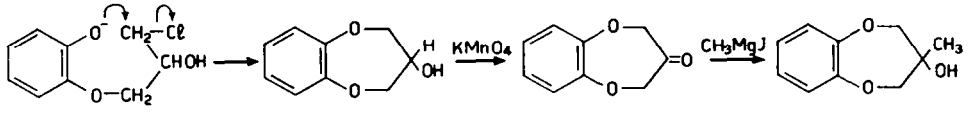
A different type of polymerization occurs, when 2-formyl-1,4-benzodioxane is treated with a trace of alkali; immediately a white amorphous polymer is formed, which shows in the I.R. spectrum a very weak band in the carbonyl region. This polymerization appears irreversible either by warming or by treatment with acids. The structure of the carbonyl compound $C_9H_8O_3$, isolated during the oxidation of alcohol (I), was finally established by the N.M.R. spectrum. (Fig. 4). It became evident, that the carbonyl-compound cannot be an aldehyde, since no peak is present in the lowest fields, where an aldehyde hydrogen should be detectable.[13] Instead, only two peaks are present in the spectrum: one at 3·04 p.p.m., due to the four equivalent aromatic hydrogens,[14] and the other at 5·75 p.p.m., which is associated with four equivalent aliphatic hydrogens.

Therefore, the carbonyl function is a keto-group. Since from the I.R. spectrum it is evident that the partial structure  is present, the incorporation of a keto-group, two extra carbon atoms, and four equivalent aliphatic hydrogens, can be interpreted only by the structure (XIII) of the unknown 3-keto-3,4-dihydro-2H-1,5-benzodioxepin.

The direct synthesis of this compound was tried by the following routes: condensation of pyrocathechine and 1,3-dichloro-acetone (or its diketal), Dieckmann reaction on ethyl phenylendioxy-diacetate, thermal decomposition of the lead salt of the phenylendioxy-diacetic acid. Unfortunately, only from the last reaction was a small quantity of compound (XIII) isolated and characterized as its semicarbazone. Finally, the structure of ketone (XIII) was definitely proved by Wolff-Kishner reduction of its semicarbazone to the known 3,4-dihydro-2H-1,5-benzodioxepin (XV).

Consequently, structure (XIV) of 3-methyl-3-hydroxy-3,4-dihydro-2H-1,5-benzodioxepin has been assigned to the methyl carbinol obtained from the reaction of ketone (XIII) with methyl-magnesium iodide.

The mechanism of formation of the benzodioxepin (XIII) can possibly be explained, by considering the method of preparation of the 2-hydroxymethyl-1,4-benzodioxane used in the oxidation reaction. As illustrated in Chart II, during the course of the alkaline condensation of pyrocathechine and 1,3-dichloro-2-hydroxy-propane, from



A XII XIII XIV

the same intermediate anion (A), alcohol (I) as well as alcohol (XII) may be formed; the former through the formation of an intermediate epoxide,[15] the latter directly by the seven membered ring closure, a chlorine anion being displaced. According to this view, ketone (XIII) is formed by the oxidation of some 3-hydroxy-3,4-dihydro-2H-1,5-benzodioxepin (XII) originally present as an impurity of alcohol (I). In fact, when the

[15] O. Stephenson, *J. Chem. Soc.* 1571 (1954).

oxidation is carried out on pure 2-hydroxymethyl-1,4-benzodioxane (prepared by lithium-aluminium hydride reduction of ethyl-1,4-benzodioxane-2-carboxylate)[16] no ketone (XIII) can be isolated.

In connection with the I.R. spectra of 3,4-dihydro-2H-1,5-benzodioxepins, no data are available in the literature. The frequencies of the most significant bands present in the spectra of three such benzodioxepins is summarized in Table 2. A comparison of these with the corresponding figures of a number of 1,4-benzodioxane derivatives (Table 1) results in the following observations:

TABLE 1. I.R. FREQUENCIES (cm^{-1}) OF SOME BANDS IN 1,4-BENZODIOXANE DERIVATIVES

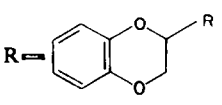
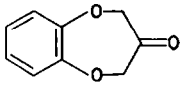
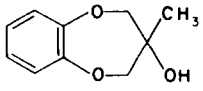
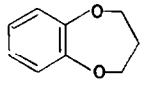
	Solvent	>C=C< Stretching vibrations	C=C—O—R Stretching vibrations	1000–800 cm^{-1}
H[5]	CCl_4	1594 1493	1250	928 893 833
CH_3	CCl_4	1603 1499	1250	997 938 926 874 845
CH_2OH	$CHCl_3$	1603 1499	1266	940 926 903 841
CHO	CCl_4	1597 1493	1258	950 927 849
COOH[16]	Nujol mull	1600 1497	1252	939 923 893 853 833
$CH(OH)CH_3$	$CHCl_3$	1600 1497	1266	926 909 875 852
$CH(OH)CH_2OH$	$CHCl_3$	1593 1493	1266	909 853 837
$CH(OH)CH_2Cl$[10]	$CHCl_3$	1603 1499	1271	939 918 862 852 838
$COCH_3$	$CHCl_3$	1605 1499	1271	963 927 916 903 857
$COCH_2Cl$[10]	$CHCl_3$	1603 1497	1261	920 902 844
$COCH_2OCOCH_3$	$CHCl_3$	1606 1499	1264	967 940 912 857

TABLE 2. I.R. FREQUENCIES (cm^{-1}) OF SOME BANDS IN 3,4-DIHYDRO-2H-1,5-BENZODIOXEPIN DERIVATIVES

Compound	Solvent	>C=C< Stretching vibrations	C=C—O—R Stretching vibrations	1000–800 cm^{-1}
 XIII	CCl_4	1597 1585 1493	1259	932 832
 XIV	$CHCl_3$	1597 1582 1493	1255	955 933 912 862 828
 XV	CCl_4	1595 1582 1493	1250	984 967 951 932 826

[16] A. W. Johnson, A. Langemann and J. Murray, *J. Chem. Soc.* 2136 (1953).

(a) In the case of benzodioxane derivatives, only two bands are present in the region of C=C stretching vibrations (Table 1); instead, in the case of the three benzodioxepins, in addition to these two bands, a third band appears at 1585–1582 cm^{-1};

(b) The strong band due to the stretching vibrations of the =C—O—R groupings is practically coincident in both molecules;

(c) In the region 1000–800 cm^{-1} benzodioxepins (XIV) and (XV) as well as all the benzodioxane derivatives, show several bands, which cannot be assumed to be characteristic of the ethylendioxy system of benzodioxane, as previously supposed;[6] in the case of benzodioxepin (XIII), the presence of only two bands in the above region can possibly be explained by the almost planar configuration of its seven membered ring, due to presence of the keto group.

EXPERIMENTAL*

2-*Acetoxyacetyl*-1,4-*benzodioxane* (V)

Method 1. 1,4-Benzodioxane-2-carboxylic acid chloride[1] (97 g) was dissolved in anhydrous ether (650 cc) and the solution added dropwise at 2–3° to a stirred ethereal solution of diazomethane prepared from 162 g of nitroso-methyl-urea.[17] After standing 12 hr, the ether was removed and the residue treated with acetic acid (250 cc). A vigorous reaction took place and when evolution of nitrogen ceased, the mixture was refluxed 1 hr. After removal of the solvent (red press), the oily residue was distilled *in vacuo*; the crude compound was obtained as a yellow oil (90 g; b.p. 133–138° at 0·3 mm). This product was purified chromatographically on an alumina column (elution: benzene–petrol ether 1:1); the pure compound boiled at 97–99° at 0·08 mm. (Found: C, 61·03; H, 5·12. $C_{12}H_{12}O_5$ requires: C, 61·01; H, 5·12%). *Infra-red absorption* ($CHCl_3$): 3030, 1765 (s), 1740 (s), 1606 (m), 1499 (vs), 1468, 1422, 1374, 1362 (m), 1309, 1289 (m), 1279 (s), 1264 (s), 1209 (s), 1193 (m), 1170 (m), 1153, 1119 (s), 1095 (m), 1073, 1052 (m), 1013, 967 (m), 940 (m), 912, 857 cm^{-1}.

Method 2. A solution of chloroketone VI[10] (18 g) and fused potassium acetate (16·5 g) in acetic acid (300 cc) was refluxed with stirring for 2 hr. After filtration and removal of the solvent (red press), the residue was taken up in ether and the solution dried over $CaCl_2$. After removal of the solvent, the residue was distilled *in vacuo*. The crude product obtained was a yellow oil (17 g; b.p. 103–110° at 0·1 mm), which upon redistillation gave pure V (b.p. 98–100° at 0·1 mm). (Found: C, 61·06; H, 5·05. $C_{12}H_{12}O_5$ requires: C, 61·01; H, 5·12%). Infra-red spectra of the compounds prepared with the methods 1 and 2 were identical.

2(1′,2′-*Dihydroxy*)-*ethyl*-1,4-*benzodioxane* (VIII)

Method 1. A stirred solution of VII[10] (18 g) and sodium formate (10·2 g) in ethylenic glycol (60 cc) was heated at 155° in a nitrogen atmosphere for 1·5 hr. After removal of the solvent (red press), the residue was treated with water (30 cc), exhaustively extracted with chloroform and the organic layer dried over Na_2SO_4. After removal of the solvent, the residue was distilled *in vacuo*. Compound VIII was obtained as a colourless oil (15 g; b.p. 145–148° at 0·09 mm). Upon redistillation it boiled at 125–127° at 0·06 mm. (Found: C, 61·24; H, 6·13. $C_{10}H_{12}O_4$ requires: C, 61·21; H, 6·17%). *Infra-red absorption* ($CHCl_3$): 3546 (m), 3390 (m), 2899, 2857, 1593 (m), 1493 (vs), 1465, 1302, 1266 (s), 1190, 1149, 1105, 1073 (s), 1042, 1016, 909, 853, 837 cm^{-1}.

Method 2. Compound V (33 g) dissolved in anhydrous ether (200 cc) was added slowly to a suspension of $LiAlH_4$ (13 g) in anhydrous ether (1000 cc). After refluxing for 5 hr, the reaction mixture was cooled and the excess $LiAlH_4$ was decomposed carefully by adding dropwise 40% NaOH. The ethereal layer was separated, dried over K_2CO_3 and the solvent removed. The oily residue was fractionated *in vacuo*. The first fraction (10·5 g; b.p. 80–95° at 0·015 mm) gave upon repeated redistillations a fraction boiling constantly at 90–92° at 0·06 mm. Its I.R. spectrum showed a band

(*) Melting and boiling points are uncorrected. Infra-red absorption spectra were recorded on a Perkin Elmer 21 spectrophotometer. N.M.R. spectra were recorded on a Varian Model U-4300B high-resolution spectrometer.

[17] *Organic Synthesis* Coll. vol. II; p. 165. John Wiley, New York (1948).

at 3610 cm^{-1} in the —OH region and no bands in the carbonyl region. (Found: C, 68·47; H, 6·76; O, 24·85%)*. The second fraction (10 g; b.p. 120–130° at 0·015 mm) consisted of the diol VIII, which showed after redistillation b.p. 124–126° at 0·05 mm. (Found: C, 61·30; H, 6·23. $C_{10}H_{12}O_4$ requires: C, 61·21; H, 6·17%). Infra-red spectra of the compounds prepared with the methods 1 and 2 were identical.

2-*Formyl*-1,4-*benzodioxane* (IX)

A solution of periodic acid (25 g) in water (100 cc) was added dropwise at 20–25° to a stirred solution of compound VIII (10 g) in a water-dioxane mixture 2:1 (150 cc). The reaction mixture was then treated with solid $NaHCO_3$ until neutral. After removal of the solvents (red. press), the residue was treated with water (10 cc) and exhaustively extracted with ether. The organic layer, washed with $Na_2S_2O_3$ solution, was dried over $CaCl_2$. Removal of the solvent gave an oily residue which was distilled *in vacuo*. Compound IX was obtained as a colourless oil (6 g; b.p. 64–67° at 0·02 mm). Upon redistillation it boiled at 63° at 0·09 mm. (Found: C, 65·68; H, 5·03. $C_9H_8O_3$ requires: C, 65·85; H, 4·91%). Infra-red and N.M.R. spectra: see Figs. 1 and 2.

4-*Nitro-phenyl-hydrazone:* m.p. 152–153° dec. from methanol. (Found: C, 60·30; H, 4·60; N, 14·04. $C_{15}H_{13}N_3O_4$ requires: C, 60·19; H, 4·38; N, 14·04%).

2,4-*Dinitro-phenyl-hydrazone:* m.p. 154–156° dec. from methanol. (Found: C, 52·58; H, 3·54; N, 16·46. $C_{15}H_{12}N_4O_6$ requires: C, 52·53; H, 3·51; N, 16·28%).

Semicarbazone: 183–185° dec. from ethanol. (Found: C, 54·35; H, 5·05; N, 18·88. $C_{10}H_{11}N_3O_3$ requires: C, 54·29; H, 5·01; N, 19·00%).

2-*Acetyl*-1,4-*benzodioxane* (XI)

Acid chloride III[1] (160 g) was dissolved in anhydrous ether (500 cc) and added dropwise at 2–3° to a stirred ethereal solution of diazomethane prepared from 200 g nitroso-methyl-urea.[17] After standing of 24 hr, the excess of diazomethane was removed (red press) and the residual solution treated carefully with 450 cc of 50% hydriodic acid. A vigorous reaction took place and, when evolution of nitrogen ceased, the ethereal solution was washed with diluted solutions of $Na_2S_2O_3$ and Na_2CO_3, with water and finally dried over Na_2SO_4. After removal of the solvent, the residue was fractionated *in vacuo*. The first fraction (104 g) was collected between 89–95° at 0·04 mm as a colourless oil, which on standing solidified completely. Repeated recrystallizations from hexane gave pure crystals of XI, m.p. 33°. (Found: C, 67·68; H, 5·45. $C_{10}H_{10}O_3$ requires: C, 67·40; H, 5·66%). *Infra-red absorption* ($CHCl_3$); 1734 (s), 1605 (m), 1499 (vs), 1471, 1420, 1362 (m), 1316, 1295 (m), 1271 (s), 1261 (s), 1244 (s), 1189, 1152, 1115 (m), 1096 (m), 1067, 1057, 1011, 963, 927, 916, 903, 857 (m), cm^{-1}. The second fraction (63 g; b.p. 150–160° at 0·1 mm) was a yellow oil, very difficult to be purified by repeated redistillations. (Found: C, 38·03; H, 3·52; I, 34·80. $C_{10}H_9IO_3$ requires: C, 39·50; H, 2·98; I, 41·75%). Its I.R. spectrum showed a band at 3446 cm^{-1} in the —OH region and no bands in the carbonyl region. Conclusive evidence that the above compound was 2(1′-*hydroxy*-2′-*iodo*)-*ethyl*-1,4 *benzodioxane* was obtained by its reaction with alkali, as follows. The second fraction (63 g) was dissolved in ethanol (180 cc) and treated at 10° with KOH (12 g) dissolved in ethanol (300 cc). After neutralization with CH_3COOH, the removal of the solvent (red press) left an oil which was taken up in ether. The ethereal layer was washed with water, dried over $CaCl_2$ and the solvent removed. The residue by distillation gave 2-*ethylen-oxide*-1,4-*benzodioxane* as a colourless oil (33 g; b.p. 90° at 0·07 mm). (Found: C, 67·15; H, 5·75. $C_{10}H_{10}O_3$ requires: C, 67·40; H, 5·66%). *Infra-red absorption* (CCl_4): 3030, 2959, 2899, 2857, 1595 (m), 1493 (vs), 1466, 1326, 1304, 1287 (m), 1266 (vs), 1255 (vs), 1239 (s), 1198, 1148, 1111, 1099, 1088, 1062, 1038, 947 (m), 924, 868 (m), 858, 828.

2(1′-*Hydroxy*)-*ethyl*-1,4-*benzodioxane* (X)

Method 1. A solution of IX (4·4 g) in ether (20 cc) was added dropwise to a stirred ethereal solution of methyl magnesium iodide prepared from methyl iodide (7 g). The mixture was refluxed for 3 hr and, after cooling, poured into ice and acidified with HCl. The organic layer, washed with $NaHCO_3$ solution and dried over Na_2SO_4, gave an oily residue, which was distilled *in vacuo*. Compound X was thus obtained as a colourless oil (4 g; b.p. 88–90° at 0·05 mm). After redistillation: b.p. 80–82° at 0·05 mm. (Found: C 66·73; H, 6·85. $C_{10}H_{12}O_3$ requires: C, 66·65; H, 6·71%).

(*) These data were correct for a molecular formula $C_{22}H_{36}O_6$, however this interpretation seems very improbable.

Infra-red absorption ($CHCl_3$): 3605, 2967, 2882, 1600 (m), 1497 (vs), 1469, 1401, 1383, 1305, 1294, 1266 (s), 1149, 1111, 1073 (m), 1047, 1033, 1016, 1000, 926, 909 (m), 875, 852 cm^{-1}.

Method 2. Sodium borohydride (1·2 g) was added cautiously at 15–20° to a stirred solution of 2-acetyl-1,4-benzodioxane (10 g) in methanol (50 cc). After 1 hr standing, the mixture was neutralized with acetic acid and the solvent removed (red press). The residue was treated with water (10 cc), then exhaustively extracted with ether and the organic layer dried over $CaCl_2$. After removal of the solvent, the oily residue was distilled *in vacuo*. Carbinol X (9 g) was collected between 100–102° at 0·12 mm. (Found: C, 66·47; H, 6·85. $C_{10}H_{12}O_3$ requires: C, 66·65; H, 6·71%). Infra-red spectra of the compounds prepared with the methods 1 and 2 were identical.

Catalytic reduction of 2-*formyl*-1,4-*benzodioxane*

A solution of the aldehyde IX (0·4 g) in ethanol (50 cc) was reduced in a Parr hydrogenator in the presence of 0·05 g platinum oxide. After filtration of the catalyst and removal of the solvent (red press), the residue was distilled *in vacuo*. 2-Hydroxymethyl-1,4-benzodioxane was obtained as a colourless oil (0·3 g; b.p. 90–95° at 0·03 mm; m.p. 84–86°). (Found: C, 64·82; H, 5·88. $C_9H_{10}O_3$ requires: C, 65·05; H, 6·07%). These crystals showed no depression on admixture with authentic 2-hydroxymethyl-1,4-benzodioxane. The infra-red spectra of both these samples were also identical.

3-*Keto*-3,4-*dihydro*-2H-1,5-*benzodioxepin* (XIII)

In a 10 l. flask fitted with a mechanical stirrer, separatory funnel, condenser, thermometer and a gas inlet tube, was placed pyrocathechine (1100 g) and, under a current of nitrogen, KOH 35% (3350 cc) was added. The mixture was gently heated at 100° and 1,3-dichloro-2-hydroxy-propane (1410 g) was added dropwise, in such a way to maintain a gentle boiling (3–4 hr). The heating was continued for 3–4 hr more, under the nitrogen current. The reaction mixture was then cooled to 60° and chloroform (2·5 l.) was added slowly. After cooling to room temp, the chloroform layer was separated, replaced by another 2·5 l. of chloroform and the mixture refluxed for 1 hr. The chloroform solutions were combined, exhaustively extracted with 20% NaOH, washed with water and dried over $CaCl_2$. After removal of the solvent, distillation of the residue gave 850–930 g of crude 2-hydroxymethyl-1,4-benzodioxane with b.p. 134–150° at 12 mm.

450 g of this material were suspended in 4% KOH (4200 cc) and $KMnO_4$ finely powdered (560 g) was slowly added at 4–5°, under stirring, during 3–4 hr. The alkaline solution was filtered from the MnO_2, from which about 180 g of the starting material were recovered by exhaustive extraction with methanol. Conc HCl (550 cc) was added dropwise at 20–25° to the filtered alkaline solution with stirring and the crude 1,4-benzodioxan-2-carboxylic acid was filtered (168 g; m.p. 108–120°). If the acid was added too quickly and the temp was not carefully maintained, a mixture of approximately equal amount of acid II and its potassium salt separated. In this case, the acid II was separated from the mixture by ether extraction, leaving a residue of *potassium* 1,4-*benzodioxan*-2-*carboxylate* (m.p. 198–202° dec. from ethanol). (Found: C, 49·80; H, 3·53. $C_9H_7KO_4$ requires: C, 49·53; H, 3·23%). The remaining mother-liquors were saturated with $(NH_4)_2SO_4$ and exhaustively extracted with ether. The combined ether layers were washed with conc Na_2CO_3 solution. The aqueous solution, upon subsequent acidification, gave a further amount of acid II (42 g). The remaining ether solution was dried over $CaCl_2$, the solvent removed and the residue fractionated *in vacuo*. Two fractions were collected; the first (23 g) between 78–92° at 0·1 mm, the second fraction (6·5 g) between 100–105° at 0·1 mm. The latter was identified as alcohol I by mixed m.p. and I.R. spectrum. The first fraction was a colourless oil, which on standing solidified completely. Crystallization from hexane gave crystals of 3-*keto*-3,4-*dihydro*-2H-1,5-*benzodioxepin* with m.p. 40–42°. (Found: C, 65·85; H, 4·91. $C_9H_8O_3$ requires: C, 65·84; H, 4·86%). I.R. and N.M.R. spectra: see Figs 3 and 4.

4-*Nitro-phenyl-hydrazone:* m.p. 210–211° dec. from ethanol (Found: C, 60·04; H, 4·34; N, 14·19. $C_{15}H_{13}N_3O_4$ requires: C, 60·19; H, 4·38; N, 14·04%).

2,4-*Dinitro-phenyl-hydrazone:* m.p. 164° dec. from methanol. (Found: C, 52·23; H, 3·35; N, 16·25. $C_{15}H_{12}N_4O_6$ requires: C, 52·53; H, 3·51; N, 16·28%).

Semicarbazone: m.p. 230–233° dec. from ethanol. (Found: C, 54·23; H, 5·24; N, 18·74. $C_{10}H_{11}N_3O_3$ requires: C, 54·29; H, 5·01; N, 19·00%).

3,4-*Dihydro*-2H-1,5-*benzodioxepin* (XV)

A mixture of semicarbazone of ketone XIII (3 g), potassium hydroxide (7·5 g), hydrazone hydrate (2 cc of a 90% solution) and diethylenglycol (75 cc) was heated at 160–170° for 1 hr. After distillation

of the fraction boiling under 120°, the reaction mixture was heated at 180–190° for 2 hr. After cooling, it was diluted with water (100 cc) and exhaustively extracted with ether. The combined ether layers were dried over $CaCl_2$ and the solvent removed. The oily residue by distillation gave 3,4-dihydro-2H-1,5-benzodioxepin as a colourless oil (1·5 g; b.p. 100–102° at 16 mm). (Found: C, 71·73; H, 6·68. Calc. for $C_9H_{10}O_2$: C, 71·98; H, 6·71%). Its I.R. spectrum was identical with the I.R. spectrum of an authentical sample of 3,4-dihydro-2H-1,5-benzodioxepin, prepared from pyrocathechine and 1,3-dibromo-propane.[18]

3-*Hydroxy*-3-*methyl*-3,4-*dihydro*-2H-1,5-*benzodioxepin* (XIV)

A solution of compound XIII (4 g) in ether (50 cc) was added dropwise to a stirred ethereal solution of methyl-magnesium iodide prepared from 4·5 g CH_3I. The mixture was refluxed for 1/2 hr, then cooled and treated with ice and conc HCl (3 cc). The ether layer was separated, washed with water and dried over Na_2SO_4. After removal of the solvent, the residue was purified by repeated crystallizations from benzene–hexane 1:3. Pure crystals (2·5 g) of XIV were obtained with m.p. 77–79°. (Found: C, 66·77; H, 6·60. $C_{10}H_{12}O_3$ requires: C, 66·65; H, 6·71%). *Infra-red absorption* ($CHCl_3$): 3546, 2933, 2899, 1597, 1582, 1493 (vs), 1453 (m), 1381, 1299 (s), 1255 (vs), 1239 (s), 1178 (m), 1160, 1149, 1120, 1098 (s), 1048 (s), 1042 (s), 1020 (s), 955, 933, 912 (m), 862, 828 (m).

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