Tetrahedron, 1966, Vol. 22, pp. 931 to 939. Pergamon Press Ltd. Printed in Northern Ireland

1,4-BENZODIOXINS—I

PREPARATION OF 1,4-BENZODIOXIN AND ITS 2-METHYL AND 2-PHENYL DERIVATIVES

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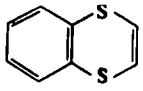
(*Received* 7 *September* 1965)

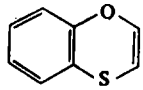
Abstract—1,4-Benzodioxin and its 2-phenyl derivative can be prepared by the dehydration of their respective 2-hydroxy compounds under suitable conditions. 2-Methyl-1,4-benzodioxin can be similarly prepared but is more readily obtained by the isomerization of 2-methylene-1,4-benzodioxan. The structures of these compounds have been authenticated by analysis, UV, PMR and IR spectroscopy and by hydrogenation experiments. 2-Hydroxy-1,4-benzodioxans are shown to exist as such rather than as their open-chain carbonyl tautomers. Previous descriptions of the preparation and structures of the above compounds are discussed.

INTRODUCTION

1,4-BENZODIOXINS are of interest because of possible electron delocalization in the hetero-ring. The corresponding dithia (I)[1] and oxathia (II)[2] compounds have been studied[3] and electrophilic substitutions have been observed to occur in the hetero-ring.



I



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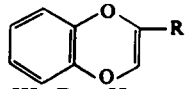
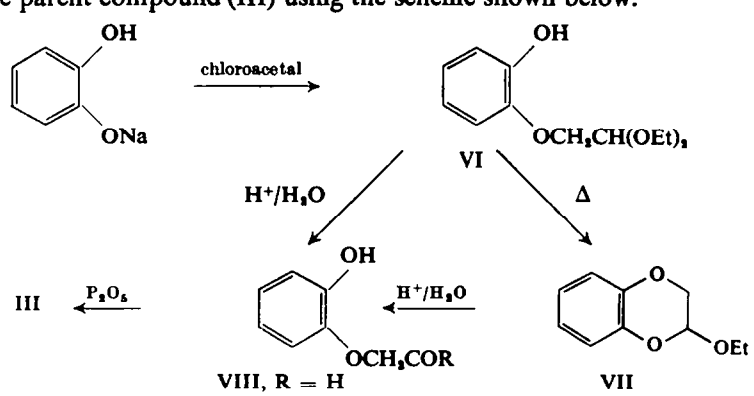


III, R = H
IV, R = CH_3
V, R = C_6H_5

1,4-Benzodioxins have only occasionally been reported in the literature. Moureu prepared[4] the parent compound (III) using the scheme shown below.



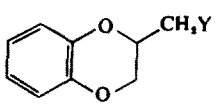
[1] W. E. Parham, T. M. Roder and W. R. Hasek, *J. Amer. Chem. Soc.* **75**, 1647 (1953).
[2] W. E. Parham and J. D. Jones, *J. Amer. Chem. Soc.* **76**, 1068 (1954).
[3] W. E. Parham and G. L. Willette, *J. Org. Chem.* **25**, 53 (1960).
[4] C. Moureu, *Bull. Soc. Chim. Fr.* **21**, 294 (1899); *C.R. Acad. Sci. Paris* **128**, 559 (1899); *Ann. Chim. Phys.* **18**, 76 (1899).

He reported that direct hydrolysis of the acetal (VI) to the compound ascribed structure VIII was much less efficient than the two-step preparation *via* the 2-ethoxy derivative (VII). Compound III was produced in unstated yield by the dehydration of VIII with phosphorus pentoxide in quinoline. Its preparation is not otherwise recorded in the literature.

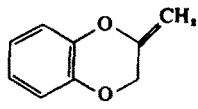
Moureu also claimed[5] to have prepared 2-methyl-1,4-benzodioxin (IV) by the dehydration of a compound considered to be *o*-hydroxyphenoxy acetone (IX) either with phosphorus pentoxide or with acetyl chloride in triethyl orthoformate. Compound IX was prepared directly from chloroacetone and the monosodium salt of catechol.

In 1909, Lazennec[6] prepared 2-phenyl-1,4-benzodioxin (V) by the carefully controlled thermal decomposition of a compound suggested to be ω-(*o*-hydroxyphenoxy)acetophenone (X). He failed to dehydrate this compound under the conditions described by Moureu for its methyl analogue.

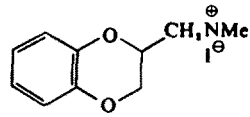
In 1956, Marini-Bettolo *et al.*[7] claimed to have prepared 2-methyl-1,4-benzodioxin by the action of ethanolic potassium hydroxide on 2-chloromethyl-1,4-benzodioxan (XI, Y = Cl). They also reported that the isomeric 2-methylene-1,4-benzodioxan (XII)



XI

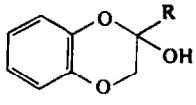


XII

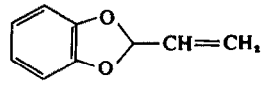


XIII

was produced by the alkaline decomposition of the quaternary salt (XIII). The hydrolysis of the "2-methylbenzodioxin" in aqueous hydrochloric acid gave a compound identical with that produced by the action of chloroacetone on the sodium salt of catechol and the Italian workers showed that this had the structure XV rather than the open-chain form IX.



XIV, R = H
XV, R = CH_3
XVI, R = C_6H_5



XVII

They also described the hydrogenation of the "methylbenzodioxin" to 2-methyl-1,4-benzodioxan (XI, Y = H) but reported neither the hydrogenation nor the hydrolysis of their claimed 2-methylene compound (XII). In 1957, the analogous preparation of 7-chloro-2-methyl-1,4-benzodioxin was described.[8]

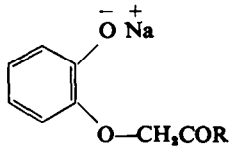
An initial report[9] of part of the present work indicated that the compound considered by the above workers to be the methylbenzodioxin (IV) was in fact XII while the isomeric compound obtained from the quaternary salt was 2-vinyl-1,3-benzodioxole (XVII).

[5] C. Moureu, *C.R. Acad. Sci. Paris* **128**, 670 (1899); *Ann. Chim. Phys.* **18**, 134 (1899).
[6] I. Lazennec, *Bull. Soc. Chim. Fr.* **5**, 509 (1909).
[7] G. B. Marini-Bettolo, R. Landi Vittory and L. Paolini, *Gazzetta* **86**, 1336 (1956).
[8] G. B. Marini-Bettolo and R. Landi Vittory, *Gazzetta* **87**, 1038 (1957).
[9] A. R. Katritzky, A. M. Monro, G. W. H. Potter, R. E. Reavill and M. J. Sewell, *Chem. Comm.* 58 (1965).

RESULTS AND DISCUSSION

1,4-*Benzodioxin*

We followed the preparation described[4] by Moureu but with two major modifications. (a) The reaction of the sodium salt of catechol with chloroacetal was found to proceed smoothly in dimethylsulphoxide at 85–90°, thus avoiding the repetitive use of sealed tubes and the lower yields obtained when the reaction was conducted in ethanol at 170°. The product was a mixture of the acetal (VI) and the ether (VII). (b) We found that hydrolysis of the mixture without further separation gave satisfactory yields of the compound claimed to be VIII. The erroneous suggestion that it was better to purify VII as an intermediate arose because insufficient time was allowed in the earlier work for the acetal to hydrolyse. We repeated this alternative procedure and obtained the identical compound. This compound was, however, found to exist as 2-hydroxy-1,4-benzodioxan (XIV) rather than as the open-chain tautomer (VIII), a result analogous to that reported[7] for the 2-methyl derivative. Thus the IR spectrum contained no $\nu_{C=O}$ absorption and the PMR spectrum confirmed the hydroxy form. The compound did however, as previously noted by Moureu, dissolve in aqueous alkali but was regenerated on acidification. We suggest that it gives the salt (XVIII)



XVIII, R = H
XIX, R = CH_3
XX, R = C_6H_5

of the open-chain tautomer in alkali; stronger evidence is adduced for a similar result with the 2-methyl and 2-phenyl derivatives discussed below.

Dehydration of the hydroxy compound with phosphorus pentoxide in quinoline gave only moderate yields of the benzodioxin but the use of thionyl chloride in pyridine, which is effective for both the 2-methyl and 2-phenyl compounds, led merely to extensive decomposition. The structure of the 1,4-benzodioxin was confirmed by elemental analysis, an IR spectrum showing $\nu_{C=C}$ at 1675 cm^{-1} and other characteristic bands as expected and the simple PMR spectrum showing only benzenoid protons with band centre at τ3·37 and a 2H singlet at τ4·25.

2-*Methyl*-1,4-*benzodioxin*

The preparation of this compound has been claimed[7] by the action of ethanolic potassium hydroxide on 2-chloromethyl-1,4-benzodioxan (XI, Y = Cl). We repeated this work, and our product had the properties as reported in the literature. An identical product was obtained from the 2-bromomethylbenzodioxan (XI, Y = Br) and, in better yield, by the action of potassium t-butoxide on 2-tosyloxymethyl-1,4-benzodioxan (XI, Y = tosyl) in t-butanol. PMR evidence (see below) showed conclusively that the compound was 2-methylene-1,4-benzodioxan (XII) which would also hydrogenate to 2-methyl-1,4-benzodioxan and hydrolyse to the 2-hydroxy compound (XV). Both these reactions were confirmed.

Treatment of the methylene compound with dry potassium t-butoxide in anhydrous dimethylsulphoxide gave an isomer in quantitative yield. This second compound

differed markedly (VPC, IR, UV, PMR, n_D etc.) from the methylene benzodioxan but gave the same products on hydrogenation and hydrolysis. It could thus only be 2-methyl-1,4-benzodioxin and this was confirmed by the IR spectrum containing a $\nu_{C=C}$ absorption at 1714 cm^{-1}, and the PMR spectrum. The methylene compound showed benzenoid protons at τ3·12, a singlet at τ5·70 due to the ring methylene group and an AB system with centres at τ5·30 and τ5·80 (J = 1·8c/s) arising from the terminal methylene group. The second isomer had aromatic proton resonance near τ3·30, a quartet at τ4·40 (J = 1·6 c/s) due to the hetero-ring proton and a doublet at τ8·47 (J = 1·6 c/s) due to the methyl group.

The isomerization of XII to IV is analogous to the known[10] conversion of allyl ethers to their vinyl isomers under similar conditions. The treatment of the 2-tosyl-

$$CH_2 = CH - CH_2 - OR \xrightarrow[DMSO]{KO^tBu} CH_3 - CH = CH - OR$$

oxymethylbenzodioxan directly with potassium t-butoxide in dimethyl sulphoxide gave a mixture of the two isomers presumably because the liberated toluene sulphonic acid makes the medium more ionic.

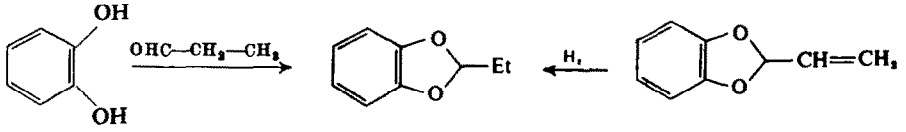
2-Hydroxy-2-methyl-1,4-benzodioxan (XV) was prepared (a) by hydrolysis of either of the two isomers above and (b) from chloroacetone and catechol.[7] Its structure was confirmed by the lack of a carbonyl absorption in the IR and by a PMR spectrum showing aromatic protons at τ3·08, an AB quartet centred at τ6·03 due to the two hetero-ring protons, a broad hydroxyl proton peak at τ6·54 and a singlet at τ8·43 arising from the methyl protons. The compound was reported,[7] without explanation, to be soluble in aqueous alkali. We produced an anhydrous sodium salt, by the interaction of equimolar amounts of aqueous sodium hydroxide and XV and subsequent evaporation of the water, and found that its IR spectrum showed a strong carbonyl absorption at 1730 cm^{-1}. The original compound can be recovered on acidification. We thus consider the salt to have the open-chain structure (XIX). The hydroxy compound also gives a semicarbazone which analyses as the derivative of the open chain form. (Moureu prepared[5] both an oxime and a phenylhydrazide and therefore considered the compound to exist in the carbonyl form.)

The hydroxyl compound was recovered unchanged after several attempts to dehydrate it with phosphorus pentoxide in quinoline.[5] The other reported procedure[5] using acetyl chloride in triethylorthoformate gave a mixture of several compounds. Removal of the phenolic components left a product evidently containing small amounts of both isomers IV and XII but the only product that could be isolated was 2-ethoxy-2-methyl-1,4-benzodioxan. Heating the hydroxy compound with sulphuric acid caused extensive pyrolysis and while dehydration did occur on heating in dimethyl sulphoxide at 160°, there was much concurrent decomposition. The best method of dehydration found was to reflux the compound with thionyl chloride in pyridine but the 2-methyl-1,4-benzodioxin obtained was contaminated by the isomeric methylene compound. The preparation of 2-methyl-1,4-benzodioxin by isomerization of the methylene compound as described above is far superior. A subsequent paper in this series will cover more fully the acid and alkali catalysed equilibrium and the relative stability of these two isomers.

The preparation of the compound produced[7] by the alkaline decomposition of the quaternary salt (XIII) was also repeated. The product was found to be isomeric with

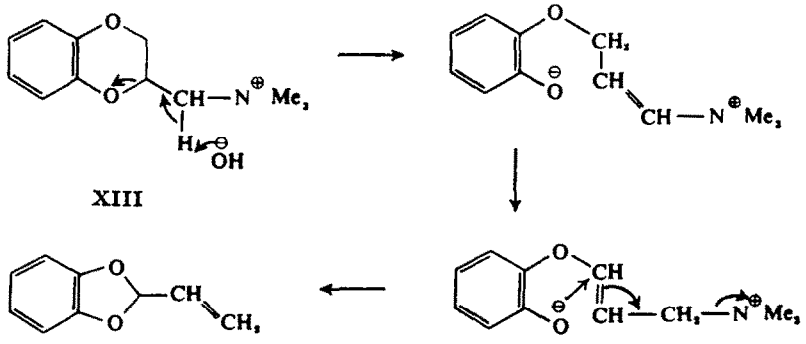
[10] J. Cunningham, R. Gigg and C. D. Warren, *Tetrahedron Letters* 1191 (1964); T. J. Prosser, *J. Amer. Chem. Soc.* **83**, 1701 (1961); C. C. Price and W. H. Synder, *Ibid.* **83**, 1773 (1961).

the two above but hydrogenation gave the previously unreported 2-ethyl-1,3-benzodioxole (XXI) as authenticated by an independent synthesis from catechol and propanal.



XXI XVII

That the compound produced in the quaternary salt decomposition was 2-vinyl-1,3-benzodioxole was confirmed by IR, UV and PMR results. The latter showed aromatic protons at τ3·30 and a complex multiplet, arising from the other four protons, from τ3·58–4·98. The IR showed a $\nu_{C=C}$ peak at 1625 cm^{-1}. The mechanism of the rearrangement of XIII to XVII is still under investigation but a plausible scheme is shown below.



XIII XVII

2-Phenyl-1,4-benzodioxin

2-Hydroxy-2-phenyl-1,4-benzodioxan (XVI) was prepared by the reaction of phenacyl bromide with the sodium salt of catechol. Its structure was confirmed by the absence of a carbonyl absorption in its IR spectrum and it thus does not exist as X as previously claimed.[6] Like its methyl analogue, the sodium salt does show a carbonyl absorption and doubtlessly exists in the open-chain structure (XX); the cyclized neutral form (XVI) can be recovered on acidification.

Dehydration of this hydroxy compound to the dioxin (V) was accomplished with thionyl chloride in pyridine. This method was found to be more satisfactory than thermal decomposition.[6] The compound obtained had a m.p. in agreement with that reported[6] by Lazennec and its structure was confirmed by elemental analysis and a $\nu_{C=C}$ absorption at 1680 cm^{-1} in the IR.

The reactions of the benzodioxins described above are being investigated and will be described in a later paper, together with a discussion of the possible aromatic character of the dioxin rings in these compounds.

EXPERIMENTAL

M.ps are uncorrected. IR spectra were measured as smears (liquids) or nujol mulls (solids) using a Perkin–Elmer 237 spectrometer. UV spectra were recorded as solutions in MeOH with a Perkin–Elmer 137 UV spectrophotometer. Proton chemical shifts are expressed in τ units and were measured

for the pure liquids, unless otherwise stated, with a Perkin–Elmer 40 Mc/s instrument using TMS as an internal reference. Analytical gas chromatography was performed on a Perkin–Elmer 452 chromatograph using a 10% Apiezon on Celite Column and preparative VPC separations were carried out on a silicone MS 710 on embacel column using a Wilkens Autoprep 700 instrument. Extracts were dried over anhydrous $MgSO_4$.

1,4-*Benzodioxin* (III)

2-*Hydroxy*-1,4-*benzodioxan* (XIV). A solution of NaOEt (produced from 13·8 g of Na dissolved in 260 ml of abs. EtOH) was added over 2 hr to a stirred solution of catechol (66 g) in refluxing EtOH (140 ml), the reaction being performed under dry O_2-free N_2. The EtOH was then distilled off and the remaining monosodium salt of catechol dried by heating under vacuum. The salt was dissolved in anhydrous dimethyl sulphoxide (400 ml) and chloroacetal (91·6 g) added while maintaining the N_2 atm. The mixture was kept at 85–90° for 70 hr, cooled and filtered. Addition of 3M HCl (200 ml) liberated a heavy oil which was extracted into ether. The ether extract was washed with water, dried and the ether evaporated. Distillation of the residue gave unreacted chloroacetal (18·0 g), b.p. 60–65°/14 mm, and a fraction (59·6 g), b.p. 90–158°/1 mm, which was shown (IR, PMR) to be a mixture of VII and VI. This mixture (referred to as A below) was refluxed for 20 hr with 12 g of conc. H_2SO_4 in 600 ml water. Steam distillation then allowed the removal of unchanged VII. The residual solution was extracted with ether (10 × 100 ml) and the total ether extract was washed with water, dried and the solvent evaporated. Distillation of the residue gave 2-hydroxy-1,4-benzodioxan, b.p. 108–110°/1·5 mm. (Moureu[5] listed b.p. 139°/9 mm for the compound that he considered to be the open-chain tautomer.) The yield was 28·35 g, ca. 40% based on chloroacetal consumed. (Found: C, 63·43; H, 5·43. $C_8H_8O_3$ requires: C, 63·15; H, 5·30%.) The IR spectrum showed a broad ν_{OH} absorption centered at 3400 cm^{-1}, aromatic ring modes at 1600 and 1500 cm^{-1} and a strong peak at 750 cm^{-1} indicative of an *ortho* substituted benzene derivative but no $\nu_{C=O}$ absorption. The PMR spectrum (10% in CCl_4) had peaks at 3·30 (4H), 4·72 (triplet, 1H), 6·20 (doublet, 2H) and a very broad hydroxyl proton resonance.

The compound could be extracted into 10% NaOHaq from an ethereal solution. Acidification of the extract liberated the compound which could be recovered by ether extraction and was identical (b.p., IR) with the original material.

The reaction of chloroacetal with the monosodium salt of catechol in EtOH at 170° under press.[5] gave lower yields and was unsatisfactory for large scale preparations. The use of a shorter hydrolysis time (15 hr) in the second part of the preparation above resulted in lower yields of the hydroxy compound with an increase in the amount of VII recovered. Hydrolysis of VII under similar conditions also gave XIV.

2-*Ethoxy*-1,4-*benzodioxan*. This was obtained: (a) By recovery from the steam distillate obtained from the hydrolysis mixture above; (b) By heating the mixture A to above 230°, thereby converting[5] VI into this compound with the liberation of EtOH; (c) By extracting the acetal from mixture A with 10% NaOHaq. It had b.p. 63–66°/0·1 mm, n_D^{23} 1·5245, Lit.[5], b.p. 119°/8 mm. (Found: C, 66·66; H, 6·79. Calc. for $C_{10}H_{12}O_3$: C, 66·65; H, 6·71%.) The IR spectrum had aromatic ring modes at 1600 and 1500 cm^{-1} and a peak at 750 cm^{-1} indicative of an *ortho* substituted benzene but containing neither ν_{OH} nor $\nu_{C=C}$ absorptions. The PMR spectrum (10% in CCl_4) had peaks at 3·20 (4H), 5·02 (triplet, 1H), 6·08 (doublet, 2H), 6·42 (quartet, 2H) and 8·79 (triplet, 3H).

1,4-*Benzodioxin*

2-Hydroxy-1,4-benzodioxan (21 g) was stirred (1 hr) under N_2 with P_2O_5 (23·4 g) in quinoline (63 g). The whole was then gradually warmed (oil-bath) to 70° and the apparatus then arranged for distillation under red. press. A fraction (ca. 50 ml) b.p. 112–125°/16 mm was collected and added to 4N HCl (150 ml) and ice (ca. 50 g). The organic material was extracted with ether (250 ml) and the extract was washed with water (2 × 100 ml) and dried. Distillation gave 2·72 g (15%) of the dioxin, b.p. 81–83°/16 mm, n_D^{23} 1·5473, Lit.[5], b.p. 76°/13 mm. (Found: C, 71·77; H, 4·70. Calc. for $C_8H_6O_2$; C, 71·64; H, 4·51%.) The IR spectrum showed a $\nu_{C=C}$ absorption at 1675 cm^{-1}, ν_{Ar} at 1600 and 1500 cm^{-1} and $\nu_{C_{Ar}-H}$ at 745 cm^{-1}. The PMR spectrum (10% in CCl_4) had only two peaks at 3·37 and 4·25 (singlet, 2H).

2-*Methyl*-1,4-*benzodioxin* (IV); 2-*Methylene*-1,4-*benzodioxan* (XII)

(a) *From* 2-*tosyloxymethyl*-1,4-*benzodioxan.* A solution of potassium t-butoxide (prepared by dissolving 10·0 g K in 350 ml t-butanol) was refluxed with the tosyl compound[11] (60·0 g) for 4 hr. The mixture was shaken with ether (500 ml) and water (1 l). The organic layer was separated, washed with water (3 × 200 ml) and dried. Distillation gave the *methylene compound* (23·9 g, 86%), b.p. 88–90°/18 mm (b.p. 213–214° at normal press. but with slight dec.) n_D^{19} 1·5630 (Marini-Bettolo *et al.*[7] give b.p. 70–76°/3 mm, n_D^{21} 1·5611 for the compound that they considered to be 2-methyl-1,4-benzodioxin). The compound was shown to be pure by VPC. It tends to polymerize above 200° or in contact with agents such as H_2SO_4 but can be steam distilled without dec. Its IR spectrum shows $\nu_{C=C}$ at 1670 cm^{-1}, ν_{Ar} at 1600 and 1500 cm^{-1} and $\nu_{C_{Ar}-H}$ at 750 cm^{-1} UV, λ_{max} 278 (ε = 2255) and 283 (ε = 1990) (Marini-Bettolo reported[7] λ_{max} 277·5 (ε = 2300) and 283 (ε = 2020) for his claimed methyl isomer). The PMR spectrum has peaks at 3·12 (aromatic protons), 5·70 (singlet, 2H) and ca. 5·55 (quartet, 2H).

Sodium t-butoxide was less satisfactory than the K-salt in the above preparation since larger volumes of t-butanol were required but the yield (76%) was comparable. The use of NaOH in EtOH caused predominant substitution. Thus the 2-tosyloxymethyl benzodioxan (26·2 g) was refluxed with a solution of the hydroxide (prepared from 13 g NaOH dissolved in 250 ml EtOH) for 3 hr. The mixture was poured into ice (1 l) and then extracted with ether (500 ml). The organic extract was dried and then distilled to give a fraction (1·5 g), b.p. 73–78°/1·5 mm, n_D^{21} 1·5578 containing (VPC) mainly the methylene compound and 6·25 g of 2-*ethoxymethyl*-1,4-*benzodioxan*, b.p. 98–103°/1·5 mm, n_D^{21} 1·5207. (Found: C, 68·09; H, 7·22. $C_{11}H_{14}O_3$ requires; C, 68·02; H, 7·27%.) The IR spectrum showed no $\nu_{C=C}$, $\nu_{C=O}$ or ν_{OH} absorptions.

(b) *From* 2-*halomethyl*-1,4-*benzodioxans.* The methylene benzodioxan was produced (ca. 32%) by the action of ethanolic KOH on 2-bromomethyl- or 2-chloromethyl-1,4-benzodioxan. Small amounts (3%) of 2-hydroxymethyl-1,4-benzodioxan, b.p. 82°/0·5 mm, m.p. 89–91·5° (from pet. ether, b.p. 60–80°) were also produced. This compound has IR identical with an authentic specimen. (The Italian workers[7] claimed to get 2-hydroxy-2-methyl-1,4-benzodioxan as a by-product.)

2-*Methyl*-1,4-*benzodioxin*

Anhydrous potassium t-butoxide (prepared from 0·3 g K in t-butanol and dried by heating under vacuum) and 2-methylene-1,4-benzodioxan (17·5 g) were reacted for 2 hr in anhydrous dimethyl sulphoxide (50 ml). The solution was added to water (250 ml) and extracted with ether (2 × 125 ml). The total ethereal extract was washed extensively with water (7 × 100 ml) and dried. Distillation gave 14·4 g of the *dioxin*, b.p. 87°/18 mm (b.p. 205–208° at normal press. with slight dec. n_D^{25} 1·5395. (Found: C, 72·93; H, 5·53. $C_9H_8O_2$ requires: C, 72·96; H, 5·44%.) The compound tends to polymerize above 200° or in the presence of agents such as H_2SO_4 but can be steam distilled unchanged. The IR spectrum shows $\nu_{C=C}$ at 1714 cm^{-1}, ν_{Ar} at 1602 and 1496 cm^{-1} and $\nu_{C_{Ar}-H}$ at 750 cm^{-1}. UV, λ_{max} 297 (ε = 1840). The PMR spectrum shows an aromatic proton resonance at 3·30, a peak at 4·40 (quartet, 1H) and at 8·47 (doublet, 3H). Moureu[5] listed b.p. 97–102°/18 mm for this compound but it probably contained some of the methylene isomer—see discussion. IR results show that the conversion is effectively quantitative.

The direct reaction of 2-tosyloxymethyl-1,4-benzodioxan with anhydrous potassium t-butoxide in dry dimethyl sulphoxide gave a mixture of the dioxin and its methylene isomer.

2-*Methyl*-1,4-*benzodioxan*

(a) *From* 2-*methylene*-1,4-*benzodioxan.* The compound (2 g) in EtOH (25 ml) was hydrogenated at room temp and press. over 10% Pd/C (0·2 g). The XI obtained (Y = H) had b.p. 33°/0·2 mm, $n_D^{24.5}$ 1·5314, UV λ_{max} 279 (ε = 2480) and 285 (ε = 2205), Lit.[7], b.p. 60–70°/0·2 mm, n_D^{25} 1·5331, λ_{max} 278 (ε = 2510), 284 (ε = 2180). (Found: C, 71·91; H, 6·85. Calc. for $C_9H_{10}O_2$: C, 71·98; H, 6·71%.) The IR spectrum was identical with that previously reported.[7]

(b) *From* 2-*methyl*-1,4-*benzodioxin.* Hydrogenation under identical conditions to those described in (a) gave the same product (VPC, IR, UV). 2-*Hydroxy*-2-*methyl*-1,4-*benzodioxan* (XV). (a) 2-Methylene-1,4-benzodioxan (2 g) was hydrolysed by refluxing for 4 hr with 5M HCl (7 ml). On

[11] J. Augstein, S. M. Green, A. M. Monro, G. W. H. Potter, C. R. Worthing and T. I. Wrigley, *J. Med. Chem.* **8**, 446 (1965).

cooling, the required compound crystallized out, m.p. 100° (from pet. ether, b.p. 60–80°), Lit.[7], 99°. The IR spectrum agreed with that reported[7] and the PMR spectrum (10% in $CDCl_3$) had peaks at 3·08, 6·03 (quartet, 2H), 6·54 (broad) and 8·43 (singlet, 3H).

Identical material was obtained by (b), hydrolysing 2-methyl-1,4-benzodioxin under the same conditions, (c) from the monosodium salt prepared from catechol (11 g) by refluxing with chloroacetone (9·25 g) as previously described.[7] The yield was 7·8 g, b.p., 135–145°/20 mm.

The compound was dissolved in the calculated quantity of NaOHaq and the water evaporated to yield the *sodium salt* (XIX), ν_{O-O} 1730 cm^{-1}. Acidification with HCl liberated the original compound which was recovered by ether extraction.

The compound also gave a semicarbazone, m.p. 155–157°, under normal conditions. (Found: C, 54·48; H, 5·88; H, 18·56. $C_{10}H_{13}N_3O_3$ requires: C, 53·80; H, 5·87; H, 18·83%.)

Dehydration of 2-hydroxy-2-methyl-1,4-benzodioxan

The compound (6·0 g) was refluxed for 1·5 hr with redistilled $SOCl_2$ (4·7 g) in pyridine (40ml). The mixture was added to ether (100 ml) and washed free of pyridine with 2M HCl. The ether extract was then washed with water, dried and the ether removed. Distillation gave a fraction (3·1 g), b.p. 85–90°/18 mm, which was shown (IR, VPC) to be a mixture of 2-methyl-1,4-benzodioxin (ca. 95%) and its methylene isomer (ca. 5%).

The hydroxy compound distilled at atm. press. without significant dec. while heating with conc. H_2SO_4 led to almost complete pyrolysis. Heating in dimethyl sulphoxide (7–48 hr) at 160° caused some dehydration to a mixture of IV and XII but yields were low and hard to purify. Attempts to eliminate water from XV using P_2O_5 in quinoline[5] under various conditions always left the compound unchanged (the IR showed no evidence for even traces of the required products). (Reaction of XV with acetyl chloride in triethylorthoformate proceeded exothermically as reported[6] but the material obtained contained several products (VPC).) Steam distillation from 10% aqueous alkali gave the non-phenolic fraction which contained (IR, VPC) small amounts of IV and XII. The only compound that could be isolated was 2-ethoxy-2-methyl-1,4-benzodioxan, b.p. 123–125°/15 mm, Lit.[5], b.p. 124–125°/15 mm. (Found: C, 68·11; H, 7·40; Calc. for $C_{11}H_{14}O_3$: C, 68·02; H, 7·27%.) There were no ν_{OH}, ν_{O-O} or $\nu_{O=O}$ absorptions in the IR spectrum. The PMR (10% in $CDCl_3$) showed peaks at 3·10, 6·25 (multiplet), 8·52 (singlet, 3H), 8·92 (triplet, 3H).

2-*Vinyl*-1,3-*benzodioxole* (XVII)

Treatment of 2-bromomethyl-1,4-benzodioxan with dimethylamine in an autoclave gave 2-(dimethylaminomethyl)-1,4-benzodioxan, b.p. 78–80°/0·01 mm, n_D^{20} 1·5278, Lit.[7], b.p. 112–114°/1 mm, n_D^{21} 1·5246. Methylation with MeI gave the quaternary salt (XIII), m.p. 207–209°, Lit., 214–215°[12]. (Found: I, 37·81. Calc. for $C_{12}H_{18}INO_2$: I, 37·87%.) Decomposition[7] of this salt with KOHaq gave the *vinyl compound*, b.p. 85–87°/14 mm, n_D^{26} 1·5330, UV λ_{max} 226 (ε = 3495) 283 (ε = 3430) (Marini-Bettolo *et al.*[7] reported b.p. 87–88°/14 mm, n_D^{22} 1·5330, UV λ_{max} 230 (ε = 3520) and 283 (ε = 3570) but considered the compound to be XII). The IR showed ν_{O-O} at 1625 cm^{-1} while the PMR spectrum had peaks at 3·30 and 3·58–4·98 (complex multiplet).

2-*Ethyl*-1,3-*benzodioxole*

(a) Hydrogenation of the vinyl compound above (2 g) by the method reported for the isomers above gave this *dioxole* (preparative VPC); b.p. 30°/0·3 mm, n_D^{24} 1·5107; UV λ_{max} 233 (ε = 3090), 284 (ε = 3565); PMR peaks (10% in $DCCl_3$) at 3·24 (singlet, 4H), 3·96 (triplet, 1H), 8·05 (complex multiplet, 2H) and 8·97 (triplet, 3H).

(b) The compound was also synthesized by refluxing catechol (11 g) and redistilled propanol (6 g) in benzene (100 ml) containing toluene-*p*-sulphonic acid (0·1 g) for 18 hr (the theoretical quantity of water was collected in a fitted Dean-Stark tube). The reaction mixture was shaken with 2N NaOH and the organic layer washed with water and dried. Distillation gave 1·9 g of colourless oil, b.p. 41°/0·5 mm, $n_D^{23.5}$ 1·5110, identical (VPC, IR) with the above. (Found: C, 71·24; H, 6·66. $C_9H_{10}O_2$ requires: C, 71·98; H, 6·71%.)

[12] M. W. Baines, D. B. Cobb, R. J. Eden, R. Fielden, J. N. Gardner, A. M. Roe, W. Tertiuk and G. L. Willey, *J. Med. Chem.*, **8**, 81 (1965).

2-*Phenyl*-1,4-*benzodioxin* (V)

2-*Hydroxy*-2-*phenyl*-1,4-*benzodioxan* (XVI). Sodium (4·6 g) was added to a solution of catechol (22 g) in EtOH (80 ml) under a N_2 atm. The temp. was controlled by use of an ice-water bath. After the evolution of H_2 had ceased, a solution of phenacyl bromide (39·8 g) in EtOH (100 ml) was added dropwise with stirring at room temp. Stirring was continued for a further 1 hr and the EtOH then partly evaporated. The mixture was filtered and the solid obtained recrystallized from benzene to give 18·6 g (40%) of the *compound* as white needles, m.p. 109·5–110°, Lit.[6], 111° for the compound reported to have the tautomeric open-chain structure. The IR shows ν_{OH} at ca. 3460 cm^{-1} but no $\nu_{C=O}$ absorption.

The Na-salt was prepared by stirring the compound with the calculated quantity of NaH in dimethyl sulphoxide, followed by evaporation of the solvent. It had $\nu_{C=O}$ 1700 cm^{-1}. The original compound was recovered on acidification.

2-*Phenyl*-1,4-*benzodioxin*. The 2-hydroxy derivative XVI (4·7 g) was refluxed for 5 hr with redistilled $SOCl_2$ (3·0 g) in pyridine (15 ml). The mixture was poured into 100 ml of ether and the pyridine removed by washing with 2N HCl. The ethereal extract was washed with water, dried and the ether was evaporated to leave the crude product as an oily solid. It was found to polymerize on attempted distillation under red. press. and was therefore purified by chromatography on alumina using ether as eluent. The compound (2·8 g) had m.p. 69° raised to 73° on recrystallization from 10% aqueous MeOH Lit.[6], m.p. 73°. (Found: C, 80·34; H, 4·96. Calc. for $C_{14}H_{10}O_2$: C, 79·98; H, 4·79%.) The IR showed $\nu_{C=O}$ 1680 cm^{-1}, ν_{Ar} 1600, 1498 cm^{-1} and $\nu_{C_{Ar}-H}$ 750 cm^{-1}. Dehydration by heating XVI in a vacuum as described by Lazennec[6] was found to be less satisfactory.

Acknowledgements—R. D. T. is grateful for the award of a Nuffield Travelling Fellowship, and M. J. S. for an S.R.C. Studentship. Thanks are due to Mr. J. Zoro for competent technical assistance.