Tetrasubstituted 2,5-Hydrofuranols and Their Anomerism[1]

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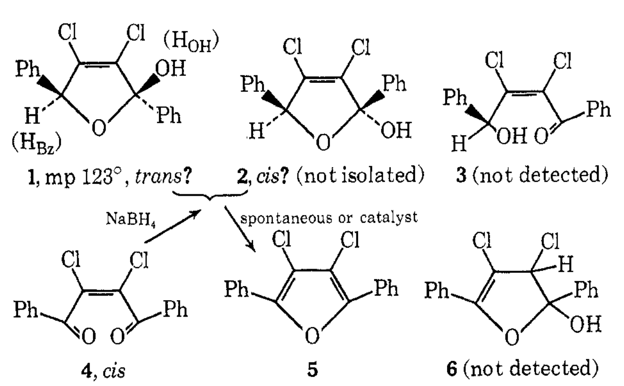
Four *cis*-2,3-disubstituted 1,4-diaryl-unsaturated 1,4 diketones were reduced by $NaBH_4$ to metastable 2,5-hydrofuranols. The solid 3,4-dichloro-2,5-diphenyl-2,5-hydrofuranol upon dissolving underwent equilibration within minutes between *cis* and *trans* forms. Detailed nmr study delineated solvent, concentration, and temperature effects. Reactions included facile dehydration to the furan and reduction by $NaBH_4$ to the *cis* unsaturated glycol. The stabilities of the hydrofuranols are related to the degrees of stabilization by substituents of the hydrofurylium ion intermediate to aromatization.

Many unsaturated 1,4-diketone reactions[4] such as the facile "*cis*-reductive-furanization"[4a] of dibenzoylstilbene by sodium borohydride and by phosphorus trichloride[4b] under conditions which are without effect upon the *trans* isomer, appear to be dependent upon *cis*-group interactions and participation involving cyclic transition states and intermediates such as the unstable 2,5-hydrofuranol **1**. Actual isolation of two metastable intermediates of this type have been reported, α-hydroxy-α,α'-diphenyldihydroisobenzofuran[5] and 2,5-di(*p*-bromophenyl)-3,4-diphenyl-2,5-hydrofuranol (**14**).[6]

Reduction of *cis*-dibenzoyldichloroethylene **4** by one-fourth molar equivalent of sodium borohydride followed by ice–water quench gave a single metastable crystalline compound which is one of the two possible anomers of 3,4-dichloro-2,5-diphenyl-2,5-hydrofuranol (**1**) (*trans*-dibenzoyldichloroethylene did not react under the same conditions). The second anomer **2** appears only in solution where equilibration occurs; it has not been isolated. These anomers are intramolecular hemiketals of the acyclic ketol **3** which may be involved or intermediate in the reduction of **4** and in the equilibration **1** $\rightleftharpoons$ **2** but which has not been isolated or detected in solution by spectral means.[7] The hydrofuranols **1** and **1** $\rightleftharpoons$ **2** underwent the expected slow spontaneous and rapid catalyzed elimination of water with aromatization to the furan **5**.



1, mp 123°, *trans*? **2**, *cis*? (not isolated) **3** (not detected)

4, *cis* **5** **6** (not detected)

That the product of borohydride reduction of **4** was indeed the hydrofuranol **1–2** was demonstrated by analysis and by ir, uv, and nmr spectra. The ir spectrum showed a moderately intense band at 1645 cm^{-1} attributable to a double bond bearing an electronegative substituent,[8] a hydroxyl band at 3450 cm^{-1}, and no carbonyl or enol ether group absorptions in the 1690- or 1640-cm^{-1} regions, respectively. That it was the 2,5- and not the conceivable 2,3-hydrofuranol **6** was established by its lack of uv absorption above 220 nm (**6** would have absorbed strongly at *ca.* 250 nm). The nmr spectrum observed immediately after solution (60 mg/0.4 ml of $CDCl_3$) showed a ten-proton aromatic multiplet at *ca.* δ 7.5, a benzyl proton singlet (H_{Bz}) at 5.75, and a hydroxylic proton singlet (H_{OH}) at 3.55, the latter shown to be hydroxylic by disappearance upon treatment with D_2O.

Equilibration of the *cis* and *trans* anomers 1 $\rightleftharpoons$ 2 was first noticed when nmr solutions of **1** in $CDCl_3$ (60 mg/0.4 ml) had been allowed to stand after spectral determination. Over 34 hr the benzylic proton-5 (H_{Bz}) singlet integrating for one proton (which was subsequently recognized as being composed of two overlapping singlets) slowly separated into and became two individual singlets very close together with total integration intensities of one proton. This separation of peaks was subsequently shown to be due to an unequal effect on the anomers of the change in solvent brought about by slow spontaneous generation of water accompanying furanization to **5**. This same separation of the one-proton H_{Bz} singlet into two singlets occurred *immediately* when a microdrop of water, D_2O, or DMSO-d_6[9] was added to a freshly prepared solution of **1** in pure $CDCl_3$.

That equilibration of the anomers **1** and **2** was indeed involved was shown as follows. The nmr spectrum of **1** in DMSO-d_6 at the low concentration of 10 mg/0.4 ml, observed *immediately* upon solution, showed a single benzylic proton peak at δ 5.96. A second peak then appeared upfield at δ 5.88 (for **2** H_{Bz}) which grew while the first peak diminished, until a constant peak integration ratio of *ca.* 1.5 for **1**/**2** was reached within 56 min. The first and stronger downfield peak must

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[1] Supported by research grants from the National Science Foundation.

[2] W. M. Hankins, Ph.D. Dissertation, University of Virginia, 1969.

[3] E. L. Anderson, M. S. Thesis, University of Virginia, 1964.

[4] (a) R. E. Lutz, C. R. Bauer, R. G. Lutz, and J. S. Gillespie, *J. Org. Chem.*, **20**, 218 (1955); (b) R. E. Lutz and W. J. Welstead, Jr., *J. Amer. Chem. Soc.*, **85**, 755 (1963); (c) R. E. Lutz and J. S. Gillespie, *ibid.*, 344 (1950); (d) *ibid.*, 2002 (1950).

[5] A. Guyot and J. Catel, *Bull. Soc. Chim. Fr.*, **35**, 1124 (1906).

[6] H. H. Freedman and G. A. Doorakian, *Tetrahedron*, **20**, 2181 (1964).

[7] *Cf.* examples of this type of interconversions: B. G. Hudson and R. Barker, *J. Org. Chem.*, **32**, 2101 (1967); B. Casu, M. Geggiani, G. G. Gallo, and A. Vigevani, *Tetrahedron Lett.*, No. 27, 2253 (1965).

[8] G. Eglinton in "Physical Methods in Organic Chemistry," J. C. P. Schwartz, Ed., Oliver and Boyd, Edinburgh and London, 1964, p 76.

[9] (a) Because of its strong hydrogen-bonding effect DMSO has been used in carbohydrate chemistry to lower the anomerization rate and thereby to make possible the detection and analysis of the anomers: B. Casu, *et al.*, *Tetrahedron*, **22**, 3061 (1966). *Cf.* also (b) O. L. Chapman and R. W. King, *J. Amer. Chem. Soc.*, **85**, 1256 (1964); (c) C. P. Rader, *ibid.*, **88**, 1713 (1966); (d) C. S. Springer and P. W. Meek, *J. Phys. Chem.*, **70**, 481 (1956); (e) R. J. Oulett, *J. Amer. Chem. Soc.*, **86**, 3089, 4378 (1964); (f) N. Bagett, *et al.*, *Chem. Ind. (London)*, 106 (1961); (g) Y. Aito, T. Matsuo, and C. Aso, *Bull. Chem. Soc. Jap.*, **40**, 130 (1967); (h) R. A. Newark and C. R. Cantor, *J. Amer. Chem. Soc.*, **90**, 510 (1968).

therefore represent the anomer of the solid state, **1**, and the smaller second and upfield peak therefore must represent the anomer **2** which has not been isolated. At the higher concentration of substrate of 60 mg in 0.4 ml of DMSO-d_6, a similar equilibrium ratio was reached but in the *much shorter time* of 15 min. This greater speed of equilibration in the more concentrated solution is presumably due in large part to increased catalysis by, or involving, the weakly acid substrate.

This same anomer equilibrium ratio of *ca.* 1.5 for **1**/**2** was attained in $CDCl_3$ more rapidly than in DMSO-d_6, but it was visible by nmr only at concentrations of substrate *less* than 60 mg in 0.4 ml of $CDCl_3$ At the concentration of 20 mg in 0.4 ml of $CDCl_3$, only the upfield and larger of the two anomer peaks of the mixture at equilibrium was seen immediately upon solution of the solid **1**; this peak integrated for one proton and necessarily corresponds to the isomer of the solid state **1**. The second peak (as was the second peak in $CDCl_3$) was the smaller of the two peaks at equilibrium and must represent **2**. In contrast to the case in DMSO-d_6, this second peak for **2** appeared *downfield* rather than upfield of the first, and within the very short time of 9 min it grew to about the same equilibrium ratio of *ca.* 1.5 for **1**/**2** with a total integrated intensity of one for the pair. Thus, the change in solvent from the polar DMSO-d_6 to $CDCl_3$ had reversed the relative positions of the two peaks, that of **1** from downfield to upfield of **2**.

The magnitude of the differences between the chemical shifts of the respective protons H_{Bz} and H_{OH} of the two anomers is of a very low order. Furthermore, the equilibrium ratios of **1** and **2** in the two aprotic solvents of widely different dielectric constants, DMSO and $CDCl_3$, are very similar. This indicates that the differences both in polarity and in thermodynamic stability of the anomers **1** and **2** are exceedingly small.[10]

Solvent effects on nmr chemical shifts are shown in Table I where the δ of H_{Bz} and H_{OH} were followed systematically in mixtures starting with pure $CDCl_3$ and ending with pure DMSO-d_6. Addition of the first microdrop of DMSO-d_6 to the $CDCl_3$ solution caused separation of the respective one-proton H_{Bz} and H_{OH} singlets into corresponding pairs of singlets. The larger peak of **1** was slightly upfield of the corresponding and smaller peaks of **2**, each pair integrating for one proton. With further dropwise addition of DMSO-d_6 to the $CDCl_3$ solution, the larger **1** H_{Bz} peak moved very slowly downfield, and, when the solvent ratio reached 0.67 for $CDCl_3$/DMSO-d_6, this larger **1** H_{Bz} peak crossed over the corresponding and smaller **2**-H_{Bz} peak which also had been moving downfield but more slowly. The total range of variations in the positions of the H_{Bz} signals was small, *ca.* δ 0.2.

When 4 drops of DMSO-d_6 had been added, the H_{Bz} and H_{OH} pairs of singlets merged into a two-proton multiplet as the faster moving H_{OH} pair of singlets crossed over the much slower moving H_{Bz} pair. At 5 drops of added DMSO-d_6, the **1** and **2** H_{OH} singlets merged in a crossover. And at 0.67 and lower for $CDCl_3$/DMSO-d_6, the **1** H_{OH} singlet appeared just downfield of the aromatic multiplet, whereas the **2** H_{OH} peak was under the aromatic multiplet. In going from pure $CDCl_3$ to pure DMSO-d_6, the H_{OH} δ of the anomers varied from *ca.* −0.1 to +0.6 and underwent drastic downfield shift of *ca.* δ 4.

TABLE I

SOLVENT EFFECTS ON NMR OF **1** AND **2** (60 mg/0.4 ml) IN $CDCl_3$–DMSO-d_6 MIXTURES[a]

	δ			
	H_{Bz}		H_{OH}[c]	
DMSO-d_6, drops[b]	**1**	**2**	**1**	**2**
0	5.76	5.76	3.67	3.67
1	5.80	5.86	4.27	4.37
3	5.79	5.88	5.46	5.55
4	5.8 (m, 2 H)[d]			
5	5.80	5.92	6.07 (s)[d]	
7	5.80	5.92	6.57	6.51
10	5.80	5.92	7.02	6.92
Vol %				
25	5.77	5.84	7.72	*e*
50	5.82	5.85	7.78	*e*
60	5.88 (s)[d]		7.83	*e*
75	5.91	5.87	7.84	*e*
100	5.96	5.88	7.90	*ca.* 7.3

[a] Assignments of δ values specifically to **1** or **2** are based on the near constancy of the equilibrium position (**1**/**2** = 1.5), on the assumption that the progression of these values is smooth, and on the specific demonstration above, that immediately upon solution of the solid **1** in both $CDCl_3$ (40 mg/40 ml) and in DMSO-d_6, only the solid-state isomer was initially present. Solvent samples were drawn from common batches. [b] Added to 0.4 ml of $CDCl_3$; wt of microdrop, 6.2 ± 0.1 mg. [c] Deleted by D_2O. [d] Crossover point. [e] The **1** H_{OH} δ value falls under the aromatic multiplet at *ca.* δ 7.46 in $CDCl_3$ and 7.2 in DMSO-d_6.

Dropwise addition of DMF or acetone to the equilibrium mixture in $CDCl_3$ produced changes in the nmr spectrum similar with those above except that acetone caused a significantly lower rate of downfield shift of the H_{OH} signals, which is understandable in terms of the expected lesser strength of hydrogen bonding with the substrate.[11]

Concentration Effects on Nmr (10–60 mg/0.4 ml).—In DMSO-d_6 the δ values for both **1** and **2** pairs of H_{Bz} and H_{OH} protons did not change significantly, which is consistent with the observation[9c] that the chemical shift of a number of alcohol hydroxyl protons in this solvent is independent of concentration below 0.12 mol fraction of solute. This indicates that in dilute solutions the relative population of hydrogen bonded species OH–DMSO does not change significantly.

In $CDCl_3$ the **1** H_{Bz} peak did not move, while the **2** H_{Bz} peak moved upfield (δ 0.08). On the other hand, the **1**–**2** H_{OH} broad singlet moved *downfield* (δ 0.2); furthermore, there was a very large increase in the broad infrared hydroxyl absorption at *ca.* 3425 cm^{-1}. These effects suggest markedly increasing association by intramolecular hydrogen bonding at higher concentration.[9]

The effect of temperature (34 to −20°) on nmr ($CDCl_3$ with DMSO-d_6) was to shift the signals progressively downfield, slightly for H_{Bz} (δ 0.07) and considerably for H_{OH} (δ 1.0). The H_{OH} shift was approximately linear (like that with cyclohexanol in DMSO-d_6[9c]) and comparable to the effect of addition of DMSO-d_6 at room temperature. At 0°, all of the **1**–**2** H_{Bz} and H_{OH} peaks were in a multiplet close to the solvent crossover point for the H_{Bz} and H_{OH} pairs of signals. At

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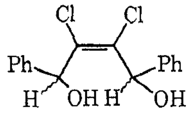
(10) *Cf.* The very dissimilar equilibrium constants of the *cis* and *trans* isomers of 2,3-dibenzoyl-1-benzylaziridine where *K* (*cis*/*trans*) varies greatly from 5.25 in DMSO to 0.32 in *t*-butyl alcohol: R. E. Lutz and A. B. Turner, *J. Org. Chem.*, **33**, 516 (1968).

(11) W. C. Drinkard and D. Kivelson, *J. Phys. Chem.*, **62**, 1494 (1958).

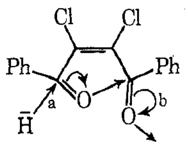
$-20°$, the H_{Bz} and H_{OH} signals were one-proton singlets. These results are consistent with supposition of exothermic hydrogen bonding.[9h]

Assignment of Configurations.—Consideration of Dreiding models, the very small effects of differences in polarity of the solvent, and the small but relatively constant equilibrium ratio K of *ca.* 1.5 for **1**/**2** suggest an overriding determinative importance of steric over polar factors. It seems reasonable, therefore, tentatively to assign the *trans* configuration to the more favored solid-state anomer **1**.

Reactions and Mechanisms.—Dehydration of **1**–**2** to furan **5** occurred slowly in chloroform, and rapidly in boiling glacial acetic acid and in moist ether containing iodine. Reduction by sodium borohydride gave only one of the diastereoisomeric *cis*-glycols **7** which was also obtainable in one step from the *cis* unsaturated diketone **4** by using an excess of borohydride. The structure of the glycol **7** was demonstrated by analysis and spectra; the broad ir bands (KBr) at 3600 and 3400 cm^{-1} indicated free and hydrogen-bonded OH groups; and the uv spectrum (EtOH) showed no absorption above 230 nm. The fact that one glycol only was obtained suggests involvement of a typical *cis* group proximity effect or participation which exerts a high degree of steric control over the configuration of the product, a very interesting subject for further study.



7 (*dl* or *meso*)



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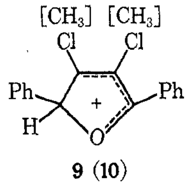
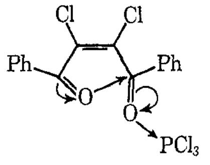


9 (**10**)



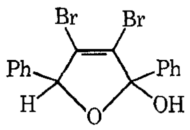
11 (→ $POCl_3$ + **5**)

Because the hydrofuranols **1**–**2** are the major products obtained upon borohydride reduction of the unsaturated diketone **4**, and because the reduction of **1** ⇌ **2** to the glycol requires an excess of borohydride, it can be said that there is a *cis*-group effect facilitating the first step in the reduction of **4** wherein the product is presumably stabilized to a very considerable extent in the intramolecular hemiketal forms **1** ⇌ **2**. The isolation of **1** as the chief product therefore supports the types of mechanism proposed earlier for borohydride "*cis*-reductive-furanizations" of unsaturated 1,4 diketones[4] the simplest of which is hydride attack at one carbonyl of **4** (**8**) with simultaneous or subsequent cyclization and protonation to the hydrofuranol.

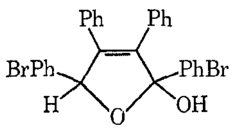
The furanizations of the hydrofuranols are presumed to require passage through hydrofurylium ions (**9**) where the inductive effects of the 3,4 halogens sufficiently destabilize this intermediate to lower the rate of dehydration and thereby to permit the isolation of the metastable intermediates. This principle should apply also in the reduction of the *cis*-2,3-dimethyl analog of **4** where several attempts have failed to yield the hydrofuranol and gave only the furan. In this case the intermediate 3,4-dimethyl cation **10** would be formed relatively easily from the 3,4-dimethyl analog of **1**–**2** because of stabilization of the positive charge by the electron-repelling methyl groups, and this would greatly facilitate the dehydration.

The reduction of the dichloro *cis* unsaturated diketone **4** to the furan **5** was accomplished in one step by refluxing phosphorus trichloride, conditions which were without effect on the *trans* isomer.[4b] This reduction is consistent with the assumption that facilitating *cis*-group interaction or participation is involved such as is depicted in **11**, which would not be possible with the *trans* isomer.[4b]

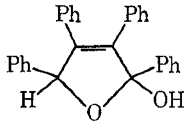
Other Hydrofuranols.—Several of these were made to show the generality of their formation and isolation where the structural setup is favorable, to test relative stabilities, and to determine whether the anomer equilibration in solution is generally involved. Like the dichlorohydrofuranol **1**, the 3,4-dibromo analog **12**[12] was easily made and isolated through borohydride reduction of the dibromo analog of *cis* unsaturated diketone **4**.[12] It was metastable as was **1**, and the anomer equilibration **12** ⇌ **13** in solution was demonstrated by nmr. The structure **12** is supported by analysis, spectral data, and reactions. Hot glacial acetic acid quickly converted it into the corresponding furan, and nmr tracking in $CDCl_3$ showed the spontaneous loss of water upon standing at a rate comparable with that of **1**–**2**. As with **1**–**2**, a series of nmr spectra in $CDCl_3$ with added increments of DMSO-d_6 showed separation of the H_{Bz} and H_{OH} one-proton singlets into two signals for each. In pure DMSO-d_6 the H_{Bz} signals for **12** and **13** were at δ 5.87 and 5.98, respectively, but for H_{OH} there was only a broad one-proton singlet at δ 7.8.



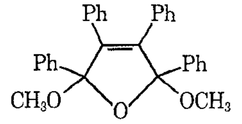
12, mp 129°, *trans*?
13, *cis* (not isolated)



14[6]



15, mp 161°, *trans*?
16, *cis* (not isolated)



17, **18**
cis, *trans*

3,4-Diphenyl-2,5-di-(*p*-bromophenyl)-2,5-hydrofuranol (**14**)[6] was remade by borohydride reduction of *cis*-di(*p*-bromobenzoyl)stilbene. Although moderately stable, it was somewhat less stable than **1** and **12** as shown by nmr tracking in $CDCl_3$. The ir spectrum of the hydrofuranol **14** displayed associated hydroxyl absorption at 3425 cm^{-1} but none for a carbonyl; its uv spectrum in ethanol was very similar to that of the cyclic diketal of the corresponding *cis* unsaturated diketone. The nmr spectrum in $CDCl_3$ contained six discrete lines: four peaks in the phenyl region (δ 7.1–7.5 integrating for 18 protons), and two singlets integrating for one proton each for H_{Bz} and H_{OH} at δ 6.35 and 3.45, respectively, the latter shown to be hydroxylic by disappearance upon addition of D_2O. Dropwise

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[12] The work on **12** was carried out by L. Hayes.

addition of 10 drops of DMSO-d_6 did not change the H_{Bz} peak position but did shift the H_{OH} peak rapidly downfield to δ 6.74, crossing over the nearly stationary H_{Bz} peak at 5 drops of DMSO-d_6. Using both the HA-100 and R-20 instruments, addition of DMSO-d_6 dropwise to a $CDCl_3$ solution of **14** (60 mg/0.4 ml) failed to bring about separation of either the H_{Bz} or H_{OH} peaks into a pair of peaks, as happened in the cases of **1** and **12**. Only the one sharp singlet each was observed for H_{Bz} and for H_{OH} in both solvents and at several concentrations.

2,3,4,5-Tetraphenyl-2,5-hydrofuranol (**15**) (not isolated in earlier attempts)[3,6] was prepared by borohydride reduction of *cis*-dibenzoylstilbene in methanol. It proved to be unstable and attempts to purify it always entailed partial spontaneous dehydration to tetraphenylfuran.[6] From the reaction solution a small amount of a mixture of the *cis* and *trans* cyclic diketals **17** and **18** was obtained and separated on a Florisil column; evidently these had been formed by reaction with the solvent in competition with reduction.

The hydrofuranol **15** was characterized by analysis and spectral data. The ir (KBr) showed broad hydroxyl absorption at *ca.* 3400 cm^{-1} and no carbonyl absorption. Nmr (60 mg/0.4 ml) in $CDCl_3$ showed two singlets, H_{OH} (eliminated by D_2O) at δ 3.46, and H_{Bz} at δ 6.35, and a 20-proton aromatic multiplet centered at *ca.* δ 7.2. Upon seven dropwise additions of DMSO-d_6 the H_{Bz} singlet was unchanged while the H_{OH} singlet moved downfield to δ 6.53. Only in pure DMSO-d_6 did there appear an anomer peak (corresponding to **16**); the H_{Bz} peak consisted of two separate peaks close together at δ 6.33 and 6.48 with total integration for one proton.

The hydrofuranol **15** was easily converted to tetraphenylfuran, spontaneously in solution, and rapidly by hot glacial acetic acid. It is relatively unstable compared with the 3,4-dihalo analogs **2** and **12**, but was not far different in stability from **14**. These stability differences are consistent with electronic and steric effects expected in the presumed intermediate carbonium ions of type **9**.

All of the four hydrofuranols studied were metastable. Nmr data show that three of them, **1**, **12**, and **15**, underwent anomer equilibration in solution but did not reveal anomerism in the *p*-dibromohydrofuranol **14**. This uniqueness of **14** might be explained by the effect of the *para* bromines in significantly increasing the polarity in the *cis* configuration, thus making the *trans* isomer relatively the more stable and predominent at equilibrium. However, it is not excluded that the *para* bromines have increased stabilization of the anomer intermediate and made equilibration too rapid to observe by nmr, or have diminished the differences in chemical shifts for the anomer signals and made them indistinguishable under the conditions and instrumentation used. Further studies in this field would be interesting.

Experimental Section[13]

3,4-Dichloro-2,5-diphenyl-2,5-hydrofuranol (1). Reduction of *cis*-2,3-Dichloro-1,2-dibenzoylethylene (4).—A solution of 52 mg of $NaBH_4$ in 19 ml of absolute methanol was added slowly to a stirred solution of 1.5 g of **4**[14] in 20 ml of absolute methanol at room temperature. After continued stirring for 15 min, addition of 1 ml of acetone, pouring into ice water, extracting with ether, and evaporating under reduced pressure at 40°, the product was dissolved in the minimum amount of benzene and chromatographed on 50 g of Florisil, eluting with petroleum pentane containing increasing percentages of benzene. Hydrofuranol **1** was in the 40–50% benzene effluent and was recrystallized from *n*-hexane to give 0.9 g (60%): mp 120–121°; ir ($CHCl_3$) 3425, 1645 cm^{-1}, no absorption in the region of 1690 cm^{-1}; λ_{EtOH}, no absorption above 220 nm; nmr (in $CDCl_3$, Table I) ten-proton aromatic multiplet at δ 7.5.

Anal. Calcd for $C_{16}H_{12}O_2Cl_2$: C, 62.56; H, 3.94. Found: C, 62.65; H, 4.26.

Dehydration of 1. Nmr Tracking of Spontaneous Dehydration in $CDCl_3$ (60 mg/0.4 ml).— The spectrum of a freshly prepared solution showed singlets for both H_{Bz} and H_{OH}. Over 24 hr at room temperature there was progressive separation of the H_{Bz} peak into a pair of peaks with total integration for one proton, but the H_{OH} singlet progressively broadened greatly and began to diminish in integrated intensity to *ca.* 0.75. Then diminution of the H_{Bz} peaks began and that of H_{OH} continued, the latter more rapidly until after 131 hr the H_{Bz} peaks had separated further and almost disappeared, and the broadened H_{OH} peak had completely disappeared.[15] The spectrum also showed a growing broad aromatic multiplet centered at δ 7.6 which was assigned to the *ortho* protons of furan **4** on the basis of a comparison with the nmr spectrum of pure **5**. Furthermore there was a growing peak at δ 4.8 assignable to water.

Dehydration of 1 (15 mg) in 0.5 ml of refluxing glacial acetic acid (5 min) and pouring the mixture into ice gave 12 mg of **5**, mp 94–95°. In another experiment a solution of **1** in moist ether containing iodine, after shaking for 5 min and evaporating, gave **5**.

Attempted autoxidations[5] of **1–2** were unsuccessful, unchanged material being recovered in which no carbonyl group impurities were detected by ir. Conditions: dry air bubbled through solutions of **1** in (a) ethanol (1 hr), (b) ethanol containing triethylamine (overnight), and (c) $CHCl_3$ containing benzoylperoxide.

Reduction of *cis*-1,2-dichloro-1,2-dibenzoylethylene (4) by PCl_3 (0.5 g in 50 ml), refluxing for 32 hr followed by hydrolysis in ice, chromatographing over Al_2O_3, and elution with 10% benzene–petroleum pentane gave 0.24 g of **5** (mp 91–93°) and 0.19 g of starting material (mp 66–68°). The *trans* isomer of **5** was recovered unchanged (86%) under these conditions.

1,4-Diphenyl-2,3-dichloro-2-butene-1,4-diol (7). A. By Borohydride Reduction of 5.—A stirred solution of 1 g of **5** in 25 ml of methanol was treated with a large excess of $NaBH_4$ (250 mg) in two portions (30 min). Pouring into water, extraction with ether, washing with water, drying over Na_2SO_4, evaporation, and crystallization from $CHCl_3$ gave 0.87 g of **7**, mp 139.5–141.5°.

B. By Borohydride Reduction of 1.—Compound **1** (100 mg in 10 ml of methanol), with excess $NaBH_4$ (25 mg), was worked up as above, and, after crystallization from *n*-hexane, gave 90 mg of **7**: mp 139–141°; ir (KBr) 3600, 3400 (broad), 1630 cm^{-1}, no absorption in the 1690-cm^{-1} region; λ_{EtOH}, no absorption above 230 nm; nmr ($CDCl_3$) δ *ca.* 7.4 (m, 10, aromatic), 6.2 (s, 2, CH–OH), 3.1 (hydroxyl envelope, 2, disappearing on treatment with D_2O).

Anal. Calcd for $C_{16}H_{14}Cl_2O_2$: C, 62.15; H, 4.56. Found: C, 62.42; H, 4.63.

3,4-Dibromo-2,5-diphenyl-2,5-hydrofuranol (12). Borohydride reduction of *cis*-dibenzoyldibromoethylene (0.4 g in 5 ml of CH_3OH by 1.6 mg of $NaBH_4$ in 5 ml of CH_3OH, 15 min), quenching in ice water, and recrystallization from hexane gave 0.2 g (50%) of **12**: mp 128–129°; ir (KBr) 3400 cm^{-1} (b, OH), none in 1650–1700-cm^{-1} region; $\lambda_{max}^{CHCl_3 \text{ or } EtOH}$, none above 220 nm. For nmr [60 mg/0.4 ml $CDCl_3$ + drops of DMSO-d_6 (wt per drop, 6.2 ± 0.1 mg)], see Table II.

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[13] Melting points were taken on a Thomas-Hoover apparatus (corrected), ir on a Perkin-Elmer 137 (KBr pellet), uv on a Perkin-Elmer 4000A Spectracord or Beckman DK-2, and nmr on a Varian A-60 and HA-100 and Hitachi Perkin-Elmer R-20, TMS. Identifications were by mixture melting point and/or ir.

[14] R. E. Lutz and F. N. Wilder, *J. Amer. Chem. Soc.*, **56**, 978, 2145 (1934).

[15] The observation that the loss of the H_{OH} resonance was faster than that of H_{Bz} during the spontaneous dehydration may be explained by proton exchange with DOH which is commonly present in $CDCl_3$. Trace amounts of DOH as impurity in $CDCl_3$ have been utilized to identify absorption bands from other OH groups which undergo slow reversible proton exchange with H_2O: J. Feeney and A. Henrich, *Chem. Commun.*, **10**, 295 (1966).

TABLE II

DMSO-d_6, +drops	δ			
	H_{Bz}		H_{OH}	
	12	**13**	**12**	**13**
0	5.85	5.85	3.53	3.53
1	5.84	5.87	4.51	4.61
2	5.83	5.90	5.49	5.58
3	5.82	5.90	6.28	6.28
4	5.82	5.90	6.75	6.68
Pure DMSO-d_6	5.98	5.87	7.8 (s, broad)	

Anal. Calcd for $C_{16}H_{12}Br_2O_2$: C, 48.48; H, 8.03. Found: C, 48.51; H, 3.19.

Dehydrations of **12**, and also **14** and **15**, to the corresponding furans were practically quantitative in warm glacial acetic acid (15 min).

2,3,4,5-Tetraphenyl-2,5-hydrofuranol (15). Borohydride reduction of *cis*-dibenzoylstilbene[3,6] (2.8 g in 200 ml of absolute methanol with 2 g of $NaBH_4$ warmed with stirring for 20 min), followed by ice-water quench, and crystallization from hexane gave 2.5 g of **15** (90%), mp 160-161°.

Anal. Calcd for $C_{28}H_{22}O_2$: C, 86.12; H, 5.69. Found: C, 86.01; H, 5.67.

Preparation of 2,5-di-(4-bromophenyl)-3,4-diphenyl-2,5-hydrofuranol (14) was done by $NaBH_4$ reduction of the *cis* unsaturated diketone[4b] (91%, recrystallized from hexane, mp 158-160°): ir (KBr) 3425 cm^{-1} (associated OH), none between 1650 and 1700 cm^{-1} (C=O).

Registry No.—**1**, 25244-40-0; **2**, 25244-41-1; **5**, 25244-42-2; **7**, 25244-43-3; **12**, 25244-44-4; **14**, 1888-40-0; **15**, 25244-46-6.

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Aldol Condensations of Leucoquinizarin

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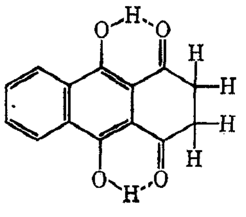
Hydrochloric acid was found to be an effective catalyst for condensation of leucoquinizarin with aromatic mono- and dialdehydes but ineffective with aliphatic aldehydes; monoaldehydes gave 2-alkylquinizarins; *o*-dialdehydes gave polycyclic compounds. Piperidinium acetate was found to be effective for both aliphatic and aromatic aldehydes. 2-Alkylleucoquinizarins likewise gave 2,3-dialkylquinizarins. They are presented in relationship to previously reported alkaline dithionite condensations. A mechanism is proposed in which the dehydration step is suggested to be rate determining.

Leucoquinizarin has been shown by proton magnetic resonance studies to exist, in solution, entirely as the diketo tautomer, 2,3-dihydro-9,10-dihydroxy-1,4-anthracenedione **1**.[1] This diphenolic diketone is known to undergo aldol condensations with aldehydes.



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Earlier workers[2,3] investigated the condensation of leucoquinizarin with aldehydes in alkaline dithionite solution under nitrogen at 90-95° and then allowed the products to interact with air. Under these conditions formaldehyde gave 2,3-dimethylquinizarin; however, other aliphatic aldehydes up to C_8 and aromatic aldehydes gave condensation products involving only one molecule of aldehyde per molecule of leucoquinizarin. Aldehydes above C_8 failed to give condensation products.

Marschalk, *et al.*,[2] were able to reduce 2-ethylquinizarin with dithionite and then to react the reduced product with formaldehyde; 2-ethyl-3-methylquinizarin was obtained. As will be shown later the failure of most aldehydes (except formaldehyde) to give 2,3-disubstituted products in the alkaline dithionite procedure cannot be attributed to steric hindrance of the monocondensation product, *i.e.*, 2-alkylquiniazrin.

Alkaline Dithionite Condensations.—In the present investigation, we repeated the condensation of leucoquinizarin with a large excess of butyraldehyde in alkaline dithionite and then followed the fate of the aldehyde.

Vapor phase chromatography revealed the absence of butyraldehyde at the end of the reaction; the only product isolated had one molecule of aldehyde per mole of quinizarin as observed by the previous investigators. We conclude that the alkaline dithionite procedure is not a general method for introducing two molecules of aldehyde in quinizarin owing to the competing self-condensation of aldehydes having α hydrogens. The observation that aldehydes above C_8 fail to react at all may simply reflect lack of solubility of these aldehydes in the reaction medium.

Aqueous Hydrochloric Acid Catalyzed Condensations.—We have studied the reactions of leucoquinizarin with a variety of aldehydes in 2-propanol using concentrated hydrochloric acid as catalyst with the following results. Aliphatic aldehydes[4] C_4 through C_{12} failed to give condensation products. This failure cannot be attributed to the destruction of the aldehyde prior to its condensation with leucoquinizarin, since, at least in the case of butyraldehyde, considerable excess of the aldehyde remained after a 20-hr reaction period. Aromatic monoaldehydes including those with electron-releasing and -withdrawing substituents gave condensation products **2**, **3**, **4**, **5**, involving one molecule of aldehyde per molecule of leucoquinizarin.

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[1] S. M. Bloom and R. H. Hulton, *Tetrahedron Lett.*, No. 28, 1993 (1963).

[2] Ch. Marschalk, F. Koenig, and N. Ouroussoff, *Bull. Soc. Chim., Fr.*, 1545 (1936).

[3] A. T. Peters, Jr., and A. T. Peters, *J. Chem. Soc.*, 1125 (1960).

[4] In the present investigation we were concerned only with aldehydes C_4 through C_{12}.