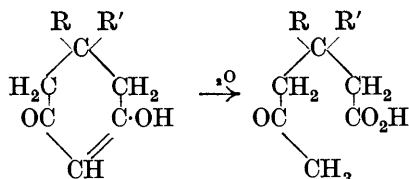


CXIV.—*The Intramolecular Strain in Substituted Dihydroresorcinols. Part I.*

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THE velocity of ring fission by hydrolysis has been employed in several instances as a measure of the stability of a cyclic system. Experiments on the velocity of hydrolysis of substituted hydantoins have been made by Ingold, Sako, and Thorpe (J., 1922, **121**, 1177) and of substituted glutarimides, succinimides, paraconic acids, and butyro- and valero-lactones by Sircar (J., 1927, 602, 1252, 1257; 1928, 898), for the purpose of examining the effect of substituents on ring stability from the standpoint of the valency deflexion hypothesis.

A dihydroresorcinol in alkaline solution exists in the keto-enol form and when subjected to alkaline hydrolysis undergoes ring fission at the double bond, forming a δ -keto-hexoic acid (Vorländer and Knotzsch, *Annalen*, 1897, **294**, 317).

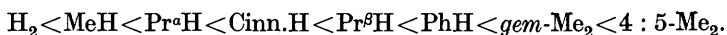


The dihydroresorcinols thus furnish an example of ring fission in a homocyclic system, contrasting with the compounds cited above, which are all heterocyclic systems. The intensity of strain in the double bond and hence the rate of ring fission will be influenced by the number and character of the substituent groups, since the strain in the cyclic system will be shared by the double bond.

Dihydroresorcinols in dilute ice-cold solution are oxidised readily by potassium permanganate solution, whereas under these conditions the δ -keto-hexoic acids are not appreciably attacked; consequently the course of hydrolysis can be followed by the use of this reagent.

The hydrolysis in the presence of a large excess of alkali becomes unimolecular, the velocity having been found to be independent of the initial concentration of the dihydroresorcinol. The velocity coefficient is therefore given by the expression $1/t \cdot \log_e a/(a-x)$, where a is the initial concentration of the dihydroresorcinol and $a-x$ the concentration after the time t . The volumes of potassium permanganate solution required to oxidise equal volumes initially and after a given time t are taken as measures of a and $a-x$ respectively.

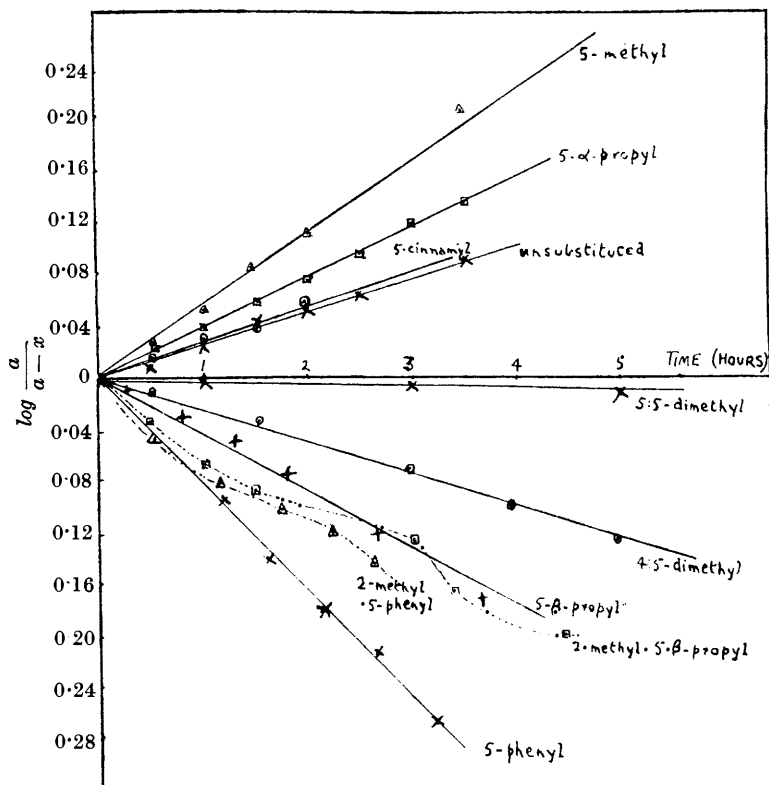
The hydrolysis of ten dihydroresorcinols with standard potassium hydroxide solution has been examined and when the results are expressed graphically, $\log a/(a - x)$ being plotted against t , eight of the compounds yield straight-line relationships, from which the values of the velocity coefficients of the compounds have been derived. The two exceptions contain substituents in the 2-position and will be considered later. The eight compounds which behave normally contain, with the exception of 4:5-dimethyldihydroresorcinol, only 5-substituents; and of the substituents studied, the spatial effects of the cinnamyl and phenyl groups have not hitherto been considered. The cinnamyl group is regarded as having an effect approximating to, but greater than, that of the *n*-propyl group, since it has a phenyl group in the place of the methyl group of the latter and, further, the unsaturated link will bring the sphere of influence of its β -carbon atom nearer to the cyclic system. The phenyl group is somewhat analogous to the isopropyl group, since with each a forked carbon chain is attached to the cyclic system, but the additional carbon atoms of the former, together with the spatial condensation of the nucleus, should give the phenyl group the greater spatial effect (compare $\text{Pr}^\alpha > \text{Et}$). With these additions to the normal sequence of the remaining substituents, taken from the series cited by Gane and Ingold (J., 1929, 1694), and placing the two dimethyl groups in accordance with the observation of Spiers and Thorpe (J., 1925, 127, 543), that two alkyl groups attached to different carbon atoms produce a greater effect on the dissociation constant of succinic acid than when attached to the same atom, the spatial influences of the substituents studied may be correlated as follows:



Comparison of this series with one showing the sequence of ease of rupture of the dihydroresorcinols (see experimental) appears to indicate some parallelism, but the results receive a more adequate explanation by the application of the principle of the attainment of a maximum stability (Dickens, Kon, and Thorpe, J., 1922, 121, 1499), as exemplified by the varying stability of substituted cyclobutadiones (compare Staudinger, *Ber.*, 1911, 44, 521).

In a dihydroresorcinol the system undergoing fission is a cyclohexenone nucleus and the stability of the six-membered ring is degraded by the presence of the cyclic and semicyclic double bonds, the latter appearing, from parachor measurements, to shift the position of maximum stability in the cycloketone series towards cycloheptanone (compare Mumford and Phillips, J., 1929, 2114). The cyclohexenone nucleus must therefore be regarded as possessing

a *positive* strain, *i.e.*, a tendency to open outwards, and substituents of increasing spatial influence should gradually relieve the strain until the optimum stability is reached. After this, substituents of greater spatial influence should lead to the appearance of an increasing *negative* strain. That such a negative strain can exist in a six-membered ring without necessarily being relieved by the assumption of a multiplanar strainless configuration is evident from the results



Hydrolysis of substituted dihydroresorcinols.

of Baker and Ingold (J., 1923, **123**, 122; compare Ingold and Thorpe, J., 1928, 1320) and from the recent demonstration by Rao (J., 1930, 1162) that the *cyclohexane* nucleus must possess appreciable strain.

In accordance with this hypothesis, the velocity coefficients of the methyl-, *n*-propyl-, and cinnamyl-dihydroresorcinols progressively diminish towards a minimum, which is found with the *gem*-dimethyl compound, this being followed by an increase with the 4 : 5-dimethyl compound. The coefficients for the remaining three dihydro-

resorcinsols, however, do not agree with conceptions based on the above spatial sequence, since they place the unsubstituted among the substituted and the *isopropyl* and phenyl above the dimethyl compounds, as shown in the following series :

	diminishing stability ←				→ diminishing stability			
Substituent:	MeH	Pr ^α H	Cinn.H	H ₂	<i>gem</i> -Me ₂	4 : 5-Me ₂	Pr ^β H	PhH
k.....	0.128	0.085	0.064	0.059	0.004	0.050	0.097	0.175

Whilst in this series the monosubstituted dihydroresorcinsols occur in the order anticipated from spatial considerations, they are displaced relatively to the unsubstituted compound, and the disubstituted relatively to the monosubstituted compounds. Similar displacements, although to a lesser degree, are postulated by Gane and Ingold (*loc. cit.*) in a series of substituted malonic acids, the internal polar influence of the alkyl groups acting as a disturbing influence on a series corresponding to the normal spatial relations. Although the compounds studied by Gane and Ingold and the measurements involved are very different from those examined here, this common feature suggests that polar influences may also be responsible for the apparent anomalies with the dihydroresorcinsols.

The hydrolysis of 2-methyl-5-*isopropyl*- and 2-methyl-5-*phenyl*-dihydroresorcinsols has also been studied. The reactions are characterised by the rapid intervention of secondary reactions not observed in the previous cases, but the initial velocities are greater than those of the corresponding *isopropyl* and phenyl compounds, in accordance with the demands of the valency deflexion hypothesis. The results obtained for these 2-methyl compounds indicate, as shown by the close approximation of the two curves in the graph, that the 2-methyl group exerts an influence largely outweighing the difference shown by the *isopropyl* and phenyl groups alone. These compounds also decompose on keeping in a manner analogous to that described for other compounds of this type (Vorländer and Erig, *Annalen*, 1897, **294**, 302; Becker and Thorpe, J., 1922, **121**, 1305; Mattar, Hastings, and Walker, J., 1930, 2457).

During the course of this investigation the following new compounds have been prepared: γ -methyl- Δ^{β} -penten- δ -one, 2-methyl-5-*isopropyl*- and 4 : 5-dimethyl-dihydroresorcinsols, the latter in two forms. 5-*n*-Propyl- and 2-methyl-5-*phenyl*-dihydroresorcinsols were obtained prior to the recent publications of Eccott and Linstead (J., 1930, 915) and Mattar, Hastings, and Walker (*loc. cit.*) respectively, both in better yield, the former being also obtained as its monohydrate.

EXPERIMENTAL.

γ -Methyl- Δ^{β} -penten- δ -one.—A solution of methyl ethyl ketone (265 g.) and acetaldehyde (150 g.) was cooled to -5° , saturated with

dry hydrogen chloride, and kept over-night. It was then washed with dilute sodium hydroxide solution, dried, and distilled. During distillation a rapid evolution of hydrogen chloride occurred, and in order to effect complete removal of this from the distillate the latter was boiled with quinoline. Fractionation of the distillate yielded γ -methyl- Δ^{β} -penten- δ -one, b. p. 138°, as a yellow liquid of peppermint odour (yield, 46%) (Found: C, 73.2; H, 10.3. $C_6H_{10}O$ requires C, 73.5; H, 10.2%). The *semicarbazone*, prepared in the usual manner, was obtained as colourless needles, m. p. 201° (decomp.) (Found: C, 53.9; H, 8.7. $C_7H_{13}ON_3$ requires C, 54.2; H, 8.4%). The *oxime*, prepared in the usual manner, was obtained as colourless needles, m. p. 75–76° (Found: N, 12.7. $C_6H_{11}ON$ requires N, 12.4%).

4 : 5-Dimethyldihydroresorcinol.—Molecular proportions of γ -methyl- Δ^{β} -penten- δ -one, ethyl malonate, and sodium ethoxide in alcohol were mixed and heated over a water-bath. The subsequent procedure adopted was similar to that described for 5-isopropyl-dihydroresorcinol by Crossley and Pratt (J., 1915, 107, 173). The oil obtained upon acidification of the dihydroresorcylic acid was extracted with ether. The residue obtained after evaporation of the ether was dissolved in acetone, and the solution evaporated under reduced pressure. This process of addition and removal of acetone was repeated until crystallisation began. The solid was removed from the accompanying tarry matter by treatment with hot water and was finally purified by crystallisation from acetone and subsequent washing with ethylene dibromide.

When the condensation was arrested after one hour, the final crystalline product consisted of colourless needles of the *monohydrate* of 4 : 5-dimethyldihydroresorcinol, m. p. 55° (Found: C, 60.9; H, 8.8. $C_8H_{12}O_2 \cdot H_2O$ requires C, 60.8; H, 8.9%). After standing in a vacuum over concentrated sulphuric acid, the anhydrous *dihydroresorcinol* was obtained, m. p. 68–70° (Found: C, 69.2; H, 8.5. $C_8H_{12}O_2$ requires C, 68.6; H, 8.6%).

When the condensation was continued for periods varying between 1 and 22 hours, the final product consisted of either the needles (described above) or a second form of 4 : 5-dimethyldihydroresorcinol, crystallising in colourless prisms, m. p. 109° (Found: C, 68.1; H, 8.8%). The latter compound was also obtained from ethylideneacetone and methylmalonic ester (yields in both preparations, less than 10%).

2-Methyl-5-isopropyldihydroresorcinol.—Molecular proportions of β -methyl- Δ^{γ} -hepten- ϵ -one (50 g.) (Thoms and Kahre, *Arch. Pharm.*, 1925, 263, 245), ethyl malonate, and sodium ethoxide in alcohol were condensed by heating over a water-bath for 7 hours. The

subsequent procedure was similar to that previously adopted and the product (29 g.; 43.5%), crystallised from aqueous acetone, yielded 2-methyl-5-isopropyl-dihydroresorcinol as white leaflets, m. p. 186° (Found: C, 71.2; H, 9.6. $C_{10}H_{16}O_2$ requires C, 71.4; H, 9.5%).

5-n-Propyl-dihydroresorcinol.—n-Butylideneacetone (18 g.), prepared by a slight modification of the method of Grignard and Dubien (*Ann. Chim.*, 1924, **2**, 287), was condensed with ethyl sodio-malonate by heating for 6 hours. The product, treated as before, crystallised from aqueous acetone, yielding 5-n-propyl-dihydroresorcinol monohydrate as colourless needles, m. p. 76° (Found: H_2O , 10.2. $C_9H_{14}O_2 \cdot H_2O$ requires H_2O , 10.5%), which on standing over concentrated sulphuric acid in a vacuum yielded the anhydrous compound, m. p. 107° (compare Eccott and Linstead, *loc. cit.*, who obtained a 16% yield, using sodium carbonate solution for hydrolysis of the resorcylic ester) (Found: C, 70.3; H, 9.2. Calc.: C, 70.1; H, 9.1%) (yield, 24%).

2-Methyl-5-phenyl-dihydroresorcinol.—Condensation of styryl ethyl ketone (Harries and Müller, *Ber.*, 1902, **35**, 966) was carried out by heating for 22 hours and employing the proportions and procedure previously adopted. Crystallisation of the product from aqueous alcohol yielded colourless prisms, m. p. 215° (Found: C, 76.9; H, 7.2. Calc.: C, 77.2; H, 6.9%) (yield, 80%).

This dihydroresorcinol (m. p. given as 212—213°) was obtained in 32% yield by Mattar, Hastings, and Walker (*loc. cit.*), who, however, employed the earlier method of hydrolysis of the resorcylic ester by means of alcoholic caustic potash instead of 10% aqueous alkali for a shorter time (compare Crossley and Pratt, *loc. cit.*).

Measurement of the Rates of Hydrolysis.—Standard solutions of the dihydroresorcinols were made by dissolving 0.0133 g.-mol. of the dihydroresorcinol in 100 c.c. of 3.91*N*-potassium hydroxide solution. Each solution was placed in a flask fitted with an upright condenser and the temperature was kept at 100° by means of a water-bath. During the hydrolysis a slow stream of nitrogen was passed through the solution to prevent secondary reactions due to atmospheric oxidation. Titrations were made normally at 0.5 hour intervals for the first 3 hours of the reaction, except for those compounds which hydrolyse very slowly. At suitable intervals 10 c.c. of the solution were withdrawn, diluted with 100 c.c. of iced water, acidified with 25 c.c. of 4*N*-sulphuric acid, and immediately titrated with 0.8*N*-potassium permanganate solution, the solution being kept at 0°. For the first half of the titration the oxidation was rapid. The end-point was denoted when a pink colour persisted in the solution for at least one minute after the addition of 0.2 c.c. of 0.8*N*- or 0.5 c.c.

of 0.2*N*-potassium permanganate solution, the latter strength being found preferable in the case of the unsubstituted dihydroresorcinol.

It was found necessary to modify the method of titration in the cases of the 5-cinnamyl-, 2-methyl-5-phenyl-, and 2-methyl-5-*iso*-propyl-dihydroresorcinols. With the cinnamyl and methyl-phenyl compounds the extracted solution was added to a litre of water, acidified, and titrated at room temperature; with the methyl-*iso*propyl compound the extracted solution was added to 500 c.c. of iced water, acidified, and titrated as before. 0.8*N*-Permanganate solution was used in each case.

The results obtained for the eight compounds which behave normally are summarised in the first table, *t* representing the duration of the experiment in hours, *n* the number of observations made, and *k* the mean value for the velocity coefficient derived from the rectilinear relationship obtained by plotting $\log a/(a - x)$ against *t*.

The results obtained for the two 2-methyl compounds are given more fully in the subsequent tables in order to indicate the resemblance between the results, *t*, *v*, and *k* representing the time in hours, the respective volume of permanganate solution required, and the corresponding value for the velocity coefficient respectively. In each case the initial velocity is greater than that of the corresponding compound without the 2-methyl group.

Dihydro-resorcinol.	<i>t</i> .	<i>n</i> .	<i>k</i> .	Dihydro-resorcinol.	<i>t</i> .	<i>n</i> .	<i>k</i>
5-Phenyl-	3.25	5	0.175	5-Cinnamyl- ...	2.0	4	0.064
5-Methyl-	3.5	5	0.128	Unsubstituted ...	3.5	6	0.059
5- <i>iso</i> Propyl-	4.75	7	0.097	4 : 5-Dimethyl- ...	5.5	6	0.050
5- <i>n</i> -Propyl-	3.5	7	0.085	5 : 5-Dimethyl- ...	5.0	3	0.004

2-Methyl-5-phenyldihydro-resorcinol.

<i>t</i> .	<i>v</i> .	<i>k</i> .
0	12.8	—
0.5	11.6	0.197
1.25	10.7	0.143
1.75	10.4	0.119
2.25	10.0	0.110
2.75	9.4	0.112

2-Methyl-5-*iso*propyldihydro-resorcinol.

<i>t</i> .	<i>v</i> .	<i>k</i> .
0	30.5	—
0.5	28.1	0.164
1.0	26.3	0.148
1.5	25.0	0.133
3.0	23.1	0.093
3.5	21.0	0.107
4.5	19.2	0.103

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