

CCLVII.—*Studies of Dynamic Isomerism. Part XXII.*
Methyl Alcohol as an Amphoteric Solvent for the
Mutarotation of the Sugars.

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SINCE oxygenated solvents, such as ethyl acetate, acetone, and cresol, and even a nitrogenous base like pyridine, have been proved to be inert (J., 1925, **127**, 1385, etc.), water has for a brief period occupied a unique position as the only compound which could with reasonable confidence be classed as a "complete catalyst" for the mutarotation of the sugars.* Our theory of mutarotation suggested, however, that other amphoteric compounds might possess catalytic properties, such as we have already recorded in dry mixtures of pyridine and cresol (J., 1925, **127**, 2883). The most obvious compounds to test were the alcohols, which are certainly amphoteric in the sense that they can liberate either hydrogen or hydroxyl to suitable chemical agents, but which do not necessarily possess sufficiently strong acidic and basic properties to enable them to act as complete catalysts for the mutarotation of the sugars. Since, however, the residual activity of the most highly purified solvents can always be attributed to imaginary impurities, direct experiments can only lead to conclusive results when the compound is *not* a catalyst; thus, our earlier experiments (J., 1925, **127**, 1396) only enabled us to assert that *if* methyl alcohol is a complete catalyst, its activity cannot be greater than 1/30 of that of water. In the present experiments, therefore, we have sought to reach a definite conclusion by finding out whether methyl alcohol is sufficiently basic to act as a complete catalyst when mixed with cresol, and sufficiently acidic to act as a complete catalyst with pyridine. The

* The reservation still holds, however, that "if the solution could by extreme purification be rendered non-conducting, it is possible that the mutarotation would not take place" (J., 1903, **83**, 1320).

positive results recorded below enable us to conclude that the alcohol must also be capable of acting as a complete catalyst when used alone, although we can now assert that its catalytic activity is less than 1/60 of that of water.

EXPERIMENTAL.

(a) *Direct Method*.—The sugar used was tetramethyl glucose, the purity of which had been tested as already described (this vol., p. 721; compare J., 1925, **127**, 1387, footnote). We have already recorded (*ibid.*, p. 1397) a velocity coefficient of 0.00039 for the mutarotation of this sugar in a sample of methyl alcohol containing about 0.5% of water, as compared with one of 0.0128 for pure water (this vol., p. 722); the corresponding value for a glucose of normal purity was 0.00060. A sample of methyl alcohol specially purified by Hartley for measurements of electrical conductivity, and very kindly sent to us by him in a sealed flask, has now been found to give an almost identical velocity coefficient, viz., 0.00041, when used as a solvent for the mutarotation of tetramethyl glucose. Since the same low velocity coefficient was given by our own, obviously wet, sample of methyl alcohol, it is clear that intensive drying is probably not the most important factor in the process of reducing the catalytic activity of the alcohol to a minimum. This conclusion is in accord with our recent observations on aqueous acetone (this vol., p. 720), as well as with the fact that, in the lower range of concentrations, the addition of 1% of water to methyl alcohol produces an average increase of less than 0.0001 in the velocity coefficient of mutarotation of tetramethyl glucose in this solvent.

In the present instance a more drastic purification was attempted. Using a part of Hartley's method, a litre of methyl alcohol was first purified by boiling it for 3 hours with 5% of its weight of sodium hydroxide, fractionating, and treating the product with successive quantities of a mercury-aluminium couple, until no further action took place. Since the alcohol then had a distinct odour of methylamine, it was distilled from succinic acid in order to remove basic impurities, and finally from a fresh mercury-aluminium couple, in order to remove any water which might have been produced by esterification of the succinic acid. The product gave the lowest velocity coefficient that has yet been recorded, namely, 0.00018 (Table I A). In order to determine, however, whether the velocity could be lowered still further, 50 c.c. of the purified alcohol were sealed up at a pressure of 10 cm. Hg in an all-glass apparatus, and distilled over phosphorus pentoxide at laboratory temperature by immersing the receiver in liquid air. By this means a sample

was obtained which was dry and free from basic impurities, as well as from substances of higher boiling point, which would be left behind by distillation at this temperature. The product of this further purification gave a velocity coefficient of 0.00022 (Table I B).

It is possible that in the future even lower values may be recorded; but, in view of the concordance of the velocities before and after the final stage of the purification, it is reasonable to think that the velocity coefficient will not be reduced much below 0.0002. This conclusion is supported by the fact that a solution which had been stored in a silica flask for 48 hours showed the same rotation (within 0.03°) as the part of the solution which had been transferred to the glass polarimeter tube; and that, even in the most highly purified sample, mutarotation began immediately, without any lag or period of induction, showing that it was due to the solution itself and not to impurities derived from the containing vessels.

TABLE I.

The Effect of Intensive Drying on the Velocity of Mutarotation of Tetramethyl Glucose in Methyl Alcohol.

(5% Solution in 2 dem. tube at 20°.)

(A) Methyl alcohol dried with Hg-Al couple.			(B) Methyl alcohol dried with P ₂ O ₅ .		
Time.	α_{5461} .	k .*	Time.	α_{5461} .	k .*
5	12.06°	—	10	11.94°	—
40	12.04	—	130	11.89	0.00018
1410	11.56	0.00020	250	11.83	0.00022
4320	11.07	0.00017	420	11.78	0.00020
6060	10.78	0.00018	660	11.71	0.00019
7260	10.60	0.00019	1290	11.50	0.00020
Final.	10.09	—	1530	11.36	0.00022
	Mean	0.00018	1770	11.29	0.00022
			2880	11.00	0.00022
			3180	10.92	0.00022
			4320	10.70	0.00022
			Final.	9.96	—
				Mean	0.00022

* $k = 1/t \cdot \{\log(a_0 - a_\infty) - \log(a_t - a_\infty)\}$; t in minutes.

In the case of *ethyl alcohol* we have been able without taking any elaborate precautions, to reduce the velocity of mutarotation to 0.00016 by mere distillation of the solvent with lime (Table II); moreover, in spite of the smallness of the velocity coefficient, the mutarotation of the solution again started immediately, without any lag or period of induction. Since this velocity coefficient is eighty times smaller than for water (as compared with sixty times in the case of methyl alcohol) it is likely that even lower values may be reached in the higher homologues; but since all the alcohols are more or less amphoteric, we must suppose that they are all

capable, in a larger or smaller degree, of acting as catalysts for the mutarotation of the sugars.

TABLE II.

Mutarotation of Tetramethyl Glucose in Ethyl Alcohol.

(5% Solution in 2 cm. tube at 20°.)

Time.	α .	k .*	Time.	α .	k .*
10 min.	11.86°	—	5760 min.	10.71°	0.00015
90	11.81	—	7200	10.50	0.00016
1380	11.46	0.00017	8640	10.34	0.00017
1920	11.36	0.00016	11,520	10.08	0.00016
2820	11.16	0.00016	Final	9.90	—
4380	10.87	0.00016	(13 days).		

Mean 0.00016

(b) *Indirect Method.*—The methods used to purify the pyridine and cresol, and to determine the velocity of mutarotation in the mixed solvents, have already been described (J., 1925, **127**, 2884). The methyl alcohol was the same sample as that used for the mutarotation recorded in Table I A. The results of the experiments are in Table III and Fig. 1.

TABLE III.

Mutarotation of Tetramethyl Glucose in Mixtures of

(A) Methyl alcohol and cresol.		(B) Methyl alcohol and pyridine.	
Methyl alcohol.	k .*	Methyl alcohol.	k .*
100%	0.0002	100%	0.0002
75	0.0008	90	0.0182
50	0.0013	80	0.0284
25	0.0018	60	0.035
10	0.0013	40	0.0216
0	0.0005	20	0.0089
		0	0.003

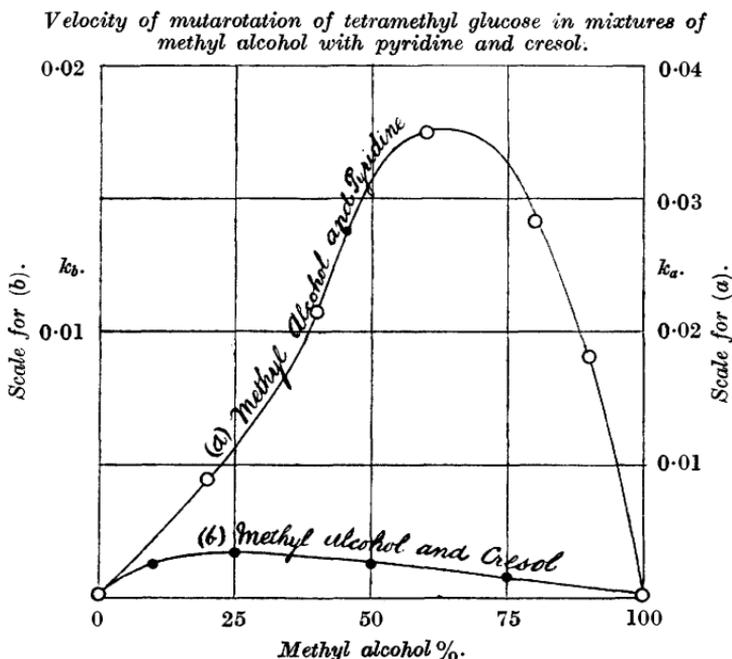
* $k = 1/t \cdot \{\log(\alpha_0 - \alpha_\infty) - \log(\alpha_t - \alpha_\infty)\}$; t in minutes.

A very striking maximum was recorded in the series of mixtures of methyl alcohol with pyridine at about 60% of the former, where the velocity was about three times as great as in pure water, although only about one-eighth as great as in the most efficient mixture of pyridine and water. This high velocity of mutarotation cannot be due to traces of water in the alcohol, since it requires nearly 20% of water to develop a similar degree of activity in aqueous pyridine; and it would be even more difficult to imagine that it was due to some substance other than water or methyl alcohol, in view of the enormous activity which it would be necessary to postulate in this hypothetical acidic impurity, which must, moreover, be supposed to have survived a prolonged treatment with an alkaline drying agent. There can therefore be no doubt that a mixture of pyridine

and methyl alcohol is a complete catalyst for the mutarotation of tetramethyl glucose.

In the case of methyl alcohol and cresol, the evidence is less striking; but we have nevertheless been able to record the occurrence of a definite maximum velocity of mutarotation in a mixture of 4 parts of cresol with 1 part of methyl alcohol (Fig. 1). Here again, we have to consider whether this increased velocity can be attributed to the presence of impurities, and in particular to water, or to some

FIG. 1.



basic impurity, which could play the part of pyridine in converting the cresol into a complete catalyst. The method of purification appears to rule out the possible presence of bases; and since 4% of water would be required in order to develop the velocity of mutarotation actually produced by 20% of methyl alcohol, the maximum which we have observed cannot be explained by the possible presence of traces of water in the "dry" solvent. We are therefore obliged to conclude again that a mixture of methyl alcohol with cresol is a complete catalyst for the mutarotation of tetramethyl glucose.

Summary.

(a) Purified methyl alcohol, which gave a velocity coefficient of 0.00018 when used as a solvent for the mutarotation of tetramethyl

glucose, gave a maximum velocity coefficient of 0.0018 when mixed with three times its weight of cresol and of 0.035 when mixed with two-thirds of its weight of pyridine. Since methyl alcohol is sufficiently acidic to form a complete catalyst with pyridine, and sufficiently basic to form a complete catalyst with cresol, it must also be able to act alone as an amphoteric solvent to promote the mutarotation of the sugars.

(b) The velocity of mutarotation of tetramethyl glucose in purified ethyl alcohol has been reduced to 0.00016 or about eighty times less than the velocity in water. Since the chemical properties of ethyl alcohol are similar to those of methyl alcohol, it is probable that a part of this velocity is again due to the solvent itself.

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