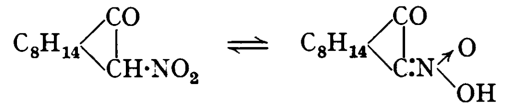
226. *Acid Catalysis in Non-aqueous Solvents. Part IX. The Mutarotation of α-Nitrocamphor in Chlorobenzene Solution.*

By R. P. Bell and J. A. Sherred.

Evidence is given which suggests that the mutarotation of nitrocamphor involves the interconversion of two stereoisomers rather than of a normal and an *aci*-nitro-form. The mechanism of catalysis by acids and bases is discussed, and kinetic data are given for catalysis by five acids in chlorobenzene solution at 25°. The reactions are of the first order and there is an approximate relation between the catalytic power of an acid and its dissociation constant in water.

It has long been known that freshly prepared solutions of α-nitrocamphor and its derivatives undergo a change of rotation on standing, and in some cases it is possible to isolate two solid forms differing in their rotations and other physical properties. Most of the experimental and theoretical work on the subject is due to Lowry and his collaborators (J., 1898—1915), who established that the change is catalysed by both acids and bases. No quantitative catalytic measurements have, however, been made. The present paper contains a discussion of the mechanism of mutarotation and some kinetic data on catalysis by acids in chlorobenzene solution. A fuller experimental study has been postponed.

The Nature of the Mutarotation Reaction.—Lowry and all subsequent writers suppose that the change of rotation observed with α-nitrocamphor is due to a partial conversion of the ordinary nitro- into the *aci*-nitro-form, (I) $\rightleftharpoons$ (II), these two structures corresponding



(I.) (II.)

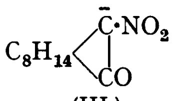
to the two solid forms which can be isolated in some cases. The only positive evidence for this assumption is based on analogies between the negative rotation of nitrocamphoric anhydride and the negative change of rotation when the mutarotation of nitrocamphor takes place. It seems more likely that both the forms have the normal nitro-structure, but differ in the configuration of the groups round the α-carbon atom. Since there are other asymmetric centres in the camphor molecule the two forms are not mirror images, but will differ in physical properties in general. The mutarotation reaction will then be analogous to the inversion of menthone (Bell and Caldin, J., 1938, 382) and to the mutarotation processes observed for the two forms of α-chloro- and α-bromo-camphor (Lowry, J., 1906, **89**, 1033; Lowry and Steele, J., 1915, **107**, 1382). The following are our chief reasons for this conclusion :

(*a*) According to Lowry, the process of mutarotation involves the partial conversion of the normal into the *aci*-form in solution, and in cases where the two forms can be isolated as solids the equilibrium solution contains comparable amounts of both forms. This behaviour would be expected for a pair of stereoisomers ; on the other hand, in all established cases of nitro–*aci*-nitro-tautomerism the *aci*-form is completely converted into the normal form at equilibrium.

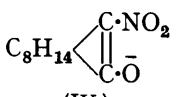
(*b*) The process of mutarotation causes no change in the weak coloration which α-nitrocamphor gives with ferric chloride. In contrast to this behaviour the *aci*-form of nitrocamphane (which is prepared by acidifying solutions of the sodium salt and reverts completely to the normal form on keeping) gives a strong coloration with ferric chloride and differs in several other respects from the normal nitrocamphane (Forster, J., 1900, **77**, 251).

(*c*) Acidification of solutions of salts of α-nitrocamphor and α-nitro-π-bromocamphor does not give chiefly the supposed *aci*-form, but a mixture of the two forms in roughly the equilibrium proportion (Lowry, J., 1899, **75**, 211).

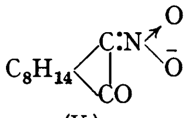
The change of configuration which we have supposed will take place by the ionisation of the hydrogen atom in the group $>CH\cdot NO_2$, this ionisation being facilitated by the possibilities of mesomerism in the resulting ion. In the first place we have the alternative structures (III) and (IV), as in all ketones. Further, the mutarotation of nitrocamphor is



(III.)



(IV.)

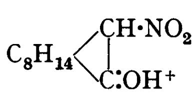


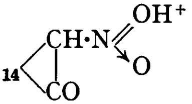
(V.)

much more facile than the prototropic reactions of simple ketones, and although this is partly due to the inductive effect of the nitro-group, it is likely that the form (V) also contributes to stabilise the ion. Information on this point might be obtained by studying the catalytic behaviour of the racemisation of active nitroparaffins.

In the base-catalysed mutarotation the proton is simply lost to the base, forming the ion described above. In catalysis by acids this process must be preceded by the addition of a proton at another point in the molecule, as in the prototropy of ketones (Pedersen, *J. Physical Chem.*, 1934, **38**, 591; *Trans. Faraday Soc.*, 1938, **34**, 237; Wilson, *ibid.*, p. 175). It is again possible that the nitro-group plays an essential part; *i.e.*, the proton may add on to give either (VI) or (VII). The nitro-group certainly has weak basic properties, since strong acids give conducting solutions in nitromethane (Wright, Murray-Rust, and Hartley, J., 1931, 199). There are, moreover, two points in our own experimental results which suggest that the mechanism differs essentially from that for the prototropy of simple ketones. (i) Both acids and bases are more effective as catalysts for the mutarotation of nitrocamphor than for the racemisation of ketones under the same conditions, whereas a purely polar effect would be expected to influence the two types of catalysis in opposite directions. (ii) The relation between catalytic power and acid strength appears to differ considerably from the corresponding relations for simple ketones. It is thus probable that the nitro-group plays an essential part in the mechanism of mutarotation by means of the structures (V) and (VII).

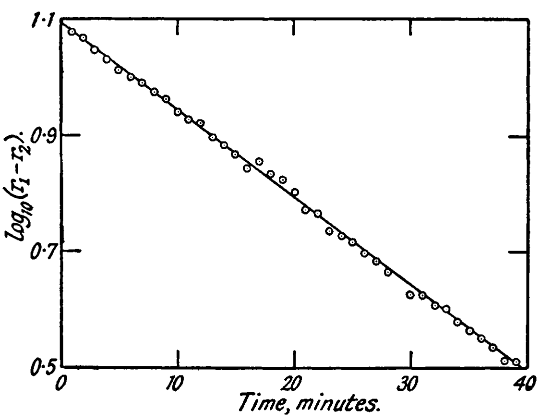
(VI.)





(VII.)

FIG. 1.



EXPERIMENTAL.

Materials.—The purification of the chlorobenzene and the acids has been described in earlier papers of this series. α-Nitrocamphor was prepared by oxidation of *iso*nitrosocamphor with the theoretical quantity of dilute permanganate solution at 0° (Lowry, J., 1898, **73**, 995); the resulting solution was filtered and acidified with acetic acid, and the oil which separated out solidified on standing and was recrystallised from methylated spirit, m. p. 102°. The best yields (40%) were obtained by using small quantities (about 10 g.).

In chlorobenzene solution α-nitrocamphor had $[\alpha]_{\mathrm{D}}^{25^\circ} + 105^\circ$, decreasing on mutarotation to + 78°. These solutions were very stable in the absence of catalyst, and exhibited no measurable change in rotation for at least 24 hours. It was found possible to recover about 90% of the nitrocamphor in the original state from solutions which had undergone mutarotation. The chlorobenzene solution was extracted with a slight excess of 2N-potassium hydroxide solution, and the aqueous layer washed twice with ether. After removal of dissolved ether by a current of air, the solution of the potassium salt was worked up for nitrocamphor as above.

Kinetic Measurements.—The polarimeter and thermostat have already been described (Bell and Caldin, J., 1938, 382; Bell, Lidwell, and Wright, *ibid.*, p. 1961). The temperature was throughout 25°. The reactions were not slow enough to permit repeated readings to be taken, and the chief error in reading was due to parallax : this was partly avoided by a rubber eyepiece which fixed the position of the observer's eye. The solutions used contained about 5% of α-nitrocamphor by weight, giving an initial rotation of about 9° and a change of about 2°. Each reaction was strictly of the first order, and the velocity constants were evaluated by Guggenheim's graphical method (*Phil. Mag.*, 1926, **2**, 538). Fig. 1 shows a typical plot of this kind.

Results.—In the following table the acid concentrations c are expressed in g.-mols. per 1000 g. of solvent, and the first-order constants k in decadic logarithms and minutes. For three of the acids, k and c are related by the simple equation $k = k_A c$ (where k_A is the catalytic constant), as shown by the agreement between the observed and calculated values. In the case of β-chloropropionic acid the relation is not linear, and one of the form $k = k_A c + bc^{\frac{1}{2}}$ has been used. The values of k_A and their probable errors have been obtained from the experimental data by the method of least squares. The values of K_A given for each acid are the dissociation constants in water at 25°.

Trimethylacetic acid : $K_A = 9{\cdot}1 \times 10^{-6}$, $k_A = 0{\cdot}109 \pm 0{\cdot}003$.

100 c	3·61	6·84	10·4	14·3
100 k obs.	0·375	0·776	1·18	1·50
100 k calc.	0·392	0·742	1·12	1·55

β-Chloropropionic acid : $K_A = 8{\cdot}6 \times 10^{-5}$, $k_A = 0{\cdot}20 \pm 0{\cdot}04$, $b = 0{\cdot}11$.

100 c	0·89	1·15	2·86	3·72	5·64
100 k obs.	1·13	1·49	2·42	2·82	3·64
100 k calc.	1·20	1·36	2·40	2·83	3·69

Monochloroacetic acid : $K_A = 1{\cdot}38 \times 10^{-3}$, $k_A = 0{\cdot}62 \pm 0{\cdot}03$.

100 c	1·76	3·64	4·03	5·71	6·78
100 k obs.	1·16	2·22	2·79	3·40	4·10
100 k calc.	1·09	2·24	2·48	3·52	4·18

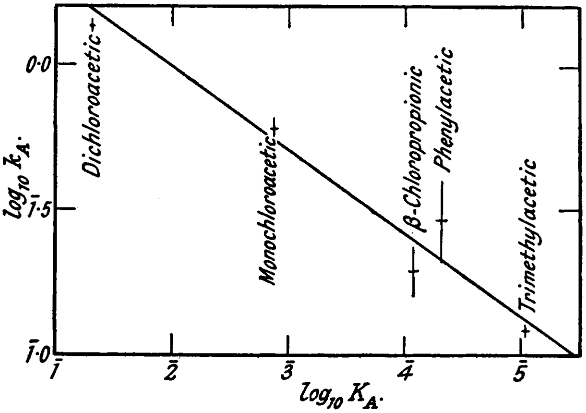
Dichloroacetic acid : $K_A = 5{\cdot}0 \times 10^{-2}$, $k_A = 1{\cdot}27 \pm 0{\cdot}03$.

100 c	0·55	0·96	1·18	1·48	1·56	1·82
100 k obs.	0·64	1·30	1·52	1·91	2·11	2·13
100 k calc.	0·69	1·22	1·50	1·88	1·98	2·31

A number of experiments with phenylacetic acid ($K_A = 4{\cdot}88 \times 10^{-5}$) gave erratic results varying by more than 100%; mean value $k_A = 0{\cdot}3 \pm 0{\cdot}1$.

Discussion.—The above results show clearly that the mutarotation of nitrocamphor is catalysed by acids in general, and there is, as usual, a parallelism between the catalytic power of an acid and its dissociation constant in water. This is illustrated by Fig. 2, which is a plot of $\log_{10}k_A$ against $\log_{10}K_A$. The lengths of the vertical lines represent the probable error in the catalytic constants. The straight line drawn has a slope of 0·3; this contrasts with the value 0·6—0·8 found for the inversion of menthone in the same solvent (Bell and Caldin, *loc. cit.*). Discussion of the detailed mechanism of catalysis must be postponed until more data are available.

FIG. 2.



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