# 380. *Activation Energy and Entropy in the Racemisation of 2,2'-Dibromobiphenyl-4,4'-dicarboxylic Acid.*

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The velocity constants for racemisation of optically active 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid in ethanol have been determined at temperatures ranging from $-20{\cdot}7°$ to $+5{\cdot}6°$, and hence experimental evaluations of $E$ and $A$, and of $\Delta H^‡$ and $\Delta S^‡$ for racemisation made. An apparatus for low-temperature polarimetric work is described.

The activation energy for the racemisation of optically active 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid was calculated by Westheimer [1] in 1947, taking into account the bending and stretching of the bonds, and the compression of the atoms which would be necessary for attainment of a planar transition state. The value arrived at was 18 kcal. mole$^{-1}$. Rieger and Westheimer [2] then applied the same method to 2,2'-dibromo- and 2,2',3,3'-tetraiodo-biphenyl-5,5'-dicarboxylic acid, obtaining calculated values for $E$ of 21·4—23·6 and 28·6—33·1 kcal. mole$^{-1}$ respectively. The last two calculated results have been compared with experimentally determined values [2,3] of $E$ for the sodium salts of the optically active acids, and satisfactory agreement has been obtained.

However, an experimental assessment of $E$ for 2,2'-dibromobiphenyl-4,4'-dicarboxylic acid, which is optically rather unstable, has hitherto rested on a single racemisation rate constant at 0° in dioxan–methanol.[4] The value corresponds with an observed free energy of racemisation $\Delta F^‡$ of 19·7 kcal. mole$^{-1}$ at 0°; if it is assumed that the entropy of activation for racemisation in this case is similar to that found [2,3] for the sodium salts of 2,2'-di- and 2,2',3,3'-tetra-iodobiphenyl-5,5'-dicarboxylic acid, that is $-7{\cdot}5$ e.u., then the enthalpy of activation $\Delta H^‡$ would be approximately 17·8 kcal. mole$^{-1}$ and $E$ would be 18·4 kcal. mole$^{-1}$. (It should be noted that Rieger and Westheimer give $\Delta S^‡$ for *inversion* and also that they use the approximation $E = \Delta H^‡$. This leads to small differences between their figures and those given here.)

Racemisation rate constants for (+)-2,2'-dibromobiphenyl-4,4'-dicarboxylic acid in ethanol have now been measured, as already briefly reported,[5] at several temperatures below 0°, a low-temperature thermostat being used to control the temperature of the

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[1] Westheimer, *J. Chem. Phys.*, 1947, **15**, 252.
[2] Rieger and Westheimer, *J. Amer. Chem. Soc.*, 1950, **72**, 19.
[3] Hall and Harris, *J.*, 1960, 490.
[4] Searle and Adams, *J. Amer. Chem. Soc.*, 1934, **56**, 2112.
[5] Harris, *Proc. Chem. Soc.*, 1959, 367.

solution in the polarimeter tube: hence the Arrhenius parameters and enthalpy and entropy of activation (for *racemisation*) have been determined. The values obtained are:

| Temp. (° c) | +5·6 | +1·0 | −3·9 | −9·25 | −15·3 | −20·7 |
|---|---|---|---|---|---|---|
| $10^5k$ (sec.$^{-1}$) * | 158 | 85·9 | 51·2 | 21·1 | 10·3 | 4·46 |

* In the preliminary communication [5] this figure appeared, owing to a misprint, as $1\text{-}^5k$ (sec.$^{-1}$); the designation above is the correct one.

$E$ = 19·0 ± 0·5 kcal. mole$^{-1}$ (graphical method; 18·9 by least squares); $\log_{10} A$ = 12·1 ± 0·4°. $\Delta F^{\ddagger}$, the free energy of activation for racemisation, calculated according to absolute reaction rate theory = 19·9 kcal. mole$^{-1}$ at 5·6°; $\Delta H^{\ddagger}$, the enthalpy of activation for racemisation = 18·5 ± 0·5 kcal. mole$^{-1}$; $\Delta S^{\ddagger}$, the entropy of activation for racemisation = −4·9 ± 1·85 e.u. (this error in $\Delta S^{\ddagger}$ is consequent upon the error in $\Delta H^{\ddagger}$). If $\Delta F^{\ddagger}$ were quoted for *inversion* and not racemisation, it would be 20·3 kcal. mole$^{-1}$, while $\Delta S^{\ddagger}_{\text{inversion}}$ would be −6·3 e.u.

In spite of the different solvent used, the rate constants fall into line with the single value obtained by Searle and Adams:[4] the entropy factor is only a little smaller than the value thought probable by Rieger and Westheimer.[2] The generalisation has been made [1,6] that in compounds owing their optical activity to restricted rotation the energy of activation and the free energy of activation for racemisation never differ by more than a few kilocalories; acceptance of this generalisation could obscure an interesting variation in entropy factors. In biphenyls and binaphthyls alone, a spread of entropy factors in racemisation from +9·2 to −16·3 e.u. has been recorded;[3,7] the difference $E_{\text{racem}} - \Delta F^{\ddagger}_{\text{racem}}$ ranges from −3·5 to +5·3 kcal. mole$^{-1}$; if other types of compound in which restricted rotation is involved are included,[8] the total spread is even larger. However, it does seem both possible and probable that the entropy factors for racemisation of such structurally similar compounds as the 2,2′-dihalogenobiphenyls (not yet measured) would be equal; added carboxylic acid groups might make a contribution to the numerical value differing, perhaps, according to whether the groups were in the 4- or the 5-position. This difference according to position in the biphenyl system has been observed with nitro-groups.[9] One kinetic observation [10] has been made on 2,2′-di-iodobiphenyl-4,4′-dicarboxylic acid in dioxan: $k^{25}$ = 0·0033. If we assume that this measurement refers to min.$^{-1}$, $\Delta F^{\ddagger}$ is 22·8 kcal. mole$^{-1}$. If $E$ is the same as that for the 5,5′-dicarboxylic acid, 21·6 kcal. mole$^{-1}$, then $\Delta S^{\ddagger}$ would be −6 e.u., *i.e.*, very close to the value now found for the dibromo-compound.

The preparation of 2,2′-dibromobiphenyl-4,4′-dicarboxylic acid was carried out by Searle and Adams [4,10] from the ethyl ester of the corresponding 2,2′-bisdiazomercuribromide: decomposition of the mercuribromide gave a very poor yield of an impure, coloured product. As an alternative method, bromination of diethyl biphenyl-4,4′-dicarboxylate in concentrated sulphuric acid in presence of silver sulphate according to the general method of Derbyshire and Waters [11] has now been tried; a mixture of bromo-esters was obtained which was difficult to separate. However, similar bromination of the dimethyl ester yielded a major portion of dimethyl 2,2′-dibromobiphenyl-4,4′-dicarboxylate; saponification of this ester yielded the corresponding acid. When the 2,2′-dibromobiphenyl-4,4′-dicarboxylic acid was dissolved in hot ethyl acetate together with one equivalent of brucine, the solution quickly deposited the monobrucine (+)-acid salt, by second-order asymmetric transformation, further crops from the mother-liquor being of the same salt.

The (+)-acid, released from the brucine, is optically very unstable ($t_{\frac{1}{2}}^{5\cdot6}$ = 7·3 min.);

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[6] Kistiakowsky and Smith, *J. Amer. Chem. Soc.*, 1936, **58**, 1043; Mills and Kelham, *J.*, 1937, 274.
[7] Theilacker and Hopp, *Chem. Ber.*, 1959, **92**, 2293.
[8] Brooks, Harris, and Howlett, *J.*, 1957, 2380.
[9] Brooks, Harris, and Howlett, *J.*, 1957, 1934.
[10] Searle and Adams, *J. Amer. Chem. Soc.*, 1933, **55**, 1649.
[11] Derbyshire and Waters, *J.*, 1950, 573.

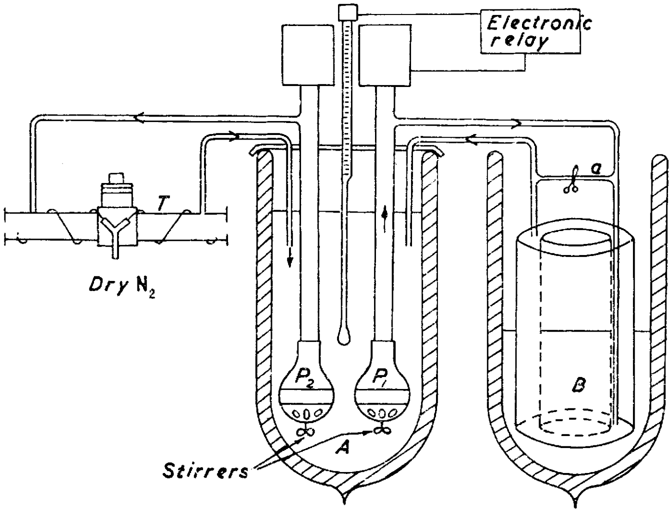
therefore, in order to measure rate constants over a sufficient range of temperature it was necessary to design a suitable thermostatically controlled polarimeter-tube to operate at temperatures lower than normal. The unit described below has proved capable of holding a solution, in the polarimeter so that it can be continuously observed, at temperatures down to −24·0° ± 0·1° for more than six hours. There is no reason to suppose that performance would be less efficient at temperatures considerably lower, or for longer periods of time.

## EXPERIMENTAL

Dimethyl biphenyl-4,4′-dicarboxylate, prepared from methyl *p*-iodobenzoate by the Ullmann reaction at 260—280°, had m. p. 214—215° (Tschitschibabin [12] gives 224°; Ullmann [13] gives 214°) after crystallisation from benzene.

*Dimethyl* 2,2′-*Dibromobiphenyl*-4,4′-*dicarboxylate*.—The preceding ester (5·4 g., 0·02 mole) was gradually added to concentrated sulphuric acid (50 c.c.), with shaking until dissolved, and then treated with silver sulphate (18·8 g.). Bromine (2·0 c.c., 0·08 mole) was added in three portions, with vigorous shaking after each addition. The colour rapidly disappeared and after 10 min. the mixture was poured into water and ice. The precipitate was extracted (Soxhlet) with ethanol for 8 hr. Fractional crystallisation from ethanol yielded the *dibromo-ester* (4·1 g.), which melted first at 114°, solidified again and re-melted at 127—128° (Found: C, 44·70; H, 2·75; O, 14·82; Br, 37·54. $C_{16}H_{12}O_4Br_2$ requires C, 44·89; H, 2·83; O, 14·95; Br, 37·34%).

FIG. 1.



This ester (5 g.) with alcoholic potassium hydroxide (5 g. in 75 ml.) gave 2,2′-dibromobiphenyl-4,4′-dicarboxylic acid (4·6 g.), m. p. 313—314° (paraffin bath; 305—306° on a Kofler block, where the crystalline form can be seen to change just before the compound melts).

*Second-order Asymmetric Transformation of* 2,2′-*Dibromobiphenyl*-4,4′-*dicarboxylic Acid by Brucine from Ethyl Acetate Solution*.—The (±)-acid (2·0 g.) was dissolved in 800 c.c. of boiling ethyl acetate, and powdered brucine (2·0 g., 1 equiv.) was then added gradually. Three crops of small needles were collected: (*a*) 2·0 g., m. p. 212—214°; (*b*) 1·0 g., m. p. 203—207°; (*c*) 0·55 g., m. p. 203—207°; all the crops were dextrorotatory and showed mutarotation in the lævo-direction in chloroform. Preparation of the brucine salt in more concentrated conditions

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[12] Tschitschibabin, *Ber.*, 1907, **40**, 1810.

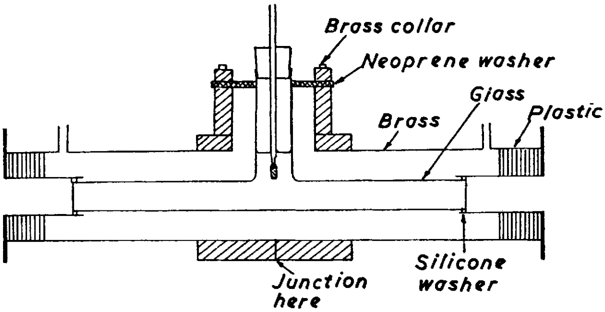
[13] Ullmann, *Annalen*, 1904, **332**, 38.

tends to cause the lævorotatory dibrucine salt [4] to crystallise together with the monobrucine (+)-acid salt.

Crop (*a*) (1·0 g.) was decomposed by stirring it with 98% formic acid at about 6° for 2 min. and then pouring the suspension into aqueous hydrochloric acid (400 c.c.). The acid (0·48 g.) thus obtained had $\alpha_{5461}^{1\cdot0}$ +0·42° (0·2 g. in 20 c.c. of ethanol) 2 min. after being wetted with solvent. Crop (*b*), similarly decomposed, yielded 0·25 g. of acid, $\alpha_{5461}^{5\cdot6}$ +0·44° in 20 c.c. of ethanol 1 min. after wetting. These figures do not, of course, represent the rotation of the optically pure acid.

*Low-temperature Polarimetric Apparatus* (in collaboration with R. K. Mitchell).—The apparatus is shown in Fig. 1. One (*A*) of a pair of gallon-size Dewar flasks contains a contact thermometer and two internal screw pumps, and the other (*B*) the heat exchanger.

Fig. 2.



The thermoregulator (contact thermometer and electronic relay [14]) controls the pump $P_1$ which drives ethanol from *A* through the hollow tin-plate cylinder which stands in *B* in a mixture of solid carbon dioxide and ethanol; the by-pass *a* permits regulation of the amount of ethanol flowing through the heat-exchanger. The second pump, $P_2$, circulates the temperature-controlled ethanol round the polarimeter tube *T*. All flexible connections are made with silicone tubing.

*T* is a standard, all-glass, centre-filling tube with adhesed end-plates, held by two silicone washers in a hollow brass outer jacket (Fig. 2). The jacket was made in two parts which were then bolted together after the two faces had been smeared with a thin coating of rubber solution; a brass cylinder surrounds the projecting part of the tube to which it is sealed by a Neoprene washer held in place by a brass collar. The jacket is long enough to project well beyond the glass; the coolant is in full contact with the tube except where the thin silicone washers touch it. Plastic ends to the outer jacket insulate the metal from warmth of contact with the polarimeter. End-plate fogging is prevented by streams of dry nitrogen, cooled in transit through metal leads coiled round the main tube, which play on the glass ends. The tube and all the leads are heavily lagged.

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[14] Easton, Hargreaves, and Mitchell, *J. Appl. Chem.*, 1957, **7**, 198.