101. *Some Racemisation Data for Compounds owing their Optical Activity to Restricted Rotation.*

By D. MURIEL HALL and MARGARET M. HARRIS.

A table of entropies and enthalpies of activation and Arrhenius parameters for the racemisation of thirty-four optically labile compounds has been compiled from the authors' and other work. In all cases the values have been calculated afresh and in a standard way from the experimental data. The table covers a wide enough field for the spread of values in compounds of this type to be apparent.

OPTICAL stability in compounds owing their optical activity to restricted rotation about one or more single bonds cannot always be assessed even qualitatively from the value of the Arrhenius activation energy for racemisation; an extreme example lies in the case of the three nitrodiphenic acids [1] (6-nitro-, 4,6′-dinitro-, and 4,6,4′-trinitro-) which all have approximately the same activation energy but whose half-lives in aqueous sodium carbonate solution at 80° are appreciably different, being 29, 91, and 208 min. respectively.

Cagle and Eyring [2] have drawn attention to the importance of the contribution of the entropy of activation ($\Delta S^{\ddagger}$) of sterically hindered compounds to their racemisation velocities; they calculated $\Delta S^{\ddagger}$ from absolute reaction rate theory for several optically active compounds, using experimental data from the literature.

Their approach, although at the time based on a small number of cases of unequal value,[3] has proved useful in helping to interpret certain apparently anomalous results. For example, the unexpected optical stability of compound 34 (see Table below) ($E =$ 14·9 kcal. mole^{-1}; $t_{\frac{1}{2}}^{20} = 3{\cdot}2$ min.) in comparison with compound 8 ($E = 19{\cdot}3$ kcal. mole^{-1}; $t_{\frac{1}{2}}^{20} = 1{\cdot}4$ min.) is explained by the latter's having an entropy of activation of $-4{\cdot}1$ e.u. compared with $-20{\cdot}9$ for the former.[4]

Our studies on optically labile compounds have led us to compile a table of values of Arrhenius parameters and entropies and enthalpies of activation for compounds of three types: (*a*) *N*-benzoyldiphenylamine-2-carboxylic acids, (*b*) *ortho*-substituted diphenyls, and (*c*) diphenyls bridged across the 2,2′-positions. These are all compounds which, under

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[1] Brooks, Harris, and Howlett, *J.*, 1957, 1934.
[2] Cagle and Eyring, *J. Amer. Chem. Soc.*, 1951, **73**, 5628.
[3] de la Mare, " Progress in Stereochemistry," Butterworths, London, 1954, Vol. I, p. 121.
[4] Brooks, Harris, and Howlett, *J.*, 1957, 2380.

ordinary conditions, racemise by mechanisms involving stretching and bending, and not breaking, of bonds. The table, which includes some work not previously published and many values not previously calculated, is published here in the belief that it may be of general interest and act as a basis for further study of racemisation in such compounds.

The table gives the Arrhenius parameters and transition-state functions obtained by using (*a*) the Arrhenius equation $k_{\text{rac}} = A \exp(-E/\boldsymbol{R}T)$ (where E is the activation energy experimentally determined and A is the non-exponential term, often called the frequency factor) and (*b*) the absolute reaction rate equation of Glasstone, Laidler, and Eyring:[5]

$$\begin{aligned} k_{\text{rac}} &= \kappa\,(\boldsymbol{k}T/\boldsymbol{h}) \exp(-\Delta F^{\ddagger}/\boldsymbol{R}T) \\ &= \kappa\,(\boldsymbol{k}T/\boldsymbol{h}) \exp(-\Delta H^{\ddagger}/\boldsymbol{R}T) \exp(\Delta S^{\ddagger}/\boldsymbol{R}) \end{aligned}$$

(where $\Delta F^{\ddagger}$ is the change in standard free energy, $\Delta H^{\ddagger}$ the change in enthalpy and $\Delta S^{\ddagger}$ the change in entropy accompanying the formation of the transition state in the racemisation process).

The compounds in the table are arranged in order of decreasing entropy of activation, and data for each are, with one exception (26), restricted to a single solvent; for a few of the compounds data for other solvents are available under the references given and show that the influence of solvent, though often slight, is large in some cases.

In compiling the table the following procedure was adopted:

(1) The transmission coefficient, κ, was taken as unity[2] and the following physical constants[6] were used: $\boldsymbol{k} = 1{\cdot}380 \times 10^{-16}$ erg/deg.; $\boldsymbol{h} = 6{\cdot}624 \times 10^{-27}$ erg-sec.; $\boldsymbol{R} = 1{\cdot}987$ cal./deg.-mole; 0° C = 273·2° K.

(2) E was determined graphically from the rate constants for racemisation; where the work has already been published, values for E are normally those given in the publication; exceptions are indicated in the table.

(3) Log$_{10}$ A was calculated from equation (*a*) in the form $\log_{10} A = \log_{10} k_{\text{rac}} + E/4{\cdot}576T$. In a few cases rate constants for inversion are given in the literature and these have been doubled to give k_{rac}.

(4) $\Delta S^{\ddagger}$ was obtained by using equation (*b*) in the form: * $\Delta S^{\ddagger} = 4{\cdot}576 \log_{10} k_{\text{rac}}/T + E/T - 49{\cdot}20$.

(5) $\Delta H^{\ddagger}$ was calculated from $\Delta H^{\ddagger} = E - \boldsymbol{R}T$.

(6) $\Delta F^{\ddagger}$ was calculated from equation (*b*) in the form: $\Delta F^{\ddagger} = 47{\cdot}22T - 4{\cdot}576T$ og$_{10}$ (k_{rac}/T).

(7) Every tabulated value for log$_{10}$ A and $\Delta S^{\ddagger}$ is the mean of those calculated for each temperature at which rates were measured. $\Delta F^{\ddagger}$, however, varies appreciably with temperature in some cases and is therefore given at a single temperature, *viz.*, the highest recorded for the range of measurement.

(8) All previously published values of log$_{10}$ A, $\Delta S^{\ddagger}$, $\Delta H^{\ddagger}$, and $\Delta F^{\ddagger}$ have been recalculated. In some cases the use of averages, as described above, or a slight difference in values of the physical constants used has led to small differences in the emergent figures.

It should be emphasised that not all the figures in the table are of equal value. In some cases E has been determined from rate measurements at only two temperatures, in one case from measurements in different solvents. Sometimes the range of temperature over which it has been convenient to study the compound has been regrettably small, and the values of the rate constants themselves are, moreover, of varying accuracies. Much depends on the actual rate, the ability to maintain a thermostat at the required temperature for a sufficient time (particularly difficult with rather low or rather high temperatures), and the quantities of optically active material available (normally less is available if the compound is fairly optically stable, and therefore resolved, than if it is highly optically labile and therefore obtained by asymmetric transformation).

* It should be noted that $\Delta S^{\ddagger}_{\text{inversion}} = \Delta S^{\ddagger}_{\text{rac}} - 1{\cdot}38$ e.u.

[5] Glasstone, Laidler, and Eyring, " The Theory of Rate Processes," McGraw-Hill, New York, 1941.

[6] Rossini, Gucker, Johnston, Pauling, and Vinal, *J. Amer. Chem. Soc.*, 1952, **74**, 2699.

Compound	E (kcal. mole^{-1})	$\log_{10} A$ (sec.$^{-1}$)	$\Delta S^{\ddagger}$ (e.u.)	$\Delta H^{\ddagger}$ (kcal. mole^{-1})	$\Delta F^{\ddagger}$ [a] (kcal. mole^{-1})	Temp. range	Solvent	Ref.
1	26·1	15·2	+9·2	25·5	22·5	20—52°	0·1N-NaOH [b]	i
2	25·4	14·5	+5·8	24·8	22·9	16·5—50	2·32N-NaOH [b]	ii
3	22·1	14·2	+4·6	21·5	20·1	2—23	Me_2CO	iii
4	30·8 [c]	13·4	+0·3	30·0	29·9	101—136	Dioxan, PhMe, PhEt	iv
5	22·6	12·6	−2·9	22·0	22·9	16·5—35	H_2O	v
6	27·8	12·7	−2·9	27·1	28·2	80—91	Aq. HCl	vi
7	22·8	12·5	−3·5	22·2	23·3	16·5—50	EtOH	ii
8	19·3	12·3	−4·1	18·7	20·0	0·5—20	$CHCl_3$–EtOH [d]	4
9	23·5 [e]	12·2	−4·6	22·9	24·4	23—43	Dioxan	vii
10	19·0	12·1	−4·9	18·5	19·9	−20·5 to 5·5	EtOH	viii
11	27·6	12·2	−5·3	26·9	28·9	79·5—100	H_2O [f]	ix
12	18·7	11·7	−6·8	18·1	20·1	0·5—17·5	EtOH	4
13	20·0 (20·0) [g]	11·6 (11·7)	−7·3 (−7·0)	19·4 (19·4)	21·7 (21·6)	0—35·5 (0·5—39)	EtOH	x
14	28·05	11·7	−7·6	27·3	30·2	80—99·5	Aq. NaOH [b]	xi
15	21·6 [h]	11·5	−7·7	21·0	23·4	20—38	$NaHCO_3$, EtOH–H_2O	xi
16	22·7 [e]	11·5	−7·9	22·1	24·6	23—43	Dioxan	vii
17	30·0	11·5	−8·3	29·2	32·7	125—145	C_6H_6	vi
18	17·7	11·2	−9·2	17·1	19·8	1—20	$CHCl_3$–EtOH [d]	xii
19	20·5	11·0	−10·2	19·9	23·1	10—41·5	EtOH	xiii
20	18·6	10·9	−10·5	18·0	21·2	0·5—30	EtOH	xiii
21	20	10·9	−10·5	19·4	22·6	0—35·5	EtOH	x
22	20	10·8	−11·2	19·4	22·9	0—35·5	EtOH	x
23	22·6	10·6	−12·3	21·9	26·4	57—87·5	2N-Na_2CO_3 [b]	1
24	25·9	10·6	−12·3	25·2	29·8	79·5—100	H_2O [i]	xiv
25	27·85	10·4	−13·3	27·1	32·2	90·5—109	EtOH [i]	xvi
26	25·8	10·4	−13·6	25·0	30·4	100—118·5	PhCl	xvii
	(25·5)	(10·2)	(−14·1)	(24·8)	(30·0)	(79·5—100)		xvi
	25·0	10·1	−14·8	24·3	29·8	79·5—100	EtOH [i]	xvi
27	16·2	10·2	−14·0	15·6	19·7	0·5—20	$CHCl_3$–EtOH [d]	4
28	22·6	10·1	−14·7	21·9	27·2	70·5—91	2N-Na_2CO_3 [b]	1
29	16·6	9·8	−15·5	16·0	20·6	6·5—25·5	$CHCl_3$–EtOH [k]	4
30	24·5	9·8	−16·0	23·7	29·7	79·5—100	EtOH [i]	xvi
31	22·6	9·7	−16·3	21·9	27·9	72·5—94	2N-Na_2CO_3 [b]	1
32	16·4	9·5	−16·9	15·8	21·0	0·5—32	$CHCl_3$–EtOH [d]	4
33	15·7	9·1	−18·6	15·1	20·8	0·5—30	$CHCl_3$–EtOH [d]	4
34	14·9	8·7	−20·9	14·3	20·6	7—27·5	$CHCl_3$–EtOH [d]	4

[a] At highest temperature at which measurements were made. [b] The free acid was dissolved in this solvent. [c] This figure was rounded off to 31 in the original paper. [d] $CHCl_3$ containing 2·5% of EtOH by volume. [e] Calc. from the rate constants given in the paper. [f] Graham and Leffler studied this compound in EtOH also. [g] The figures in parentheses were obtained from measurements by Brooks and Harris (unpublished). [h] Only those results for which at least 1 mole of $NaHCO_3$ was used per mole of acid are included. [i] Leffler and his co-workers have recently made an extensive study of medium and salt effects in the racemisation of these and other diphenyls [ix, xiv, xv, xvi]; we are grateful to Dr. Leffler for allowing us to see his work before publication. [j] The figures in parentheses were obtained from measurements by Graybill and Leffler. [k] $CHCl_3$ containing 6·9% of EtOH by volume.

i, Harris and Mellor, *Chem. and Ind.*, 1959, 949. ii, Dvorken, Smyth, and Mislow, *J. Amer. Chem. Soc.*, 1958, **80**, 486. iii, Ahmed and Hall, *J.*, 1959, 3383. iv, Hall and Turner, *J.*, 1955, 1242; Hall, *J.*, 1956, 3674. v, Mills and Kelham, *J.*, 1937, 274. vi, Ahmed and Hall, *J.*, 1958, 3043. vii, Adams and Kornblum, *J. Amer. Chem. Soc.*, 1941, **63**, 188. viii, Harris, *Proc. Chem. Soc.*, 1959, 367. ix, Graham and Leffler, *J. Phys. Chem.*, 1959, **63**, 1274. x, Li and Adams, *J. Amer. Chem. Soc.*, 1935, **57**, 1565. xi, Rieger and Westheimer, *J. Amer. Chem. Soc.*, 1950, **72**, 19. xii, Brooks and Harris, unpublished. xiii, Harris, unpublished. xiv, Leffler and Graybill, *J. Phys. Chem.*, 1959, **63**, 1457. xv, Leffler and Graham, *J. Phys. Chem.*, 1959, **63**, 687. xvi, Graybill and Leffler, *J. Phys. Chem.*, 1959, **63**, 1461. xvii, Wittig and Petri, *Annalen*, 1933, **505**, 17.

The error in the measurement of k is probably not greater than 5% and is often less: since measurements are usually made over approximately 20°, the statistical error[7] in E could be as much as $\pm 0{\cdot}6$ kcal. mole^{-1}.

Differences in E between members of the *N*-benzoyldiphenylaminecarboxylic acid series, where the whole spread is over only 4·6 kcal. mole^{-1}, would hardly be significant if

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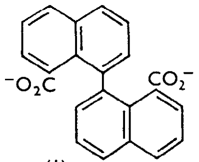
[7] Purlee, Taft, and DeFazio, *J. Amer. Chem. Soc.*, 1955, **77**, 837.



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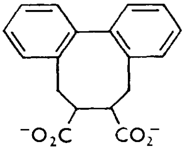

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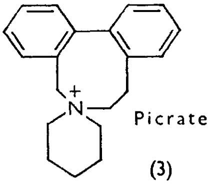

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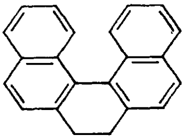

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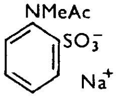

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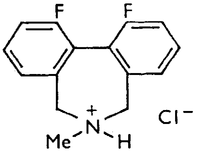

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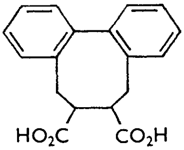

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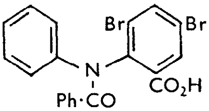

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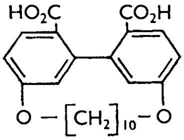

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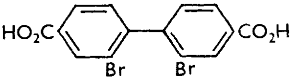

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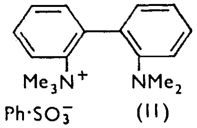

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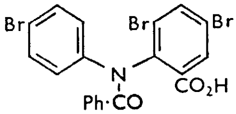

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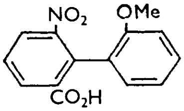

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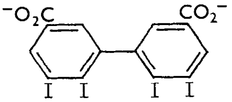

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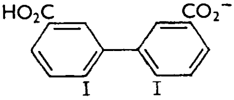

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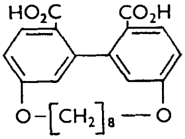

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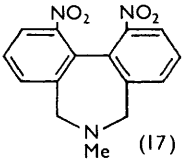

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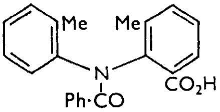

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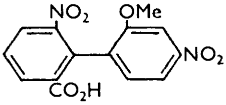

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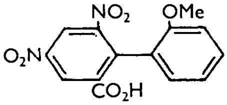

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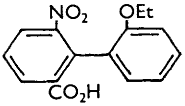

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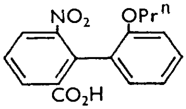

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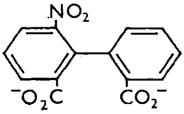

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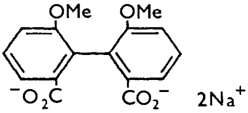

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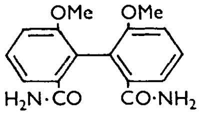

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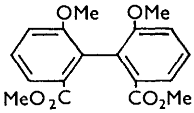

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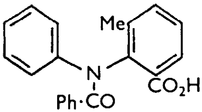

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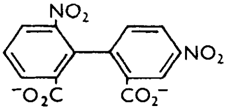

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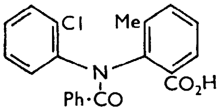

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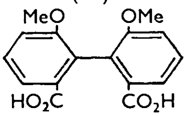

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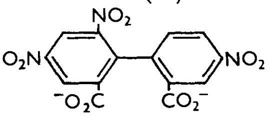

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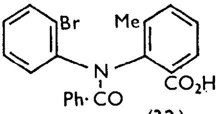

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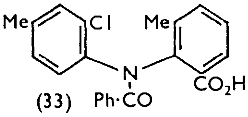

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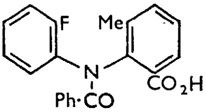

(34)

the rate constants from which they are derived had not been determined under closely comparable conditions.[4]

If E is plotted against $\log_{10} A$ for all the compounds in the table, there is a general scatter of points with a marked concentration between values of $\log_{10} A$ of 10·0 and 12·5. A line of correlation [8] between $\log_{10} A$ and E can be discerned in the *N*-benzoyldiphenylaminecarboxylic acids, as might be expected in a series of closely related compounds in the same solvent.[9,10]

Certain compounds, on which measurements have been published, have been omitted from the table, either because the rate constants were determined at rather high temperatures (at which an unusual mechanism might prevail), or because the values recorded were not sufficiently precise.

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[8] Fairclough and Hinshelwood, *J.*, 1937, 538.
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