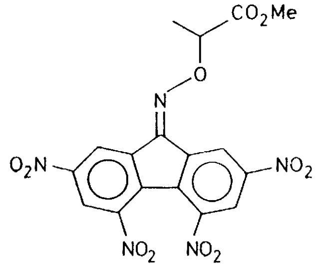
Diastereoisomeric Charge-transfer Complexes. Measurement of Thermodynamic Constants by ^{1}H Nuclear Magnetic Resonance Spectroscopy

By **Ayala Balan** and **Hugo E. Gottlieb,*** Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel

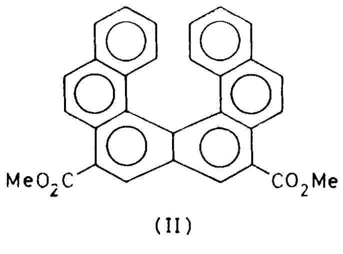
The addition of (−)-7,7'-bismethoxycarbonyl[6]helicene to a solution of (±)-2-(2,4,5,7-tetranitrofluoren-9-ylideneamino-oxy)propionic acid methyl ester (TAPM) results in the formation of two diastereoisomeric charge-transfer complexes. In the ^{1}H n.m.r. spectrum, this shifts the TAPM signals upfield and simultaneously splits them into separate groups of peaks. The chemical shifts relative to pure TAPM of solutions containing different helicene : TAPM ratios led to the determination of the equilibrium constants for the formation of the two complexes at room temperature. These measurements were then extended to a *ca.* 100 °C temperature range, and from that the enthalpies and enthropies of a complex formation were obtained. It is shown that while at low temperatures, the (−)(+)-complex is more stable than the (−)(−)-one, this is reversed at higher temperatures with a crossover point at 16 °C. These results are discussed by comparison with the chromatographic separation of helicene enantiomers.

FOR several years studies have been made in our laboratory [1] on the resolution of helicenes by h.p.l.c., using a column packed with silica gel to which (*R*)-(−)-TAPA† was bonded. Association of (*R*)-(−)-TAPA, a strong electron acceptor, with helicenes, as electron donors, leads to the formation of diastereoisomeric complexes. As the retention time of the *P*-(+)-helicene was longer than that of the *M*-(−)-isomer, it was concluded that the former has the higher stability constant with (−)-TAPA.

In order to further our understanding of the interactions involved in this phenomenon, we have investigated the helicene–TAPA system by n.m.r. N.m.r. spectroscopy has been used to probe charge-transfer complexes in solution,[2-4] since complexation is accompanied by changes in chemical shifts. In one such study, Hanna and Ashbaugh [2] have determined the association constants for 1 : 1 molecular complexes by measuring the chemical shifts of one component as the concentration of the second compound, present in large excess, is varied.



(I)



(II)

Complexation between chiral substances was studied by Pirkle *et al.*,[5] using dinitrophenyl derivatives and 1-(1-naphthyl)ethylamine or 1-(9-anthryl)-2,2,2-trifluoroethanol. Signal splitting due to formation of diastereoisomeric complexes was seen. Similar results were obtained by other authors [6] for (*R*)-(−)-TAPA–carbazole systems at −68 °C. In neither case, however, was the complexation measured quantitatively.

We report here the determination of the stability constants, enthalpies, and entropies of formation of diastereoisomeric complexes between (±)-TAPA methyl ester [(±)-TAPM] (I) and (−)-7,7'-bismethoxycarbonyl[6]helicene (II) in $CDCl_3$ solution by following proton chemical shifts.

EXPERIMENTAL

The ^{1}H n.m.r. spectra were recorded on a Bruker WH-270 spectrometer in the Fourier-transform mode. Spectral widths of 3 000 Hz and the use of 8 K data points in the real spectrum resulted in a digital resolution of ±0.001 p.p.m. All chemical shifts were referenced to internal $SiMe_4$, in $CDCl_3$ as solvent. Real probe temperatures were determined from peak separations of a methanol sample, using a calibration table, measured before and after each spectrum was run. In every case, $CDCl_3$ (500 μl) and (I) (*ca.* 10 mg) were used, with the addition of an appropriate amount of (II). Concentrations were expressed in mol kg^{-1}.

The substrates were synthesized according to known procedures.[7,8] [6]Helicene-7,7'-dicarboxylic acid was resolved by crystallization with 1-cinchonidine from an ethanol solution. Optical purity was proved to be >99% by h.p.l.c.

The thermodynamic data in Table 3 were obtained by a least-squares fit to the experimental points (see Figure 1), with the aid of an IBM 360 computer.

RESULTS

Complexation was followed by measuring the chemical shifts of 1-H of TAPM (I). The corresponding signal (a 2 Hz doublet due to *meta*-coupling) is convenient for this purpose, being at the lowest field end of the spectrum, well separated from other peaks. Furthermore, 1-H is more

---

† 2-(2,4,5,7-Tetranitrofluoren-9-ylideneamino-oxy)propionic acid.

TABLE 1

^{1}H N.m.r. chemical shifts of 1-H of (−)-TAPM with differing amounts of (±)-helicene for the determination of Δ_0[a]

Molar ratio helicene : TAPM	δ (H-1)	Δ	[TH]/[T$_0$], rel. exp.	[TH]/[T$_0$],rel. calc.[b]	Fraction of complexed TAPM[b]
(−)(+)-complex					
0	9.606	0	0	0	0
1.01	9.395	−0.211	0.227	0.227	0.133
2.08	9.232	−0.374	0.403	0.402	0.236
3.11	9.100	−0.506	0.546	0.541	0.318
4.08	9.013	−0.593	0.640	0.647	0.381
9.86	8.680	−0.926	1.000	1.000	0.588
(−)(−)-complex					
1.01	9.413	−0.193	0.229	0.228	0.135
2.08	9.265	−0.341	0.404	0.404	0.239
3.11	9.144	−0.462	0.548	0.543	0.321
4.08	9.063	−0.543	0.643	0.649	0.384
9.86	8.763	−0.843	1.000	1.000	0.592

[a] Determined at *ca.* 30 °C; see text for details. [b] Calculated for $K = 6.08$ [(−)(+)-complex] and 6.18 kg mol^{-1} [(−)(−)-complex], respectively.

strongly shifted on complexation than the protons of the side chain.

Addition of (−)-7,7′-bismethoxycarbonyl[6]helicene (II) to a solution of (±)-TAPM at *ca.* 30 °C results in an upfield shift and simultaneous splitting of the signal. Use of (−)-TAPM gave only one doublet, while interaction between the two racemic components produced slightly broadened, but not split, signals.

In order to obtain the thermodynamic parameters for the complexation, it was necessary to determine the values of Δ_0 for 1-H, *i.e.*, the chemical shift (relative to pure TAPM) for each complex. This task is not trivial, since there is fast equilibration between complexed and uncomplexed TAPM, so that the 1-H chemical shift is a weighted average of the δ values in the two species. To solve this problem, spectra were taken for varying helicene : TAPM proportions (see Table 1). The shift relative to pure TAPM, Δ, is given by $\Delta = \Delta_0[\mathrm{TH}]/[\mathrm{T}_0]$ [T], [H], and [TH] are the concentrations of TAPM, the helicene, and the complex, respectively, and [T$_0$] and [H$_0$] are the known initial concentrations of TAPM and the helicene; [TH]/[T$_0$] is therefore the mole fraction of complexed TAPM). The Δ value for each diastereoisomer in each case was divided by the corresponding Δ for the largest such proportion (9.86 : 1), as shown in Table 1. These ratios are independent of Δ_0 being only a function of the concentrations of the complexes in the various samples. If equation (1) and therefore (2) are

$$\mathrm{T} + \mathrm{H} \overset{K}{\rightleftharpoons} \mathrm{TH} \qquad (1)$$

$$K = [\mathrm{TH}]/[\mathrm{T}][\mathrm{H}] \qquad (2)$$

postulated, introduction of the balancing considerations (3) and (4) leads to equation (5).

$$[\mathrm{T}] = [\mathrm{T}_0] - [\mathrm{TH}] \qquad (3)$$

$$[\mathrm{H}] = [\mathrm{H}_0] - [\mathrm{TH}] \qquad (4)$$

$$K[\mathrm{TH}]^2 - (K[\mathrm{T}_0] + K[\mathrm{H}_0] + 1)[\mathrm{TH}] + K[\mathrm{T}_0][\mathrm{H}_0] = 0 \qquad (5)$$

Computer-generated tables for the ratios of [TH]/[T$_0$] values calculated through equation (5) for varying values of K indicated the equilibrium constants that best fit the experimental data for each diastereoisomeric complex (compare columns 4 and 5, Table 1). These equations are valid both for a pure enantiomer and a racemic mixture of TAPM as long as the K values for the two diastereoisomeric complexes are identical. Their application in the present case is an approximation that can be justified in view of the small differences in K values, which are never larger than 8%, and are <2% at room temperature.

Once K is known, and hence the percentage of complexation at each concentration, Δ_0 can easily be calculated. The values obtained for the (−)(+)- and the (−)(−)-complexes are -1.577 ± 0.013 and -1.425 ± 0.011 p.p.m., respectively, with the assignment being made by using TAPM enriched in one enantiomer. As the differences in Δ_0 values are relatively large whereas the complexation constants for the two isomeric species are about equal, the higher field signal corresponds always to the (−)(+)-complex.

The temperature-dependence of K permits the evaluation of the thermodynamic parameters. Once the Δ_0 values are known, K values for the diastereoisomers can be obtained from equation (6) (where $f = \Delta/\Delta_0$), derived from equations

$$K = \frac{f}{(1-f)([\mathrm{H}_0] - f[\mathrm{T}_0])} \qquad (6)$$

(1) and (3)—(5). Thus, spectra for a sample containing a 2 : 1 ratio of (−)-7,7′-bismethoxycarbonyl[6]helicene and TAPM were taken at several different temperatures and the K values calculated from the chemical shifts (see Table 2).

TABLE 2

Temperature dependence of δ(1-H) of (−)-TAPM in the presence of the (±)-helicene for the determination of ΔH and ΔS[a]

T/K	δ (1-H)	Δ	Fraction of complexed TAPM	K[b]
(−)(+)-complex				
236.6	8.909	−0.697	0.442	17.45
251.1	8.998	−0.608	0.386	13.41
264.7	9.075	−0.531	0.336	10.49
277.9	9.140	−0.466	0.296	8.48
293.5	9.205	−0.401	0.254	6.74
311.1	9.264	−0.342	0.217	5.35
328.5	9.312	−0.294	0.186	4.36
(−)(−)-complex				
236.6	8.999	−0.607	0.426	16.16
251.1	9.071	−0.535	0.375	12.65
264.7	9.133	−0.473	0.332	10.24
277.9	9.187	−0.419	0.294	8.40
293.5	9.243	−0.363	0.255	6.75
311.1	9.292	−0.314	0.220	5.48
328.5	9.333	−0.273	0.192	4.53

[a] For a 2.08 molar ratio of (±)-helicene : (−)-TAPM, see text for details. [b] In kg mol^{-1}.

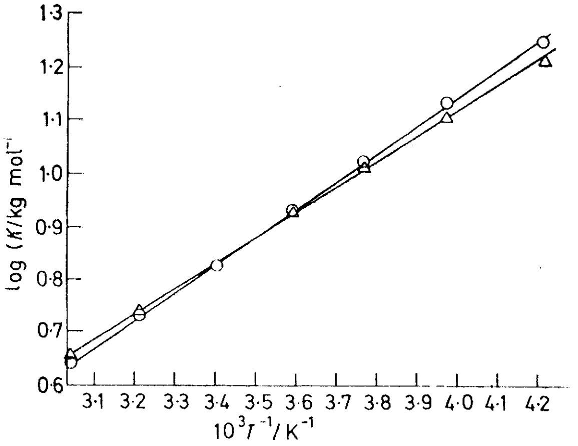
TABLE 3

Thermodynamic parameters for the formation of the charge-transfer complexes

	(−)(+)-complex	(−)(−)-complex	(−)(+) − (−)(−)
ΔH/kJ mol^{-1}	-9.14 ± 0.06	-9.94 ± 0.7	0.80 ± 0.13
ΔS_{rel}/J mol^{-1} K^{-1}	-15.2 ± 0.2	-18.0 ± 0.3	2.8 ± 0.5

A plot of log K *versus* $1/T$ gives a straight line for each diastereoisomeric complex (see Figure). The slopes yield the value of ΔH of complexation, while the intercepts are related to ΔS (see Table 3). It should be noted that K is dependent on the chosen concentration units [there are an unequal number of molecules on each side of the equilibrium represented by equation (1)], and therefore the ΔS values, which result from the intercepts, are also unit-dependent. However, their difference, $\Delta\Delta S$, is significant.

These determinations of the values of K depend on the widely used assumption that n.m.r. chemical shifts are temperature-independent. In the present case, this was checked by taking spectra of samples with different helicene : TAPM proportions at −12 °C. The K (and therefore also the Δ_0) values obtained do not significantly differ from the results presented in Table 2.



Graph of log K *versus* $1/T$ for the formation of the (−)(−)-(△) and (−)(+)-complexes (○)

DISCUSSION

The results presented above show that the formation of the (−)(+)-complex involves a larger decrease in both enthalpy and enthropy than that of the (−)(−)-complex. This would suggest a closer contact between the electron donor and the acceptor in the former complex. Based on this assumption, the larger absolute Δ_0 value for 1-H in the (−)(+)-complex would be explained by this proton being more deeply embedded in the shielding zone above and below the plane of the helicene system.

Since $\Delta\Delta H$ and $\Delta\Delta S$ are of the same sign, there is a temperature, in this case slightly below ambient (*ca.* 16 °C), where the K values coincide (see Figure). A parallel could be made with the chromatographic elution of 7,7′-bismethoxycarbonyl[6]helicene from a column containing bonded (−)-TAPA. At room temperature and below the (−)-enantiomer is first eluted, *i.e.* has lower affinity for the complexing agent fixed to the support. Upon raising the temperature, the relative retention of the two enantiomers reaches unity, however any peak reversal that might possibly occur could not be observed experimentally.[9] It should be pointed out that the TAPA molecule modified by linkage to silica gel might have a different crossover temperature to that of free TAPM. At the high temperatures involved, the retentions are so small that the resolving power of the column was insufficient to reveal any separation between the two enantiomers.

Temperature-dependent reversals of diastereoselectivity have been reported in the literature.[10] A recent further example of this phenomenon is described by Vanest and Martin.[11]

We thank Professor E. Gil-Av of this Department for many fruitful comments and discussions. A. B. gratefully acknowledges financial support from the Stiftung Volkswagenwerk.

[0/917 *Received*, 16*th June*, 1980]

REFERENCES

[1] F. Mikeš, G. Boshart, and E. Gil-Av, *J. Chromatogr.*, 1976, **122**, 205; F. Mikeš, G. Boshart, and E. Gil-Av, *J. Chem. Soc., Chem. Commun.*, 1976, 99.

[2] M. W. Hanna and A. L. Ashbaugh, *J. Phys. Chem.*, 1964, **68**, 811.

[3] R. Foster and C. A. Fyfe, *Trans. Faraday Soc.*, 1965, **61**, 1626.

[4] H. J. M. Andriessen, W. H. Laarhoven, and R. J. F. Nivard, *J. Chem. Soc., Perkin Trans. 2*, 1972, 861.

[5] W. H. Pirkle and D. L. Sikkenga, *J. Org. Chem.*, 1977, **42**, 1370.

[6] A. M. Mannschreck, P. Roza, H. Brockmann, and T. Kemmer, *Angew. Chem. Int. Ed. Engl.*, 1978, **17**, 942.

[7] P. Block, jun., and M. S. Newman, *Org. Synth.*, 1973, Coll. Vol. 5, 1031.

[8] C. Jutz and H. G. Löbering, *Ang. Chem. Int. Ed. Engl.*, 1975, **14**, 418.

[9] Y. H. Kim and E. Gil-Av, personal communication.

[10] For several examples, see J. D. Morrison and H. S. Mosher. 'Asymmetric Organic Reactions,' Prentice–Hall, Englwood Cliffs, New Jersey, 1971.

[11] J. M. Vanest and R. H. Martin, *Recl. Trav. Chim. Pays-Bas*, 1979, **98**, 113.