

Conformational Behaviour of Medium-sized Rings. Part I. 5,6,11,12-Tetrahydrodibenzo[*a,e*]cyclo-octene † (1,2,5,6-Dibenzocyclo-octa-1,5-diene †) and Heterocyclic Analogues

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The temperature dependence of the n.m.r. spectra of the eight-membered ring compound 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (1) and various aza- and thia-analogues [(7a—c), (8a—e), (9a—f), and (10b)] has been interpreted in terms of the interconversion of chair- and boat-like conformations. The values of the free energies of activation for these conformational changes are discussed in terms of probable transition state geometries and calculated strain energies.

THE conformational behaviour of medium-sized rings is generally complex,^{1,2} and experimental studies have been difficult to interpret because of the large number of available conformations of comparable energy. The situation in unsaturated ring systems is less complex^{1,3} because of the torsional rigidity of double bonds, but in spite of this simplifying factor little definitive work has been published concerning the conformations adopted in solution by medium-sized unsaturated ring systems. In this paper we discuss the conformational behaviour of 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (1) and a number of heterocyclic analogues.

It was pointed out some years ago³ that the dibenzocyclo-octene derivative (1) might be expected to adopt either a chair-like conformation (2) with C_{2h} symmetry or one of the family of boat-like conformations derived from the C_{2v} conformations (3) by a process involving rotation about the single bonds of the eight-membered ring, the boat conformation (3) and the D_2 twist-boat conformation (4) being considered as probable minimum energy points in this rotational process. The recognition that the hydrocarbon (1) in the crystalline state possesses a centre

† Throughout this paper we have used the nomenclature recommended by I.U.P.A.C. rule A-21.4 (also used by *Chem. Abs.*) rather than the alternative rule A-23.5 ('Nomenclature of Organic Chemistry,' Butterworths, London, 1966, 2nd edn., pp. 25 and 30).

¹ J. Dale, *Angew. Chem. Internat. Edn.*, 1966, **5**, 1000; J. D. Dunitz, 'Perspectives in Structural Chemistry,' vol. 2, ed. J. D. Dunitz and J. A. Ibers, Wiley, New York, 1968.

of symmetry³ was consistent with a crystal structure composed of molecules in the chair conformation (2).

A number of reports of the n.m.r. spectra of derivatives of compound (1) are relevant to its conformational behaviour. The dicyano-derivative (5) is believed on chemical grounds to have the indicated *trans*-stereochemistry and its n.m.r. spectrum shows⁴ at -40° an AB system (J_{AB} 11 Hz) for the C-5 and C-6 proton signals which coalesces to a singlet at higher temperatures. The observed coupling constant is consistent with a torsion angle (ω) of either *ca.* 0 or *ca.* 180° between the C(5)-H and C(6)-H bonds, which could mean that the molecule adopts a boat-like conformation similar to the FB conformation (see later) with ω 180° . The n.m.r. spectra of two tetrasubstituted derivatives of the hydrocarbon (1) also showed⁵ coupling of similar magnitude between

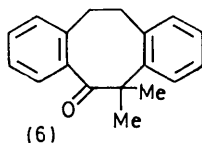
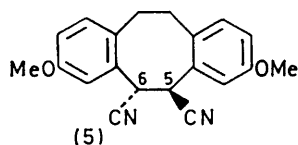
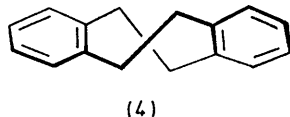
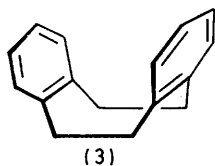
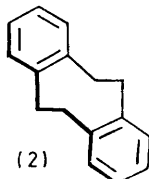
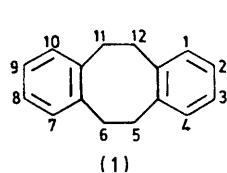
² (a) J. B. Hendrickson, *J. Amer. Chem. Soc.*, 1961, **83**, 4537; 1962, **84**, 3355; 1964, **86**, 4854; 1967, **89**, 7036, 7043, 7047; (b) K. B. Wiberg, *ibid.*, 1965, **87**, 1070; (c) N. L. Allinger, J. A. Hirsch, M. A. Miller, I. Tyminski, and F. A. Van-Catledge, *ibid.*, 1968, **90**, 1199; (d) M. Bixon and S. Lifson, *Tetrahedron*, 1967, **23**, 769; (e) C. Altona and M. A. Sunaralingham, *ibid.*, 1970, **26**, 925; (f) N. L. Allinger, M. T. Tribble, M. A. Miller, and D. H. Wertz, *J. Amer. Chem. Soc.*, 1971, **93**, 1637; (g) R. H. Boyd, *J. Chem. Phys.*, 1968, **49**, 2574.

³ W. Baker, R. Banks, D. R. Lyon, and F. G. Mann, *J. Chem. Soc.*, 1945, 27.

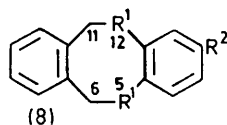
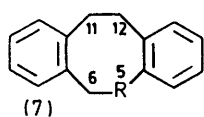
⁴ F.-H. Marquardt, *Tetrahedron Letters*, 1967, 4989.

⁵ A. T. Blomquist, Y. C. Meinwald, C. G. Bottomley, and P. W. Martin, *Tetrahedron Letters*, 1960, No. 24, 13; M. P. Cava, R. Pohlak, B. W. Erickson, J. C. Rose, and G. Fraenkel, *Tetrahedron*, 1962, **18**, 1005.

vicinal *trans*-protons of the eight-membered ring, which was considered to be consistent with a boat-like conformation. The n.m.r. spectrum of 11,12-dihydro-5,5-dimethyldibenzo[*a,e*]cyclo-octen-6(5*H*)-one (6) shows ⁶

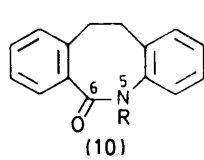
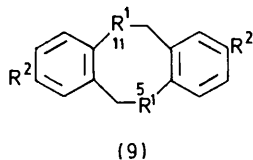


two C-methyl signals of equal intensity below 66°, indicating slow conformational inversion on the n.m.r. time scale. However, this result does not define the ground-state conformation of compound (6), which



- a; R = NAc
 b; R = NBz
 c; R = N·SO₂·C₆H₄Me-*p*
 d; R = N·CH₂Ph
 e; R = NH

- a; R¹ = NAc, R² = H
 b; R¹ = NBz, R² = H
 c; R¹ = N·SO₂·C₆H₄Me-*p*, R² = H
 d; R¹ = S, R² = Me
 e; R¹ = SO₂, R² = Me
 f; R¹ = NH, R² = H
 g; R¹ = N·CH₂Ph, R² = H



- a; R¹ = NAc, R² = Me
 b; R¹ = NBz, R² = Me
 c; R¹ = N·SO₂·C₆H₄Me-*p*, R² = Me
 d; R¹ = N·NO, R² = Me
 e; R¹ = S, R² = H
 f; R¹ = SO₂, R² = H

- a; R = H
 b; R = CH₂Ph

could be of either the chair or the boat type, or even a rapidly equilibrating mixture of more than one conformational type.

Clearly knowledge regarding the conformational

behaviour of '6,8,6-systems' [cf. (1)] is incomplete; we now report a study of the temperature dependence of the n.m.r. spectra of the hydrocarbon (1) and a number of its thia- and aza-analogues. The compounds examined fall into three main groups, all of which could be synthesised by standard procedures (Experimental section). The first group consisted of the tetrahydrodibenz[*b,f*]azocines (7a—c and e); the second of the tetrahydrodibenz[*b,f*][1,4]diazocines (8a—c, f, and g) and the tetrahydrodibenz[*b,f*][1,4]dithiocin derivatives (8d and e); and the third of the tetrahydrodibenz[*b,f*][1,5]diazocine derivatives (9a—d) and the tetrahydrodibenz[*b,f*][1,5]dithiocin derivatives (9e and f).

EXPERIMENTAL

5-Benzyl-11,12-dihydrodibenz[*b,f*]azocin-6(5*H*)-one (10b).—11,12-Dihydrodibenz[*b,f*]azocin-6(5*H*)-one ⁷ (10a) (5 g) and sodium hydride (0.6 g) in benzene were stirred and heated under reflux (30 min). Benzyl chloride (3.4 g) was added and heating was continued for a further 20 h. The mixture was treated with water (20 ml) and the benzene layer separated, dried, and evaporated. The oily residue was purified by chromatography on silica gel, with chloroform as eluant, giving the lactam (10b) (3.3 g, 47%), m.p. 131—132° (from n-hexane-benzene) [Found: C, 84.1; H, 6.4; N, 4.3%; *M* (mass spectrum), 313.1465. C₂₂H₁₉NO requires C, 84.3; H, 6.1; N, 4.5%; *M*, 313.1467; ν_{\max} 1640 cm⁻¹].

5-Benzyl-5,6,11,12-tetrahydrodibenz[*b,f*]azocine (7d).—The *N*-benzyl-lactam (10b) (1.0 g) and lithium aluminium hydride (0.3 g) in dry ether (60 ml) were heated under reflux (12 h). Excess of hydride was destroyed by the addition of water (10 ml) and aqueous sodium hydroxide (10*N*; 30 ml), and the ethereal layer was separated and combined with an ethereal extract (3 × 50 ml) of the aqueous layer. The combined extracts were dried and evaporated giving an oil. This was fractionated by chromatography on silica gel followed by short-path distillation at 130° at 0.005 mmHg yielding the azocine (7d) as an oil (0.78 g, 82%) (Found: C, 87.9; H, 7.0; N, 4.7. C₂₂H₂₁N requires C, 88.3; H, 7.1; N, 4.7%); ν_{\max} 1600 and 1495 cm⁻¹].

5-Acetyl-5,6,11,12-tetrahydrodibenz[*b,f*]azocine (7a).—The tetrahydrodibenzazocine ⁷ (7e) (1.0 g) and acetic anhydride (5 ml) in anhydrous pyridine were set aside (12 h) at room temperature. The solution was poured into water (50 ml), stirred for 30 min, and extracted with chloroform (2 × 30 ml). The extract was washed with dilute hydrochloric acid (30 ml) and aqueous sodium hydrogen carbonate (30 ml) and dried. Evaporation gave a pale yellow oil which was purified by t.l.c., followed by crystallisation from n-hexane, giving the *N*-acetylazocine (7a), m.p. 96—99° (0.67 g, 58%) [Found: C, 81.4; H, 6.9; N, 5.3%; *M* (mass spectrum), 251.1309. C₁₇H₁₇NO requires C, 81.2; H, 6.8; N, 5.6%; *M*, 251.1310]; ν_{\max} 1700 and 1690 cm⁻¹].

5-Benzoyl-5,6,11,12-tetrahydrodibenz[*b,f*]azocine (7b).—This compound was prepared as for the acetyl compound (7a) from the tetrahydrodibenzazocine (7e) (0.5 g) and benzoyl chloride (0.334 g). Purification by t.l.c. gave the *N*-benzoylazocine (7b), m.p. 110—113° (0.25 g, 33%) [Found: C, 84.1; H, 6.2; N, 4.6%; *M* (mass spectrum), 313.1468. C₂₂H₁₉NO

⁶ J. M. Davies and S. H. Graham, *Chem. Comm.*, 1968, 542.

⁷ A. M. Munro, R. M. Quinton, and T. I. Wrigley, *J. Medicin. Chem.*, 1963, 6, 255.

requires C, 84.3; H, 6.1; N, 4.5%; *M*, 313.1467; ν_{\max} , 1630 cm^{-1} .

5,6,11,12-Tetrahydro-5-*p*-tolylsulphonyldibenz[*b,f*]azocine (7c).—This compound was prepared as for the acetyl compound (7a). The tetrahydrodibenzazocine (7e) (0.3 g) and toluene-*p*-sulphonyl chloride (0.5 g) in anhydrous pyridine were heated under reflux (30 min). The product (7c) crystallised from aqueous ethanol as needles (0.46 g, 88% m.p. 152–153° [Found: C, 72.9; H, 5.9; N, 3.7; S, 8.8%; *M* (mass spectrum), 363.1298. $\text{C}_{22}\text{H}_{21}\text{NO}_2\text{S}$ requires C, 72.7; H, 5.8; N, 3.9; S, 8.8%; *M*, 363.1293; ν_{\max} , 1600 cm^{-1}).

5,6,11,12-Tetrahydro-5,12-bis-*p*-tolylsulphonyldibenzo[*b,f*]-[1,4]diazocine (8c).—This compound, prepared by the published procedure,⁸ crystallised from ethanol; m.p. 179° (lit.,^{8b} 178°) [Found: C, 64.8; H, 5.0; N, 5.6; S, 12.5%; *M* (mass spectrum), 518. Calc. for $\text{C}_{28}\text{H}_{26}\text{N}_2\text{O}_4\text{S}_2$: C, 64.9; H, 5.0; N, 5.4; S, 12.35%; *M*, 518].

5,6,11,12-Tetrahydrodibenzo[*b,f*][1,4]diazocine (8f).—The bis-*p*-tolylsulphonyldiazocine (8c) (9 g) was dissolved in *n*-butanol, and metallic sodium (15 g) was added in small portions. After the sodium had all reacted, the cooled mixture was poured into water (200 ml) and the *n*-butanol layer was separated and evaporated. The residual oil was extracted into dilute hydrochloric acid, the acidic solution was neutralised with aqueous sodium carbonate, and the product was extracted into chloroform. The extract was dried and evaporated, and the residual solid crystallised from ethanol giving the diazocine (8f) (3.0 g, 83%), m.p. 198° (lit.,^{8b} 198°) [Found: C, 79.9; H, 6.8; N, 13.5%; *M* (mass spectrum), 210. Calc. for $\text{C}_{14}\text{H}_{14}\text{N}_2$: C, 80.0; H, 6.7; N, 13.3%; *M*, 210].

5,12-Diacetyl-5,6,11,12-tetrahydrodibenzo[*b,f*][1,4]diazocine (8a).—The tetrahydrodiazocine (8f) (0.8 g) was treated with acetic anhydride (5 ml) and pyridine (1 ml). After the solution had been left for 17 h at room temperature, it was poured into dilute hydrochloric acid (20 ml) and the precipitate was collected, washed, dried, and crystallised from ethanol giving the *NN'*-diacetyltetrahydrodiazocine (8a), m.p. 238° (0.9 g, 81%) [Found: C, 73.4; H, 6.2; N, 9.3%; *M* (mass spectrum), 294. $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_2$ requires C, 73.5; H, 6.2; N, 9.5%; *M*, 294; ν_{\max} , 1655 cm^{-1}].

5,12-Dibenzoyl-5,6,11,12-tetrahydrodibenzo[*b,f*][1,4]diazocine (8b).—This was prepared as for the diacetyl derivative (8a). The tetrahydrodiazocine (8f) (0.5 g), benzoyl chloride (4 ml), and pyridine (3 ml) in benzene (30 ml) were heated under reflux (3 h) yielding the *dibenzoyl derivative* (8b) (0.7 g, 70%), m.p. 248° (from ethanol) [Found: C, 80.6; H, 5.5; N, 6.7%; *M* (mass spectrum), 418. $\text{C}_{28}\text{H}_{22}\text{N}_2\text{O}_2$ requires C, 80.4; H, 5.3; N, 6.7%; *M*, 418; ν_{\max} , 1650 cm^{-1}].

5,12-Dibenzyl-5,6,11,12-tetrahydrodibenzo[*b,f*][1,4]diazocine (8g).—The *NN'*-dibenzoyldiazocine (8b) (0.5 g) was dissolved in hot dry ether (100 ml) and lithium aluminium hydride (1 g) was added. The mixture was stirred and heated under reflux (24 h), then excess of hydride was decomposed with concentrated aqueous sodium hydroxide. The ethereal layer was separated, dried, and evaporated, and the residue was crystallised from light petroleum (b.p. 60–80°) giving the *NN'*-dibenzylidiazocine (8g) (0.36 g,

77%), m.p. 124° (Found: C, 85.9; H, 6.8; N, 7.1. $\text{C}_{28}\text{H}_{26}\text{N}_2$ requires C, 86.1; H, 6.7; N, 7.2%; τ (CDCl_3) 2.60–3.20 (18H, m, aromatic H) and 5.58 (8H, s, $2 \times \text{CH}_2\text{Ph}$ and $2 \times \text{CH}_2\text{Ar}$).

6,11-Dihydro-2-methylidibenzo[*b,f*][1,4]dithiocin (8d).—Toluene-3,4-dithiol (1.7 g) was dissolved in a solution of sodium hydroxide (0.9 g) in water (30 ml); $\alpha\alpha'$ -dibromo-*o*-xylene (2.8 g) in benzene was added and the mixture was heated under reflux (4 h). The benzene layer was separated, dried, and evaporated, and the residual oil was crystallised from ether-cyclohexane giving the *dithiocin* (8d) (0.4 g, 14%), m.p. 122–127° [Found: C, 69.6; H, 5.7; S, 25.1%; *M* (mass spectrum), 258. $\text{C}_{15}\text{H}_{14}\text{S}_2$ requires C, 69.8; H, 5.5; S, 24.8%; *M*, 258].

6,11-Dihydro-2-methylidibenzo[*b,f*][1,4]dithiocin 5,5,12,12-tetraoxide (8e).—The dithiocin derivative (8d) (200 mg) was heated under reflux (30 min) in acetic acid and hydrogen peroxide. The mixture was poured into water and extracted with chloroform. The chloroform solution was dried and evaporated giving the *bis-sulphone* (8e) m.p. 251° (from aqueous 95% ethanol) (Found: C, 55.6; H, 4.6; S, 20.1. $\text{C}_{15}\text{H}_{14}\text{O}_4\text{S}_2$ requires C, 55.9; H, 4.35; S, 19.9%).

6,12-Dihydrodibenzo[*b,f*][1,5]dithiocin⁹ (9e), 5,6,11,12-tetrahydro-2,8-dimethyl-5,11-dinitrosodibenzo[*b,f*][1,5]diazocine¹⁰ (9d), 5,11-diacetyl-5,6,11,12-tetrahydro-2,8-dimethylidibenzo[*b,f*][1,5]diazocine (9a),¹¹ 5,11-dibenzoyl-5,6,11,12-tetrahydro-2,8-dimethylidibenzo[*b,f*][1,5]diazocine (9b),¹¹ and 5,6,11,12-tetrahydro-2,8-dimethyl-5,11-bis-*p*-tolylsulphonyldibenzo[*b,f*][1,5]diazocine¹² (9c) were prepared by published methods. They had spectral properties in accord with the assigned constitutions.

6,12-Dihydrodibenzo[*b,f*][1,5]dithiocin 5,5,11,11-tetraoxide (9f).—Peroxyauric acid (5.0 g, 80%) was added to a solution of the dithiocin derivative (9e) (1.1 g) in chloroform (40 ml). After 20 h, the solution was evaporated and the residue triturated with *n*-hexane giving the *bis-sulphone* (9f) as prisms (1.2 g), m.p. 259° (from chloroform) [Found: C, 54.45; H, 4.0; S, 20.6%; *M* (mass spectrum), 308. $\text{C}_{14}\text{H}_{12}\text{O}_4\text{S}_2$ requires C, 54.6; H, 3.9; S, 20.8%; *M*, 308].

Measurement of Rates of Conformational Change by N.m.r. Spectroscopy.—The n.m.r. spectra of the compounds (1), (7a–c), (8a–e), and 9a–f) were recorded at a number of temperatures by use of a Varian HA 100 spectrometer equipped with a variable temperature probe. Solutions were generally 5–10% w/v in the stated solvents. Probe temperatures were calibrated by use of ethylene glycol and methanol standards and are probably accurate to $\pm 2^\circ$. The relevant details of the spectra are listed in Table 1; Table 2 gives details of temperature-dependent changes. Table 2 also lists the associated activation parameters (ΔG^\ddagger) based upon exchange rates obtained by the comparison of observed and calculated spectra. The latter were obtained by use of FORTRAN IV programmes, which calculated n.m.r. spectra for the following situations (a)–(c) from the stated input data.

(a) A programme for a two-site exchange process with no mutual coupling based upon the appropriate line-shape equation.¹³

The required input parameters are the site exchange rates, k_A and k_B (where k_A is the rate for the site exchange $A \rightarrow B$

⁸ (a) H. Stetter, *Chem. Ber.*, 1953, **86**, 161; (b) W. Schroth and B. Streckenbach, *Z. Chem.*, 1963, **465**; (c) E. Negishi and A. R. Day, *J. Org. Chem.*, 1965, **30**, 43.

⁹ M. Borovicka, F. Kuis, J. Chromok, and M. Protiva, *Coll. Czech. Chem. Comm.*, 1957, **32**, 1745.

¹⁰ M. A. Spielmann, *J. Amer. Chem. Soc.*, 1935, **57**, 584.

¹¹ F. C. Cooper and M. W. Partridge, *J. Chem. Soc.*, 1955, 991.

¹² F. C. Cooper and M. W. Partridge, *J. Chem. Soc.*, 1957, 2888.

¹³ M. T. Rogers and J. C. Woodbrey, *J. Phys. Chem.*, 1962, **66**, 540.

and k_B for $B \rightarrow A$ in s^{-1}), the site populations, p_A and p_B expressed as mole fractions, the chemical shifts of the two sites, ν_A and ν_B in Hz, and the two relaxation times, t_{2A} and t_{2B} in s, based upon the low temperature line-widths of the two signals. The chemical shifts ν_A and ν_B were regarded as variable input parameters in cases where the low temperature spectra indicated that they were temperature dependent.

(b) A programme for the exchange of nuclei between two sites A and B with equal populations and a mutual coupling constant, J . This programme was based upon the equation¹⁴ derived for this situation.

The input parameters are the single exchange rate k s^{-1} , the relaxation time t_2 s, the site chemical shifts ν_A and ν_B Hz, and the coupling constant J Hz. The chemical shifts ν_A and ν_B could again be regarded, in some cases, as variable parameters.

(c) A programme for the more complex case in which nuclei are exchanged between all four sites of the two AB systems, A1 and B1 and A2 and B2.

Line-shape equations of the types used for situations (a) and (b) are not available for situation (c); in this case spectra were simulated by use of the density matrix approach developed by Kaplan,¹⁵ Alexander,¹⁶ and Johnson.¹⁷ For two AB systems undergoing the exchange of nuclei between the sites illustrated in Figure 1 this method gives two sets of four simultaneous equations in the density matrix elements for the eight allowed transitions corresponding to the eight lines observed in two AB systems (Figure 2) (cf. ref. 18).

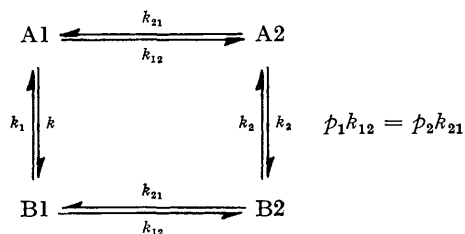


FIGURE 1 Site exchanges for programme of situation (c)

The first set of four simultaneous equations involves the density matrix elements ρ_{12}^1 , ρ_{12}^2 , ρ_{13}^1 , and ρ_{13}^2 . The subscripts have the usual significance and refer to spin states; the superscripts 1 and 2 refer to the two different AB systems of Figure 1. Then, by considering the effects of the site exchanges shown in Figure 1 upon the basis functions, the following simultaneous equations (1)–(4) in the ρ 's may be obtained for 'steady-state' conditions ($\partial\rho_{ij}/\partial t = 0$, etc).

$$k_{21}\rho_{12}^2 - k_{12}\rho_{12}^1 - k_{11}\rho_{12}^1 + k_{11}\rho_{13}^1 - \rho_{12}^1/t_{2B1} - 2\pi i\rho_{12}^1(\nu_{B1} - \nu + \frac{1}{2}J_1) + i\rho_{13}^1\pi J_1 + p_1 iC = 0 \quad (1)$$

$$k_{21}\rho_{13}^2 - k_{12}\rho_{13}^1 - k_{11}\rho_{13}^1 + k_{11}\rho_{12}^1 - \rho_{13}^1/t_{2A1} - 2\pi i\rho_{13}^1(\nu_{A1} - \nu + \frac{1}{2}J_1) + i\rho_{12}^1\pi J_1 + p_1 iC = 0 \quad (2)$$

$$k_{12}\rho_{12}^1 - k_{21}\rho_{12}^2 - k_{22}\rho_{12}^2 + k_{22}\rho_{13}^2 - \rho_{12}^2/t_{2B2} - 2\pi i\rho_{12}^2(\nu_{B2} - \nu + \frac{1}{2}J_2) + i\rho_{13}^2\pi J_2 + p_2 iC = 0 \quad (3)$$

$$k_{12}\rho_{13}^1 - k_{21}\rho_{13}^2 - k_{22}\rho_{13}^2 + k_{22}\rho_{12}^2 - \rho_{13}^2/t_{2A2} - 2\pi i\rho_{13}^2(\nu_{A2} - \nu + \frac{1}{2}J_2) + i\rho_{12}^2\pi J_2 + p_2 iC = 0 \quad (4)$$

A second set of simultaneous equations may be obtained in ρ_{24}^1 , ρ_{34}^1 , ρ_{24}^2 , and ρ_{34}^2 which differ from the first set in the

¹⁴ J. Heidberg, J. A. Weil, G. A. Janusonis, and J. K. Anderson, *J. Chem. Phys.*, 1964, **41**, 1033.

¹⁵ J. I. Kaplan, *J. Chem. Phys.*, 1958, **28**, 278; 1958, **29**, 462.

¹⁶ S. Alexander, *J. Chem. Phys.*, 1962, **37**, 967, 974; 1963, **38**, 1787; 1964, **40**, 2741.

¹⁷ C. S. Johnson, *J. Chem. Phys.*, 1964, **41**, 3277; *Adv. Magn. Resonance*, 1965, **1**, 33; *J. Magn. Resonance*, 1969, **1**, 98.

sign of the J 's. These eight complex simultaneous equations are then solved for the ρ 's at each input value of ν , and the absorption intensity at ν is proportional to the imaginary part of $\Sigma\rho_{rs}$ for all the eight allowed transitions. The simultaneous equations (1)–(4) show a resemblance to the equations derivable from the McConnell equation for a four-site exchange with no coupling. Figure 2 shows diagrammatically the site exchanges that are represented by the eight simultaneous equations used in the foregoing treatment.

This type of programme, although not as efficient as the more general programme described by Binsch,¹⁹ proved to be adequate for spectrum simulation. A spectrum consisting of the absorption intensity at 250 values of ν required a computing time of only 10 s on an I.C.L. 1907 computer.

The general procedure used to obtain exchange rates involved initially determination of the faster exchange rate

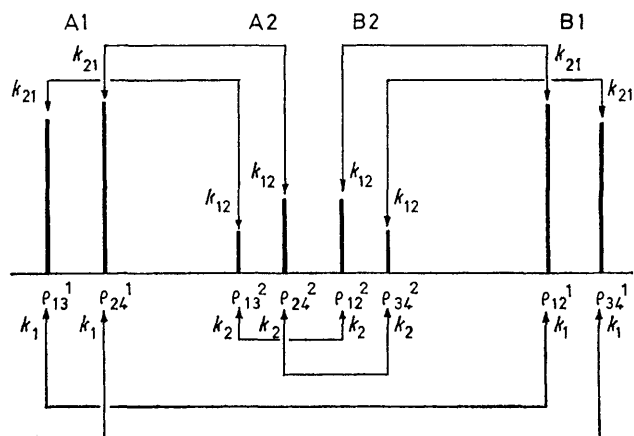


FIGURE 2 Exchange of nuclei between the four sites (A1, B1, A2, and B2) of two AB systems. The density matrix element corresponding to each transition is indicated. The double-headed arrows represent site exchanges with the appropriate rate constant given by each arrow

by setting the slower exchange rate to zero and matching the spectra by variation of the faster exchange rate. Values of the faster exchange rate could then be calculated at higher temperatures by extrapolation from the low temperature values, and the second exchange rate was obtained at higher temperature by inserting trial values into the calculation until agreement was obtained between observed and calculated spectra.

In a preliminary examination of the n.m.r. spectral site exchange rates, k_c values were calculated at coalescence temperatures from the equations (5)²⁰ and (6),²¹ suitable respectively for a two-site exchange with $p_A = p_B = 0.5$, $J_{AB} = 0$ and for the coupled two-site exchange with $J_{AB} \neq 0$.

$$k_C = \pi(\nu_A - \nu_B)/2^{\frac{1}{2}} \quad (5)$$

$$k_C = \pi[(\nu_A - \nu_B)^2 + 6J_{AB}^2]^{\frac{1}{2}}/2^{\frac{1}{2}} \quad (6)$$

$$k_A = \pi(W_A - W_{A0}), \quad k_B = \pi(W_B - W_{B0}) \quad (7)$$

¹⁸ C. J. Cresswell and R. K. Harris, *J. Magn. Resonance*, 1971, **4**, 99; C. S. Johnson, *ibid.*, 1969, **1**, 98.

¹⁹ G. Binsch, *J. Amer. Chem. Soc.*, 1969, **91**, 1304.

²⁰ H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, 1956, **25**, 1228.

²¹ M. Oki, H. Iwamura, and N. Hayakawa, *Bull. Chem. Soc. Japan*, 1963, **36**, 1542; R. J. Kurland, M. B. Rubin, and W. B. Wyse, *J. Chem. Phys.*, 1964, **40**, 2426.

TABLE 1

N.m.r. spectra (100 MHz) of chair and boat conformations of 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene and heterocyclic analogues

Compd.	Solvent	Temp. (°C)	Group	Chemical shifts ^a (τ) ± 0.01 Coupling constants (Hz) ± 0.5	Populations
(1)	CDCl ₃ -CS ₂ (1 : 1)	-86	C ₆ H ₄ CH ₂ ·CH ₂ ^b	2.86 (A), 3.13 (B) 6.86 (s), 7.01 (AA'), 7.31 (BB') ^b	$p_A \approx p_B \approx 0.5$
		+35	C ₆ H ₄ CH ₂ ·CH ₂ ^b	3.16 (AB) 7.02 (s) ^b	
(7a)	CDCl ₃ -CS ₂ (1 : 1)	-86	N·CO·CH ₃ N·CH ₂	8.16 (A), 8.28 (B) 4.11 (A1), 5.92 (B1), <i>J</i> 13.5 4.84 (A2), 6.08 (B2), <i>J</i> 15.0	p_A 0.79, p_B 0.21 p_1 0.79, p_2 0.21
	C ₆ D ₆ ·NO ₂	+63	N·CH ₂	4.32 (A12), 6.05 (B12), <i>J</i> 15.0	
(7b)	CDCl ₃ -CFCl ₃ (1 : 2)	-74	N·CH ₂	3.94 (A1), 5.50 (B1), <i>J</i> 15.0 4.42 (A2), 5.91 (B2), <i>J</i> 13.5	p_1 0.425, p_2 0.575
	CDCl ₃	+35	N·CH ₂	4.25 (A12), 5.76 (B12), <i>J</i> 14.25	
(7c)	CDCl ₃ -CFCl ₃ (1 : 1)	-85	N·SO ₂ ·C ₆ H ₄ ·CH ₃ N·CH ₂	7.49 (A), 7.72 (B) 4.58 (A), 5.81 (B), <i>J</i> 13.25	p_A 0.858, p_B 0.142
		-48			
(8a)	CDCl ₃	-43	N·CO·CH ₃ N·CH ₂	8.01 (A), 8.18 (B) 4.70 (A1), 5.95 (B1), <i>J</i> 14.5 4.82 (A2), 5.27 (B2), <i>J</i> 13.5	p_A 0.428, p_B 0.572 p_1 0.428, p_2 0.572
		+19	N·CH ₂	4.76 (A12), 5.64 (B12), <i>J</i> 14.5	
(8b)	CDCl ₃	-33	N·CH ₂	4.30 (A1), 4.88 (B1), <i>J</i> 14.5 4.35 (A2), 5.02 (B2), <i>J</i> 15.0	p_1 0.54, p_2 0.46
(8c)	CDCl ₃ -CFCl ₃ (1 : 1)	-86	N·CH ₂	4.78 (A), 5.56 (B), <i>J ca.</i> 12	<i>c</i>
(8d)	CS ₂	-74	S·CH ₂	5.92 (A1), 7.36 (B1), <i>J</i> 14.0 5.94 (A3), 7.36 (B3), <i>J</i> 14.0 5.63 (AB2) 5.70 (AB4)	$p_1 = p_3 = 0.155$ $p_2 = p_4 = 0.845$
			ArCH ₃	7.66 (A), 7.84 (B)	p_A 0.155, p_B 0.845
(8e)	CDCl ₃	-66	SO ₂ ·CH ₂	4.51 (A1), 5.20 (B1), <i>J</i> 14.0 4.58 (A2), 5.20 (B2), <i>J</i> 14.0	<i>c</i>
(9a)	(CD ₃) ₂ SO	+67	N·CH ₂	4.33 (A1), 5.98 (B1), <i>J</i> 16.0 5.07 (A2), 6.22 (B2), <i>J</i> 13.5	p_1 0.602, p_2 0.398
		+56	N·CO·CH ₃	8.40 (A), 8.48 (B)	p_A 0.622, p_B 0.378
(9b)	(CD ₃) ₂ SO	+67	N·CH ₂	4.42 (A1), 5.79 (B1), <i>J</i> 16.0 4.63 (A2), 5.90 (B2), <i>J</i> 13.5	p_1 0.50, p_2 0.50
(9c)	(CD ₃) ₂ SO	+80	N·CH ₂	5.44 (A1), 6.71 (B1), <i>J</i> 15.0 5.86 (A2), 6.20 (B2), <i>J</i> 13.5	p_1 0.48, p_2 0.52
			N·SO ₂ ·C ₆ H ₄ ·CH ₃	7.67 (A), 7.95 (B)	p_A 0.48, p_B 0.52
(9d)	CDCl ₃ -CS ₂ (1 : 1)	-74	N·CH ₂	4.56 (A1), 5.90 (B1), <i>J</i> 14.0 4.74 (A2), 5.13 (B2), <i>J</i> 15.0	p_1 0.51, p_2 0.49
		-40	ArCH ₃ N·CH ₂	7.50 (A), 7.58 (B) 4.56 (A1), 5.90 (B1), <i>J</i> 14.0 4.96 (AB2)	p_A 0.503, p_B 0.497
(9e)	CDCl ₃ -CS ₂ (1 : 1)	-66	S·CH ₂	5.09 (A1), 6.20 (B1), <i>J</i> 12.0 5.67 (A2), 5.90 (B2), <i>J</i> 13.5	p_1 0.80, p_2 0.20
(9f)	C ₆ D ₅ N	+34	SO ₂ ·CH ₂	4.14 (A), 4.75 (B), <i>J</i> 14.25	<i>c</i>

^a Sites are designated (A) and (B) for two-site systems [see Experimental section, methods (a) and (b)] and (A1), (B1), *etc.* for four-site systems where (A1) refers to the site at ν_{A1} and (B1) to the site at ν_{B1} , *etc.* [see Experimental section, method (c)]. Sites that represent two time-averaged signals are designated (AB1) [average of (A1) and (B1)] and (A12) [average of (A1) and (A2)], *etc.*
^b The CH₂·CH₂ group gives an AA'BB' system for the chair conformation and a time-averaged singlet for the boat conformation, which coalesce to a single singlet at higher temperatures. ^c Only a single conformation was observed.

For cases with $p_A \neq p_B$, site exchange rates at low temperature could also be approximately based upon the simple expression (7), where W is the observed line-width, W_0 is the line-width in the absence of exchange, k_A refers to the rate constant for the A \rightarrow B exchange and k_B to the B \rightarrow A exchange.

RESULTS AND DISCUSSION

The relevant details of the n.m.r. spectra, their temperature dependence, and the calculated activation parameters associated with site exchange processes are listed in Tables 1 and 2 for the series of compounds (1),

(7a—c), (8a—e), and (9a—f). Table 2 also specifies the method of computation used to examine site exchange rates. The values of ΔG^\ddagger obtained from the comparison of observed and computed spectra, which is generally considered to be the most accurate method of obtaining exchange rates,²² do not differ significantly from those

²² For reviews and critical discussions see (a) G. Binsch, *Topics Stereochem.*, 1968, **3**, 97; (b) J. Jonas and H. S. Gutowsky, *Ann. Rev. Phys. Chem.*, 1968, **19**, 448; (c) L. M. Jackman, T. E. Kavanagh, and R. C. Haddon, *Org. Magn. Resonance*, 1969, **1**, 109; (d) I. O. Sutherland, *Ann. Reports N.M.R. Spectroscopy*, 1971, **4**, 71.

TABLE 2
Spectral changes, rate constants, and activation parameters for the conformational changes of 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene and heterocyclic analogues

Compd.	Solvent	Group	Sites involved in exchange ^a	Method of computation ^b	Number of determinations	Temp. range (°C)	ΔG^\ddagger kcal mol ⁻¹	ΔG_{12}^\ddagger kcal mol ⁻¹ (°C)	Process ^g
(1)	CDCl ₃ -CS ₂ (1:1)	C ₆ H ₄	A ⇌ B	CT	1	-66	10.2	ca. 0 (-86)	Chair ⇌ Boat
(7a)	CDCl ₃ -CS ₂ (1:1)	N·CO·CH ₃	A → B	TLS-(a)	5	-77 to -56	11.1	+0.49 (-86)	Chair ⇌ Boat
	C ₆ D ₅ NO ₂	N·CH ₂	A12 ⇌ B12	TLS-(b)	6	+88 to +113	20.1		Boat ⇌ Boat*
(7b)	CDCl ₃ -CFCl ₃ (1:2)	N·CH ₂	A1 → A2	TLS-(c)	7	-61 to -34	11.35	-0.12 (-74)	Chair ⇌ Boat
			B1 → B2						
			A12 ⇌ B12	TLS-(b)	10	+40 to +69	17.7		Boat ⇌ Boat*
(7c)	CDCl ₃ -CFCl ₃ (1:1)	N·SO ₂ ·C ₆ H ₄ ·CH ₃	A → B	TLS-(a)	3	-63 to -53	10.6	+0.67 (-85)	Chair ⇌ Boat
	CDCl ₃ -CFCl ₃ (1:2)	N·CH ₂	A ⇌ B	TLS-(b)	7	-23 to +7	14.3		Boat ⇌ Boat*
(8a)	CDCl ₃	N·CO·CH ₃	A → B	TLS-(a)	7	-33 to -4	12.9 (13.1)	-0.13 (-43)	Chair ⇌ Boat
		N·CH ₂	A12 ⇌ B12	TLS-(b)	7	+25 to +63	16.9 (17.2)		Boat ⇌ Boat*
(8b)	CDCl ₃	N·CH ₂	A1 → A2	TLS-(c)	1	-15	14.05 (13.7)	+0.08 (-33)	Chair ⇌ Boat
			B1 → B2						
			A1 ⇌ B1	TLS-(c)	1	-15	14.3 (14.4)		Boat ⇌ Boat*
(8c)	CDCl ₃ -CFCl ₃ (1:1)	N·CH ₂	A ⇌ B	TLS-(b)	2	-75 to -62	10.1 (9.9)		Inversion
(8d)	CS ₂	ArCH ₃	A → B	TLS-(a)	7	-54 to -19	12.0 (12.2)	-0.68 (-74)	Chair → Boat
(8e)	CDCl ₃	SO ₂ ·CH ₂	A1 ⇌ B1	TLS-(b)	14	-55 to -5	11.9 (11.9)		C ⇌ C*
			A2 ⇌ B2						
(9a)	(CD ₃) ₂ SO	N·CH ₂	A1 → A2	TLS-(c)	1	+134	22.4	+0.28 (+67)	Chair ⇌ Boat
			B1 → B2						
			A2 ⇌ B2	TLS-(c)	1	+134	21.8 (22.5)		Inversion
(9b)	(CD ₃) ₂ SO	N·CO·CH ₃	A → B	TLS-(a)	8	+122 to +164	22.4 (22.1)	+0.32 (+56)	Chair ⇌ Boat
		N·CH ₂	A1 → A2	TLS-(c)	1	+112	20.8 (20.8)	0.00 (+67)	Chair ⇌ Boat
			B1 → B2						
			A2 ⇌ B2	TLS-(c)	1	+112	21.05 (21.2)		Inversion
(9c)	(CD ₃) ₂ SO	N·CH ₂	A1 → A2	TLS-(c)	1	+94	19.6 (19.3)	-0.06 (+80)	Chair ⇌ Boat
			B1 → B2						
			A2 ⇌ B2	TLS-(c)	1	+94	18.8 (18.4)		Inversion
(9d)	CDCl ₃ -CS ₂ (2:1)	N·CH ₂	A2 ⇌ B2	TLS-(b)	1	-53	10.6 (10.4)		Boat ⇌ Boat*
			A1 → AB2	TLS-(c)	6	-18 to +1	13.8 (13.4)	+0.01 (-74)	Chair ⇌ Boat
			B1 → AB2	TLS-(a)	6				
			A → B						
(9e)	CDCl ₃ -CS ₂ (1:1)	S·CH ₂	A1 ⇌ B1	TLS-(c)	2	-43 to -38	12.4 (11.9)	+0.57 (-66)	Boat ⇌ Boat*
			A1 → A2	TLS-(c)	3	-19 to -9	14.4		Chair ⇌ Boat
			B1 → B2						
(9f)	C ₅ D ₅ N	SO ₂ ·CH ₂	A ⇌ B	TLS-(b)	5	+61 to +81	18.6 (19.0)		C ⇌ C*

^a For details of the n.m.r. parameters associated with each site, see Table 1. ^b See Experimental section. CT refers to the use of the coalescence temperature approximation. TLS refers to line-shape comparison. ^c Where two rate constants are involved, the value of ΔG^\ddagger refers to the process 1 → 2 or A → B indicated in column 4. ^d The value is averaged over the number of determinations (column 6) and the temperature range (column 7). ^e The value in parentheses refers to the use of the coalescence temperature approximations. ^f ΔG for the process 1 → 2 or A → B at the temperature given in parentheses. ^g See footnote †, p. 211 and footnote ‡, p. 213.

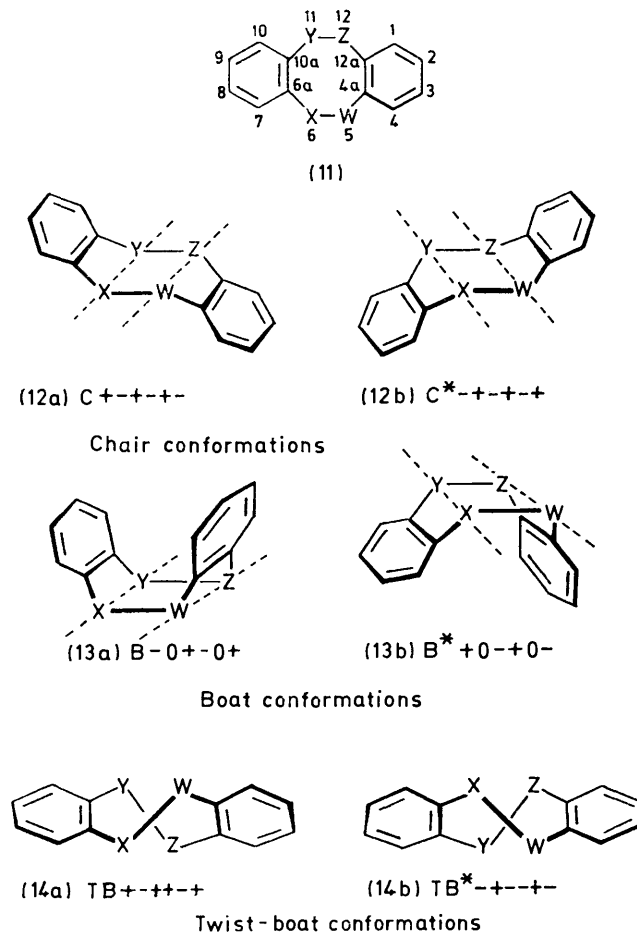
obtained by use of approximations based upon either coalescence temperatures or low temperature line-broadening [equations (5)—(7)]. The n.m.r. spectra of the diazocine derivative (8g) and the azocine derivative (7d) did not show temperature dependence down to -100° ; it is therefore probable that the conformational changes associated with these compounds are fast on the n.m.r. time scale even at this low temperature.

Examination of molecular models shows that there are three low energy conformations of 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (1) and its heterocyclic analogues (7)—(9) [represented conveniently by the general formula (11)].† The first is the chair conformation C (12a), the second is the boat conformation B (13a), and the third is the twist-boat conformation TB (14a). These conformations and their enantiomers, C* (12b), B* (13b), and TB* (14b), are shown in the appropriate conformational formulae. The C (12) and B (13) conformations are characterised by groups of atoms which lie in (or close to) planes, and the lines of intersection of these planes are indicated by the broken lines in the diagrams. In the case of the hydrocarbon (1) (11; $W = X = Y = Z = \text{CH}_2$), the conformations C and C* are identical and have C_{2v} symmetry. These conformations, C and C*, are also identical for the dibenzo[*b,f*]-[1,4]diazocine derivatives (8a—c) and have C_s symmetry. The conformations B and B* are also identical for these four compounds [(1), (8a—c)], having either C_{2v} symmetry (1) or C_s symmetry (8a—c). The TB conformations (14a) and (14b) do not have reflection symmetry so that in all cases the chiral conformations TB and TB* are related as enantiomers. In spite of the identity of the pairs of conformations C and C* and B and B* in some cases, it is convenient to maintain the distinction in all cases in the discussion that follows. This decision has been made because the environments of the individual hydrogen atoms in a ring methylene group are mutually exchanged by the inversion of any of the conformational types C, B, and TB to give the C*, B*, and TB* conformations, respectively.

These conformations (12)—(14), and other conformational types discussed in this paper, are also described below the formulae in the usual notation,^{2a,23} in which the torsional angles about each of the six single bonds of the eight-membered ring are defined as positive (15a), negative (15b), or zero (15c) when viewed from atom *n* to atom *n* + 1 [see (11)] as shown in the Newman projections (15); the curved bond represents the remainder of the eight-membered ring. This notation is used for the bonds in the order 4a—5, 5—6, 6—6a, 10a—11, 11—12, and 12—12a. Thus, for example, the C conformation (12a) is described as + - + - + -. This representation is useful in that the torsional changes that lead to the inter-

conversion between diastereomeric conformations or inversion between enantiomeric conformations may readily be recognised from the changes in the sign of individual torsional angles.

From the examination of models, it is possible to postulate twelve reasonable transition state geometries for the interconversion or inversion between any two of



the conformations C, C*, B, B*, TB, and TB*. These conformational changes are shown in Figure 3. The twelve transition states for these interconversions are shown in the formulae (16)—(21)(a—b); they are of three general types.

Those of the first type, the folded boat conformations, FB1 (16a), FB1* (16b), FB2 (17a), and FB2* (17b), are recognised by the approximate coplanarity of two groups of five atoms in the eight-membered ring, and the lines of intersection of these two planes are shown as broken lines in the diagrams (16a and b) and (17a and b). The principal non-bonded interactions in the transition state of this type (FB), which are relevant for the processes $B \rightleftharpoons TB$, $TB \rightleftharpoons B^*$, $B \rightleftharpoons TB^*$, and $TB^* \rightleftharpoons B$ (see Figure 3) are the transannular interactions between the ring atoms and their substituents located at or near the broken lines in the diagrams (16) and (17). For compounds (7a and b), (8a and b), and (9a and b), having

²³ W. Klyne and V. Prelog, *Experientia*, 1960, **16**, 521.

† The methyl substituents present in the compounds (8d and e) and (9a—d) are omitted from this formula and the general formulae (12)—(21) for simplicity. Their presence is not generally relevant to the discussion unless specifically mentioned, although the aryl-methyl signals have in two cases, (8d) and (9d) (Table 2), been used to determine the rates of interconversion of diastereomeric conformations.

an *N*-acyl group in the eight-membered ring, there are additional non-bonded interactions caused by a zero torsion angle for the N-Ar bond [(7; bond 4a-5), (8; bond 4a-5 or 12-12a), and (9; bond 4a-5 or 10a-11)].

The second type of transition state is exemplified by the four conformations TS1 (18a), TS1* (18b), TS2 (19a), and TS2* (19b). These four conformations are characterised by one coplanar group of six of the atoms of the eight-membered ring and a second group of four coplanar atoms; the lines of intersection of the two planes are shown as broken lines in the diagrams (18a and b) and



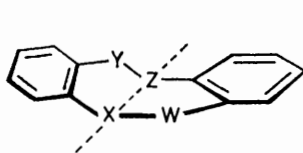
(15a) +



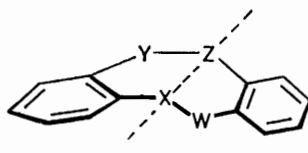
(15b) -



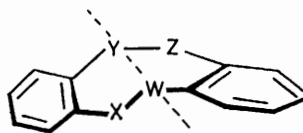
(15c) 0



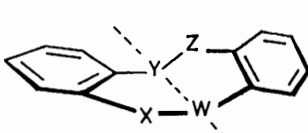
(16a) FB1 0-+0-+



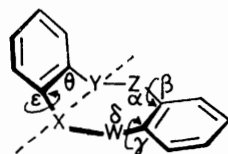
(16b) FB1* 0+ -0+ -



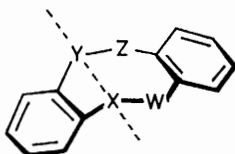
(17a) FB2 +-0+ -0



(17b) FB2* -+0 -+0



(18a) TS1 0-+-+0

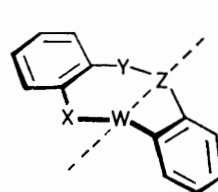


(18b) TS1* 0+ -+-0

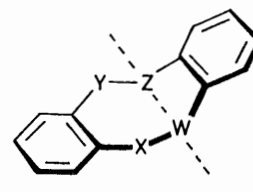
(19a and b). This geometry results in strained values for the bond angles indicated by α , β , γ , δ , ϵ , and θ in the formula (18a), the other two bond angles of the eight-membered ring having acceptable values by appropriate adjustment of the angle between the two planes. Additional important non-bonded interactions may also result in these transition states (18) and (19) if the torsion angle about one or more Ar-N-COR bonds is reduced to zero.

The third type of transition state includes the four conformations TS3 (20a), TS3* (20b), TS4 (21a), and TS4* (21b). These transition states are characterised by a single coplanar group of four atoms (4a, 5, 6, and 6a; or 10a, 11, 12, and 12a). The other four atoms of the eight-membered ring adopt a minimum energy arrangement which is related to the geometries of the appropriate C, C*, TB, and TB* conformations [see (12)—(14)] which

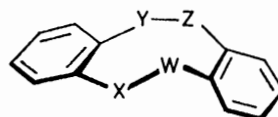
are directly interconverted by way of these transition states (see Figure 3).



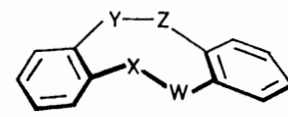
(19a) TS2 +-00+-



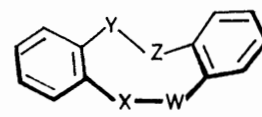
(19b) TS2* -+00--



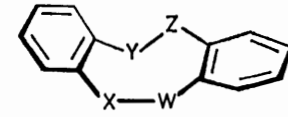
(20a) TS3 +-+000



(20b) TS3* -+-000



(21a) TS4 000+-+



(21b) TS4* 000-+-

The remaining problem is to assign the various types of possible conformational change summarised in Figure 3 to the observed temperature dependence of the n.m.r. spectra of 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (1) and the heterocyclic analogues (7)—(9). This is most easily done by considering four different types of conformational behaviour, (i)—(iv).

Type (i). 5,6,11,12-Tetrahydrodibenzo[*a,e*]cyclo-octene (1) and the 5,6,11,12-tetrahydrodibenzo[*b,f*]dithiocin derivatives (8d and e) and (9e and f). The unsubstituted hydrocarbon (1) is relatively easily placed within the scheme of conformational changes shown in Figure 3.

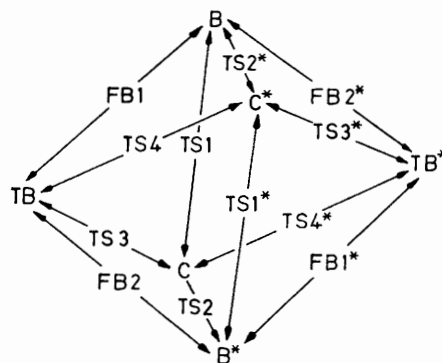


FIGURE 3 Relationships between the six ground state conformations C, C*, B, B*, TB, and TB* and the twelve transition states FB1, FB1*, FB2, FB2*, TS1, TS1*, TS2, TS2*, TS3, TS3*, TS4, and TS4*

Its n.m.r. spectrum at low temperatures indicates almost equal population of two diastereomeric conformations. These are a relatively rigid conformation for which the ring CH₂-CH₂ unit gives an AA'BB' spectrum and a mobile, rapidly inverting conformation for which a

singlet signal is observed for its ring CH_2 protons. The non-bonded interactions in the FB conformations (16) and (17) in this case are expected to be small and the mobile conformation must therefore be of the Boat † type. The more rigid conformation must be the Chair conformation, ‡ since both types of transition state [$\text{TS1} \equiv \text{TS2} \equiv \text{TS1}^* \equiv \text{TS2}^*$, (18) and (19)] and [$\text{TS3} \equiv \text{TS4}$, $\text{TS3}^* \equiv \text{TS4}^*$, (20) and (21)] for the process $\text{C} \rightarrow \text{Boat} \rightarrow \text{C}^*$, which are required for the inversion of this conformation, have considerable angle strain. The observed value of ΔG^\ddagger ($10.2 \text{ kcal mol}^{-1}$) for the process $\text{Chair} \rightarrow \text{Boat}$, based upon the coalescence of the two aryl-proton singlet signals observed at low temperatures, is in good agreement (see later) with a transition state of the former type (*cf.* TS1). The relationship between this result and the previous studies of 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (1) and its derivatives is important. In this case it is clear that the crystal structure³ is not a reliable guide to the conformational situation in solution (*cf.* refs. 4–6), since it is now established that 5,6,11,12-tetrahydrodibenzocyclo-octene (1) has the centrosymmetrical Chair conformation in the solid state,³ whereas Chair and Boat conformations are approximately equally populated in solution ($\text{CDCl}_3\text{-CS}_2$).

The foregoing discussion, which is based largely upon the examination of molecular models, is supported by calculations of steric strain in the various conformations of the hydrocarbon (1), using a computer programme based upon the Wiberg (steepest descent) procedure^{2b} for minimising strain energy. Thus, the various contributions to the strain energy of the conformational types C, TS1, B, FB, TB, and a minimum energy Boat conformation are given in Table 3. This minimum energy Boat conformation is characterised by a torsion angle of *ca.* $+26^\circ$ about the 5–6 and 11–12 bonds and is therefore situated geometrically between B^* and FB1^* in the conformational itinerary depicted in Figure 3 (there are also three other equivalent minimum energy Boat conformations associated with three equivalent positions in this itinerary).

The figures given in Table 3 should be used in a qualitative rather than a quantitative sense, but they do show clearly that the strain energy of the various conformational types is minimised by the optimum distribution of the strain energy over its components. It is also evident that the relief of torsional strain in the transition state TS1 is an important factor in determining the energy barrier for the process $\text{C} \rightarrow \text{Boat}$ in addition to the more obvious development of angle strain in the transition state. The energy barrier to the process $\text{B} \rightarrow \text{TB}$, involving the FB transition state, is low because torsional strain is also relieved to a considerable extent in this transition state and because the apparently large non-bonded interactions in an undistorted Dreiding model of the FB conformation can be effectively relieved

† The description 'Boat' used here and later in the paper refers to any conformation of the boat family. The descriptions B, B^* , TB, and TB^* are specific. Similarly, the description 'Chair' refers to both the C and C^* conformations and the descriptions C and C^* are specific.

by a distortion of the bond angles at the atoms of the eight-membered ring. It would be desirable to extend these calculations to the other compounds discussed in the paper, but this involves difficulties in selecting potential functions which have not yet been resolved, and the remainder of the discussion must therefore be limited to

TABLE 3

Strain energy in selected conformations of 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (1)

Conformation	E_R^a	E_θ^a	$E_\phi^{a,b}$	E_δ^a	E_{NBI}^a	E_s^a
$\text{C} \equiv \text{C}^*$	0.02	0.69	5.59	0.01	0.14	6.45
$\text{TS1} \equiv \text{TS1}^* \equiv \text{TS2} \equiv \text{TS2}^*$	0.62	15.05	0.06	0.04	1.23	17.90
Minimum energy boat conformation	0.10	0.35	3.72	0.63	1.89	6.69
$\text{B} \equiv \text{B}^*$	0.08	0.98	6.00	0.01	0.43	7.50
$\text{FB1} \equiv \text{FB1}^*$, $\text{FB2} \equiv \text{FB2}^*$	0.28	8.35	1.20	0.07	1.28	11.18
$\text{TB} \equiv \text{TB}^*$	0.02	0.89	6.04	0.07	0.44	7.46

^a The following energy terms are used: E_R (bond length strain), E_θ (angle strain), E_ϕ (torsional strain), E_δ (out of plane strain in the aromatic rings), E_{NBI} (non-bonded inter-actonal strain). Total strain energy ($E_s = E_R + E_\theta + E_\phi + E_\delta + E_{\text{NBI}}$). The force constants are those used by Boyd^{2a} for calculations of strain energy in cyclophanes, with a reduction by a factor of 0.7 in angle strain energy based upon the observed conformational changes of (1) and similar hydrocarbons (*cf.* ref. 2f). ^b The major component of E_ϕ is mainly associated with the 5–6 and 11–12 bonds. Torsional strain^{2a} in the aromatic rings is virtually absent.

a more qualitative approach. A number of very approximate calculations of minimised angle strain in the transition states TS1 or TS2 are summarised in Table 4. The value of these calculations is strictly limited, but they do assist in the discussion that follows in the assignment of n.m.r. spectral changes to processes involving particular conformational change.

The n.m.r. spectra of the two dithiocin derivatives (8d) and (9e) show at low temperatures evidence (see Table 1) for a more highly populated mobile conformation together with a minor, more rigid conformation. On the basis of the following analysis these two conformations have been identified as Boat and Chair, respectively.

The compound (8d) has non-equivalent C-6 and C-11 methylene groups. Its major mobile conformation gives two singlet signals (AB2 and AB4) at low temperatures. Its minor, more rigid, conformation gives two AB systems (A1, B1 and A3, B3) which coalesce with the singlets (AB2 and AB4) at higher temperatures. The kinetics of the processes associated with these n.m.r. spectral changes were more easily determined by examination of the coalescence of the two aryl-methyl group singlet signals (A and B) observable at low temperatures. This gave activation parameters which could be assigned to the process:



The calculated angle strain ($E_\theta = 14.8 \text{ kcal mol}^{-1}$ for the transition state ($\text{TS1} \equiv \text{TS1}^*$) is similar (see Table 4; $E_\theta - 2E_w = 10.5 \text{ kcal mol}^{-1}$) to the observed activation energy ($\Delta G^\ddagger = 12.0 \text{ kcal mol}^{-1}$).

The compound (9e) shows conformational behaviour

similar to that of (8d). Its equivalent C-6 and C-12 methylene groups give two AB systems at low temperatures assignable to a major, more mobile conformation A1,B1 and a minor, more rigid conformation; these two AB systems coalesce to a broad singlet at higher temperatures. In this case it is also reasonable to assume that the more mobile conformation is of the Boat type and the minor conformer has the Chair conformation. The calculated angle strain in the enantiomeric transition states $TS1 \equiv TS2$ and $TS1^* \equiv TS2^*$ (Table 4) supports this assignment. The transition states for inversion of the more mobile Boat conformation of both dithiocin derivatives (8d) and (9e) are of the FB type (see Figure 3), and the more rapid inversion of (8d) (the signals AB2 and AB4 are singlets down to -100°) is

Chair for the dithiocin (8d) (ΔG^\ddagger 12.0 kcal mol $^{-1}$). The similarity of these two energy barriers suggests that both are associated with the same type of transition state ($TS1 \equiv TS1^*$) and that the observed inversion process for the disulphone (8e) possibly involves the pathway $C \rightleftharpoons TS1 \rightleftharpoons B \rightleftharpoons B^* \rightleftharpoons TS1^* \rightleftharpoons C^*$ (with the process $B \rightleftharpoons B^*$ fast); this opinion is supported by the examination of models. The disulphone (9f) also appears to exist in a single conformation from its low-temperature n.m.r. spectrum, which shows a single AB system (A,B) from the equivalent C-6 and C-12 methylene groups which coalesces to a singlet at higher temperatures with a rather higher barrier for the inversion process (ΔG^\ddagger 18.6 kcal mol $^{-1}$) than the barrier for the inversion of the corresponding sulphide (9e) (ΔG^\ddagger 12.4 kcal mol $^{-1}$ for

TABLE 4
Approximate calculations of angle strain (E_θ) in transition state TS1 (18a)

Compounds ^a	W	X	Y	Z	E_θ ^{b,c}	E_ω ^d	$\Delta G^\ddagger_{C \rightarrow B}$ ^e
					kcal mol $^{-1}$	kcal mol $^{-1}$	kcal mol $^{-1}$ (Exptl.)
(1)	CH ₂	CH ₂	CH ₂	CH ₂	13.3	2.88	10.2 (1)
(9e)	CH ₂	S	CH ₂	S	15.4	2.13	14.4 (9e)
(8d)	CH ₂	S	S	CH ₂	18.9	2.13	
(8d)	S	CH ₂	CH ₂	S	14.8	2.13	12.0 (8d)
(8a), (8b)	NR	CH ₂	CH ₂	NR	8.3 ^f		
(8a), (8b)	CH ₂	NR	NR	CH ₂	13.2		12.9 (8a), 14.0 (8b)
(7a), (7b), (7c)	CH ₂	CH ₂	NR	CH ₂	13.2		11.1 (7a), 11.3 (7b), 10.6 (7c)
(7a), (7b), (7c)	CH ₂	CH ₂	CH ₂	NR	11.0 ^f		
(9a), (9b), (9c)	CH ₂	NR	CH ₂	NR	10.2 ^f		22.4 (9a), 20.8 (9b) 19.6 (9c), 13.8 (9d)

^a The compounds listed are those for which the transition states with given W, X, Y, and Z are relevant. ^b Calculated using $E_\theta = 0.021914 \Sigma \Delta \theta^2$ over the bond angles $\alpha, \beta, \gamma, \delta, \epsilon$, and θ (18a), where $\Delta \theta$ is the calculated deformation of these angles from their equilibrium values (ref. 27). ^c Assumed equilibrium bond lengths: Ar-N 1.45, CH₂-N 1.47, Ar-CH₂ 1.51, CH₂-CH₂ 1.54, Ar-S 1.76,

CH₂-S 1.82, C=C (in aromatic ring) 1.39 Å. Assumed equilibrium bond angles \widehat{CNC} 120°, $\widehat{C=CX}$ 120°, \widehat{CSC} 109°, \widehat{CCC} 111°. ^d Torsional barriers about 5-6 and 11-12 bonds for CH₂-CH₂ and CH₂-S bonds based upon ethane and dimethyl sulphide (ref. 28). ^e The number in parentheses indicates the compound for which the energy barrier was measured. Since torsional strain about the 5-6 and 11-12 bonds in the Chair conformation is almost totally relieved in TS1 (Table 3), $\Delta G^\ddagger_{C \rightarrow B}$ (Exptl.) should be compared with $E_\theta - 2E_\omega$. ^f A torsion angle of 0° about one or more Ar-NR bonds is involved in TS1 and ΔG^\ddagger is therefore expected to be considerably greater than E_θ for R = Ac, Bz or SO₂C₆H₄Me-*p*.

presumably a result of the smaller, transannular, non-bonded interactions between a sulphur atom and a methylene group in the FB1 \equiv FB2 and FB1* \equiv FB2* conformations of (8d) [see (16 and 17)(a and b), W = Z = S, X = Y = CH₂], as compared with the larger interaction between two sulphur atoms in the FB2 and FB2* conformations of (9e) [see (17a and b), W = Y = S, X = Z = CH₂]. The Boat conformation of (9e) accordingly shows a rather higher energy barrier to inversion (ΔG^\ddagger 12.4 kcal mol $^{-1}$) than that of (8d) (ΔG^\ddagger < 9 kcal mol $^{-1}$). These opinions are based upon the examination of models and very approximate calculations in addition to the experimental facts. Detailed calculations are difficult to carry out for compounds in which there is potential conjugation between the sulphur atoms and the aromatic rings.

The cyclic disulphones (8e) and (9f), corresponding to the dithiocin derivatives (8d) and (9e), show rather different conformational behaviour. Thus, the low temperature spectrum of (8e) shows evidence for one conformation only with an inversion barrier (ΔG^\ddagger 11.9 kcal mol $^{-1}$) similar to the barrier for the process Boat \rightleftharpoons

Boat \rightleftharpoons Boat*). This higher energy barrier could be a consequence of the larger, non-bonded interactions between the sulphonyl groups in the transition states FB2 and FB2* [see (17a and b), W = Y = SO₂, X = Z = CH₂]. However, additional temperature dependence of the low field aryl proton signals in the same temperature range in which the AB system from the methylene protons coalesces to a singlet, suggests that the inversion process involves a rate-determining interconversion to a minor conformation which then undergoes a relatively rapid inversion. These observations are consistent (see Figure 3) with the equivalent inversion pathways $C \rightleftharpoons B \rightleftharpoons C^*$ and $C \rightleftharpoons B^* \rightleftharpoons C^*$ with the rate-determining transition states TS1 \equiv TS2 and TS1* \equiv TS2* [see (18 and 19) (a and b), W = Y = SO₂, X = Z = CH₂]. The non-bonded interaction between the sulphonyl group at position 5 or 11 and the methylene group at position 12 or 6 in these transition states evidently raises their energy relative to the similar transition states for the dithiocin derivative (9e).

Type (ii). 5,6,11,12-Tetrahydrodibenz[b,f]azocine derivatives (7a-c). The n.m.r. spectra of these three

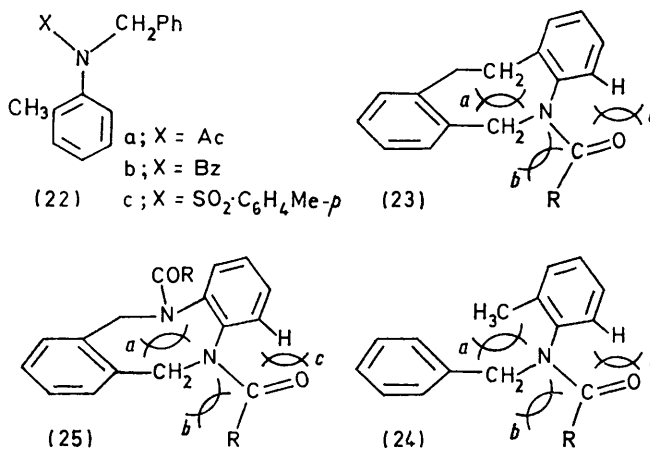
compounds all show similar temperature dependence (see Tables 1 and 2). At low temperatures the C-6 methylene group gives rise to two AB systems (A1,B1 and A2,B2), corresponding to two diastereomeric conformations, which coalesce to a single AB system (A12,B12) at higher temperatures. Finally, this single AB system coalesces to a singlet when the temperature is further raised and conformational inversion also becomes fast on the n.m.r. time-scale. The magnitudes of the energy barriers for the interconversion between diastereomeric conformations for all three compounds [(7a), ΔG^\ddagger 11.1; (7b), ΔG^\ddagger 11.4; (7c), ΔG^\ddagger 10.6 kcal mol⁻¹] are almost identical, and this process is associated with the process Chair \rightleftharpoons Boat. This interconversion probably proceeds by way of the transition states TS2 and TS2* [(19a and b), W = NAc (7a), W = NBz (7b), and W = N·SO₂·C₆H₄-Me-*p* (7c), X = Y = Z = CH₂] or TS1 and TS1*. The transition states TS1 and TS1* involve a zero torsion angle about the N-aryl (4a-5) bond with resulting severe, but varied, non-bonded interactions [see (18a and b), W = NAc (7a), W = NBz (7b), or W = N·SO₂·C₆H₄-Me-*p* (7c), X = Y = Z = CH₂]; the observed relatively small and similar free energies of activation are therefore only consistent with the pathways C \rightleftharpoons Boat* and C* \rightleftharpoons Boat involving the transition states TS2 and TS2* respectively (Figure 3). The roughly calculated angle strain in the eight-membered ring in these transition states is in agreement with this conclusion (Table 4). The inversion process, which affects the n.m.r. spectra at higher temperatures, involves free energy barriers [(7a), ΔG^\ddagger 20.1; (7b), ΔG^\ddagger 17.7; (7c), ΔG^\ddagger 14.3 kcal mol⁻¹] which are similar in magnitude to those observed²⁴ for rotation about the N-aryl bonds of the analogous *o*-toluidine derivatives (22) [(22a), ΔG^\ddagger 19.3; (22b), ΔG^\ddagger 18.1; (22c), ΔG^\ddagger 15.3 kcal mol⁻¹]. This similarity is readily understandable in terms of the structural similarity between the transition states FBI and FBI* [e.g. (23) and (16a and b), W = NAc (7a); W = NBz (7b); or W = N·SO₂·C₆H₄-Me-*p* (7c), X = Y = Z = CH₂] and the transition states [e.g. (24)] for rotation about the N-Ar bonds of the *o*-toluidine derivatives (22). The principal non-bonded interactions (*a*, *b*, and *c*) in these transition states are indicated to emphasise this similarity.

Thus, the inversion process, evident from the n.m.r. spectra of (7a-c), involves the rate-determining steps B \rightleftharpoons TB and B* \rightleftharpoons TB*, but this conclusion, although it supports the hypothesis that both Chair and Boat conformations are present in solution, does not permit the assignment of the observed n.m.r. signals to one or other of these conformations. It is also not

* Note added in proof: A paper has recently been published (A. Saunders and J. M. Sprake, *J.C.S. Perkin II*, 1972, 1660) interpreting the conformational behaviour of the compound (8a) in terms of the four folded boat conformations (16a), (16b), (17a), and (17b). This interpretation is not compatible with the experimental evidence reported in this paper, which demonstrates for the compound (8a) that there is an interconversion involving *unequally populated* conformations which are *diastereomerically* related.

possible to distinguish between the B and TB possibilities for the Boat conformers.

For the azocine derivatives (7a and b) a further possible process requiring consideration which might be involved in the interconversion of diastereomers is hindered rotation about the N-CO bonds of the amide groups. This possibility can be ruled out on a number of grounds. Thus, the energy barriers associated with these conformational changes in (7a and b) are very much lower



(ΔG^\ddagger ca. 11 kcal mol⁻¹) than those normally observed^{22a,22c,25} for rotation about the N-CO bonds (ΔG^\ddagger ca. 16–18 kcal mol⁻¹) of amides. Furthermore, the sulphonamide derivative (7c) shows similar spectral changes to the amides (7a and b) although hindered rotation about an N-SO₂ bond would not be expected to be observable. Finally, it should be emphasised that the n.m.r. spectra of the analogous *o*-toluidine derivatives²⁴ (22a and b) show no evidence for more than one populated amide configuration.

Type (iii). 5,6,11,12-Tetrahydrodibenzo[b,f][1,4]diazocine derivatives (8a-c). The n.m.r. spectra of these 1,4-diazocine derivatives show considerable differences in their temperature-dependent behaviour (Tables 1 and 2). Thus, the *N*-acetyl derivative (8a)* gives two AB systems for the equivalent C-6 and C-11 methylene groups (A1,B1 and A2,B2) at low temperatures, which coalesce to a single AB system (A12,B12) at higher temperatures, and this AB system coalesces to a singlet when the temperature is further raised. The n.m.r. spectrum of the *N*-benzoyl derivative (8b) also shows two AB systems for the C-6 and C-11 methylene groups at low temperatures (A1,B1 and A2,B2), but signal coalescences of both types occur in the same temperature range to give finally a singlet signal (AB12) at higher temperatures. The *N*-*p*-tolylsulphonyl derivative (8c) gives only a single AB system for the C-6 and C-11 methylene groups at low temperatures, which coalesces to a singlet at higher temperatures. The simplest interpretation of these

²⁴ B. J. Price, J. A. Eggleston, and I. O. Sutherland, *J. Chem. Soc. (B)*, 1967, 922.

²⁵ W. E. Stewart and T. H. Siddall, III, *Chem. Rev.*, 1970, **70**, 517.

results is that the inversion process involves the rate-determining transition states $\text{FB1} \rightleftharpoons \text{FB2}$ and $\text{FB1}^* \rightleftharpoons \text{FB2}^*$ in all three cases [(16 and 17) (a and b); $W = Z = \text{NAc}$, $X = Y = \text{CH}_2$ (8a); $W = Z = \text{NBz}$, $X = Y = \text{CH}_2$ (8b); and $W = Z = \text{N}\cdot\text{SO}_2\cdot\text{C}_6\text{H}_4\text{Me-}p$, $X = Y = \text{CH}_2$ (8c)]. The observed free energies of activation [(8a) ΔG^\ddagger 16.9, (8b) ΔG^\ddagger 14.3, (8c) ΔG^\ddagger 10.1 kcal mol⁻¹] are significantly lower than those observed for inversion of the azocine derivatives (7a—c) ($\Delta\Delta G^\ddagger$ ca. 3—4 kcal mol⁻¹) because the transannular interaction *a* in the FB transition state is between a ring nitrogen atom and a ring methylene group [*e.g.* (25)] rather than between two ring methylene groups as in (23); the interactions *b* and *c* are similar in both cases (25) and (23).

The interconversion of diastereomeric conformations is more difficult to interpret in the cases of (8a) and (8b). Thus, by analogy with the azocine derivatives (7) it seems probable that this process involves the interconversions $\text{C}^* \rightleftharpoons \text{B}$ and $\text{C} \rightleftharpoons \text{B}^*$ by way of the transition states TS2 and TS2* respectively [(19a and b), $W = Z = \text{NAc}$ (8a), or $W = Z = \text{NBz}$ (8b), $X = Y = \text{CH}_2$], but the relative free energies of activation [(8a) ΔG^\ddagger 12.9 and (8b) ΔG^\ddagger 14.1 kcal mol⁻¹] are difficult to explain. Processes involving the transition states TS1, TS3, and TS4 are improbable because they involve zero or near zero torsion angles about one or both of the *N*-aryl bonds in a distorted eight-membered ring.

Type (iv). 5,6,11,12-Tetrahydrodibenzo[b,f][1,5]diazocine derivatives (9a—d). The C-5 and C-12 methylene groups of all these compounds give rise to two AB systems (A1,B1 and A2,B2) at low temperatures (Tables 1 and 2), but the spectrum of the dinitroso-derivative (9d) shows rather different temperature dependence from those of the other three compounds and is conveniently discussed first. One of the AB systems (A2,B2) observed in the n.m.r. spectrum of the dinitroso-compound (9d) coalesces to a singlet (AB2) well below the temperature range in which the pairs of signals AB2 and A1 and AB2 and B1 coalesce. This behaviour is consistent with the presence of a mobile conformation, probably Boat, which inverts by way of the transition states FB1 and FB1* [(16a and b), $W = Y = \text{N}\cdot\text{NO}$, $X = Z = \text{CH}_2$] and FB2 and FB2* [(17a and b), $W = Y = \text{N}\cdot\text{NO}$, $X = Z = \text{CH}_2$]. The transition states FB1 and FB1* are probably rate-determining since the torsion angles about both Ar—N bonds are zero, although the barriers to torsion about the Ar—N bonds in nitrosoarylamines are generally low.²⁶ The second conformer is presumably the Chair conformation and the free energy barrier to the interconversion, Chair \rightleftharpoons Boat, of these two diastereomeric conformations (ΔG^\ddagger 13.8 kcal mol⁻¹) by way of the enantiomeric transition states TS1 \rightleftharpoons TS2 and TS1* \rightleftharpoons TS2*

[(18 and 19) (a and b), $W = Y = \text{N}\cdot\text{NO}$, $X = Z = \text{CH}_2$] is greater than that estimated (see Table 4) for the ring system lacking the nitroso-substituents because of the zero torsion angle about one of the Ar—N bonds in the transition states.

For 1,5-diazocine derivatives of the type (9a—d), inversion of the boat conformation and the interconversion of Chair and Boat conformations necessarily involve a zero torsion angle about one or both of the Ar—N bonds in all the possible transition states except FB2 and FB2* [(17a and b), $W = Y = \text{NAc}$ (9a), $W = Y = \text{NBz}$ (9b), $W = Y = \text{N}\cdot\text{SO}_2\cdot\text{C}_6\text{H}_4\text{Me-}p$ (9c), and $W = Y = \text{N}\cdot\text{NO}$ (9d), $X = Z = \text{CH}_2$]. It is not therefore surprising that the two diastereomeric conformations of the 1,5-diazocine derivatives (9a—c) are separated by large energy barriers [(9a) ΔG^\ddagger 22.4, (9b) ΔG^\ddagger 20.8, and (9c) ΔG^\ddagger 19.6 kcal mol⁻¹]. This is also consistent with the large energy barriers to conformational inversion presumed in the calculation of line-shapes, although not necessarily unambiguously, to involve exchange between the sites A2 and B2 [(9a) ΔG^\ddagger 21.8, (9b) ΔG^\ddagger 21.1, and (9c) ΔG^\ddagger 18.8 kcal mol⁻¹]. The n.m.r. spectral evidence is therefore consistent with the presence of both Chair and Boat conformational types, but signals cannot be assigned to each of these types directly. It is also not possible to determine which of the Boat conformations is the lower energy species.

Epilogue.—Our interest in the stereochemistry of '6,8,6-systems' (11) was initiated by an examination of Höhn's suggestion²⁹ that compounds of this type could exist as conformational diastereomers of the Chair (12) and Boat (13) types. This proposal was initially put forward to account for the alleged existence of the isomeric α - and β -disalicylides (26a)^{30,31} and corresponding α - and β -isomers of the *o*- (26b),³² *m*- (26c),³² and *p*-dicresotides (26d),³² and the α - and β -dithymotides (26e).³³ The existence of α - and β -disalicylides was given further consideration by Schönberg in 1948.³⁴

In a pioneering paper, Baker, Banks, Lyon, and Mann³ presented a detailed discussion of the conformational behaviour which could be exhibited by 5,6,11,12-tetrahydrodibenzo[*a,e*]cyclo-octene (1,2,5,6-dibenzocyclo-octa-1,5-diene) (1). On the basis of X-ray crystallographic information it was shown³ that the hydrocarbon (1) adopts the centrosymmetrical chair conformation (12) in the solid state, but now it has been established that Chair and Boat conformations are approximately equally populated in solution ($\text{CDCl}_3\text{-CS}_2$). This result is compatible with the approximately equal total strain energies (Table 3) calculated for the chair conformation (E_s 6.43 kcal mol⁻¹) and the minimum energy boat conformation (E_s 6.69 kcal mol⁻¹).

²⁶ A. Mannschreck and H. Muensch, *Tetrahedron Letters*, 1968, 3227.

²⁷ For general reviews, see E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis,' Wiley New York, 1965, ch. 7; J. E. Williams, P. J. Stang, and P. von R. Schleyer, *Ann. Rev. Phys. Chem.*, 1968, **19**, 531.

²⁸ J. Dale, *Tetrahedron*, 1966, **22**, 3373.

²⁹ Höhn quoted by Richter-Anschütz, 'Chemie der Kohlenstoff-Verbindungen,' 1935, vol. II [2], p. 393.

³⁰ R. Anschütz, *Ber.*, 1919, **52**, 1875; R. Anschütz and K. Reipenkroger, *Annalen*, 1924, **439**, 1; L. Anschütz and R. Neher, *J. prakt. Chem.*, 1941, **159**, 264; L. Anschütz and A. Mayer, *ibid.*, p. 343.

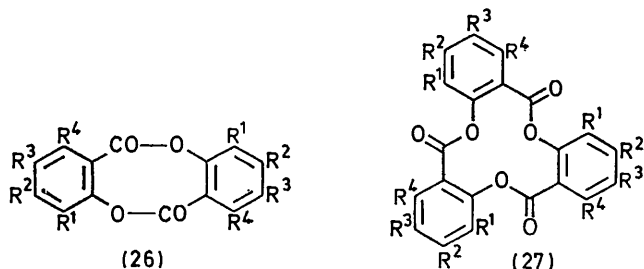
³¹ L. Anschütz and R. Neher, *Ber.*, 1944, **77**, 634.

³² L. Anschütz and G. Gross, *Ber.*, 1944, **77**, 644.

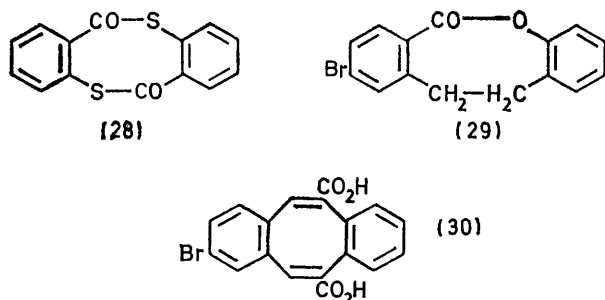
³³ R. Spallino and G. Provenzal, *Gazzetta*, 1909, **39**, II, 325.

³⁴ A. Schönberg, *J. Chem. Soc.*, 1948, 891.

Our earlier studies^{35,36} disposed of the alleged existence of α - and β -disalicylides (26a—e). In all cases it was found that the α -compounds were indeed dimers (26),



- a; $R^1 = R^2 = R^3 = R^4 = H$
 b; $R^1 = Me, R^2 = R^3 = R^4 = H$
 c; $R^2 = Me, R^1 = R^3 = R^4 = H$
 d; $R^3 = Me, R^1 = R^2 = R^4 = H$
 e; $R^1 = Pr^i, R^4 = Me, R^2 = R^3 = H$
 f; $R^1 = Me, R^4 = Pr^i, R^2 = R^3 = H$
 g; $R^1 = R^4 = Me, R^2 = R^3 = H$



whereas the β -compounds were trimers (27). These investigations³⁵ led to the discovery of the interesting compound tri-*o*-thymotide^{36,37} (27e) and subsequently it was shown³⁸ that the compounds (27e—g) participate in a conformational itinerary involving diastereomeric propeller and helical conformations. Tri-*o*-thymotide

³⁵ W. Baker, W. D. Ollis, and T. S. Zealley, *J. Chem. Soc.*, 1951, 201; W. Baker, B. Gilbert, W. D. Ollis, and T. S. Zealley, *ibid.*, 1951, 209; W. Baker, J. B. Harborne, A. J. Price, and A. Rutt, *ibid.*, 1954, 2042.

³⁶ W. Baker, B. Gilbert, and W. D. Ollis, *J. Chem. Soc.*, 1952, 1443.

³⁷ H. M. Powell, *Nature*, 1952, **170**, 155; A. C. D. Newman and H. M. Powell, *J. Chem. Soc.*, 1952, 3747; D. Lawton and H. M. Powell, *ibid.*, 1958, 2339.

³⁸ A. P. Downing, W. D. Ollis, and I. O. Sutherland, *J. Chem. Soc. (B)*, 1970, 24.

(27e) adopts a propeller conformation in the solid state³⁸ and the absolute configuration of its (+)-enantiomer has been established.³⁹ Good evidence for the boat conformation (13; $W = Y = CO, X = Z = O$) of the disalicylides (26) and dithiosalicylide (28) is provided by their dipole moments: ⁴⁰ (26a) 6.26, (26b) 6.34, (26c), 6.74, (26d) 6.67, (26e) 6.63, and (28) 6.39 D.⁴¹

The resonance demand for the ester group to be planar is also dominant in the lactone (29), whose dipole moment (μ 4.09 D)⁴² was also considered to be compatible with the boat conformation. Similarly, a desire for planarity in the lactams (10) would be expected to favour a boat conformation. The boat conformation (13: $W = N \cdot CH_2Ph, X = CO, Y = Z = CH_2$) is chiral and the lactam (10b) gave a temperature-dependent n.m.r. spectrum which was compatible with inversion (Boat \rightleftharpoons Boat*). The *N*-benzylic methylene group gave an AB system (τ_A 5.83, τ_B 6.32, J_{AB} 14.0 Hz) in [²H₅]nitrobenzene and line-shape analysis [method (b)] over the temperature range 63—170° gave $\Delta G^\ddagger = 21.4$ kcal mol⁻¹.

The existence of enantiomers of the Boat conformation of disalicylide (26) was first mentioned in 1934,⁴³ but an attempt to effect its resolution was unsuccessful.³¹ However, the resolution of the cyclo-octatetraene derivative (30), which also presumably has a Boat conformation, has been achieved and its thermal racemisation (E_a ca. 27 kcal mol⁻¹) has been studied.⁴⁴

The conformational changes observable for '6,8,6-systems' are summarised in the last column of Table 2. Their relation to Höhn's original suggestion²⁹ is clear, although the actual situation as depicted in Figure 3 is more complicated.

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³⁹ A. P. Downing, W. D. Ollis, I. O. Sutherland, J. Mason, and S. F. Mason, *Chem. Comm.*, 1968, 329.

⁴⁰ P. G. Edgerley and L. E. Sutton, *J. Chem. Soc.*, 1951, 1069.

⁴¹ W. Baker, A. S. El-Nawawy, and W. D. Ollis, *J. Chem. Soc.*, 1952, 3163.

⁴² W. Baker, W. D. Ollis, and T. S. Zealley, *J. Chem. Soc.*, 1952, 1447.

⁴³ Beilstein, 'Handbuch der Organischen Chemie,' 4th edn., 1934, vol. 19, pp. 172, 500.

⁴⁴ K. Mislow and H. D. Perlmutter, *J. Amer. Chem. Soc.*, 1962, **84**, 3591.