Nuclear Magnetic Resonance Studies of Heterocyclic Bridged Biphenyls

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Condensation reactions (a) between 1,2-diamines and biphenyl-2,2′-dicarbaldehyde or 9,10-phenanthraquinone and (b) between 2,2′-diaminobiphenyl and 1,2-diketones give polycyclic products with 5-, 6-, 7- and 8-membered heterocyclic rings, the n.m.r. spectra of which are discussed. Temperature-dependent signals for the methylene protons in the 15*H*-dibenzo[*c*,*e*]benzimidazo[1,2-*a*]azepines (2) and (3) show that these compounds are conformationally labile. The dibenzo[*a*,*c*]phenazines (4) and (5) and dibenzo[*f*,*h*]quinoxaline (6) show large downfield shifts (δ *ca.* 9·5) for some aromatic protons.

SEVERAL workers have investigated reactions between diamines and dialdehydes in attempts to prepare biphenyls such as (1) with a 10-membered heterocyclic bridging ring. However, reaction between biphenyl-2,2′-dicarbaldehyde and *o*-phenylenediamine in methanol at room temperature gives the benzimidazoazepine[1-3] (2) instead of (1), the reaction involving an intramolecular hydride shift.[3]

We find that reaction in methanol or in ethanol at room temperature or in ethylene glycol at 160° gives the same product (2) in two distinct forms, m.p. 159—160 and 192—193°, with slightly differing i.r. spectra (KBr disc). The lower melting form could be crystallised or stored without change if contamination with the higher melting form was avoided. Inoculation during crystallisation changed it to the less soluble higher melting form. Previous workers describe the product as a glass,[1] m.p. 52—57°; as two interconvertible high melting forms,[2] m.p. 188—191 (rhomboid) and 189—192° (needles), with different i.r. spectra in Nujol mulls but identical solution spectra (CS_2); and as having m.p. 160° (from reaction in acetic acid).[3]

The reaction between biphenyl-2,2′-dicarbaldehyde and ethyl 3,4-diaminobenzoate in ethanol proceeds similarly to give (3). Only one product was isolated although both the 11- and 12-ethoxycarbonyl compounds (3a and b) might have been expected.

With some samples of dialdehyde traces of the dibenzo[*a*,*c*]phenazines (4) and (5) were isolated, presumably from condensation of the amine with the phenanthroquinone present as a trace impurity. With carefully purified dialdehyde no quinoxalines were obtained, even when oxygen was passed in during the reaction. Photochemical formation of the quinone from the dialdehyde requires a peroxide as initiator.[2,4]

The dibenzophenazines (4) and (5), dibenzoquinoxaline (6), and the dibenzodiazocines (7) and (8) were made so that their n.m.r. spectra could be compared with those of the various reaction products.

N.m.r. Spectra.—The n.m.r. spectra (Table) of the benzimidazoazepines (2) and (3) show that the two protons of the ring methylene group are diastereotopic. At low temperatures they appear as an AB quartet (J_{AB} −14 Hz), becoming a doublet between 40 and 50° for (2) [*ca.* 40° for (3)] and coalescing to a singlet between 50 and 60° [40 and 50° for (3)], when conformational inversion of the twisted biphenyl system becomes rapid. Bindra and Elix[3] determined the spectrum of (2) in

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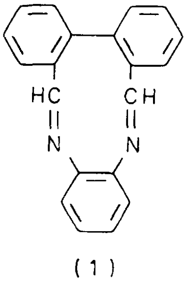
[1] F. Sparatore, *Ann. Chim.* (*Italy*), 1959, **49**, 2102.

[2] J. O. Hawthorne, E. L. Mihelic, M. S. Morgan, and M. H. Wilt, *J. Org. Chem.*, 1963, **28**, 2831.

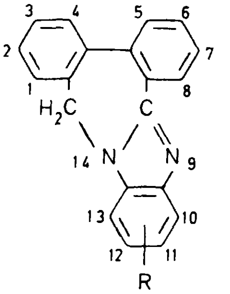
[3] A. P. Bindra and J. A. Elix, *Tetrahedron*, 1969, **25**, 3789.

[4] E. L. Mihelic, U.S.P. 2,930,742/1960 (*Chem. Abs.*, 1960, **54**, 18,461).

[$^2H_6$]DMSO–D_2O in which the two doublets are widely separated, δ 4·78 and 6·58 (J_{AB} −15 Hz).

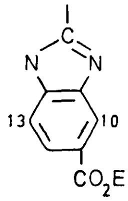


(1)

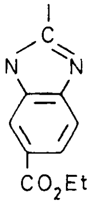


(2) R=H

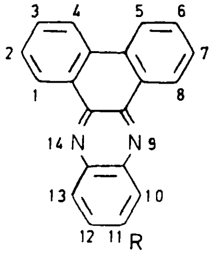
(3) R=CO_2Et



(3a)

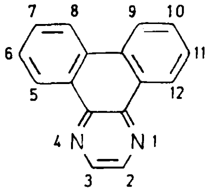


(3b)

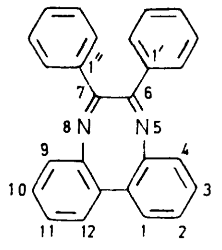


(4) R=H

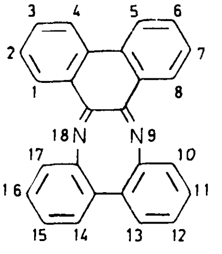
(5) R=CO_2Et



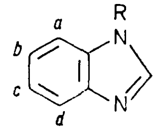
(6)



(7)



(8)



(9)

In (2) the most strongly deshielded proton, δ 8·28, is probably 10-H β to the unsaturated nitrogen atom: a number of 1-substituted benzimidazoles (9) show a signal at δ *ca.* 7·6—8·0 which is usually assigned[5] to proton *d*. The other low field signal (δ 7·83) is probably that of 8-H, which is also deshielded by the unsaturated group.

The introduction of the ethoxycarbonyl group in (3) causes a downfield shift of protons *ortho* to it; as three protons resonate in the δ 8·0—8·4 region, the structure of (3) is considered to be that of the 12-ethoxycarbonyl compound (3b) rather than that of its isomer (3a), in which only 10- and 12-H would be expected to resonate so far downfield. The downfield protons in (3b) are assigned as follows: one of the protons at δ 8·3 is 10-H, since in compound (2) 10-H is at δ 8·28; the other is 13-H, deshielded by the *o*-CO_2Et. The proton at 8·0 shows *ortho*-coupling (*J* 8·4 Hz) and either *meta*- or *para*-coupling (*J* 1·5 Hz) and can therefore only be 11-H, also deshielded by *o*-CO_2Et. (The slightly larger shift for 13-H is attributed to proximity to the imidazole ring.)

N.m.r. spectra [δ (p.p.m.)] in $CDCl_3$

Compound	Chemical shift	Assignment
(2)	4·93 (2H, q [a])	CH_2 [b]
	7·17—7·33 (5H, m)	Arom
	7·37—7·67 (5H, m)	Arom
	7·83 (1H, m)	8-H
	8·28 (1H, m)	10-H
(3)	1·44 (3H, t)	CH_3
	4·43 (2H, q)	CH_2 of Et
	5·14 (2H, q [a])	CH_2 of ring
	7·24—7·71 (7H, m)	Arom
	7·79 (1H, m)	8-H
	8·0 (1H, q)	11-H
	8·23—8·40 (2H, m)	10-, 13-H
(4)	7·62—7·90 (6H, m)	2-, 3-, 6-, 7-, 11-, 12-H
	8·17—8·61 (4H, m)	1-, 8-, 13-, 10-H,
	9·25—9·48 (2H, m)	4-, 5-H
(5)	1·49 (3H, t)	CH_3
	4·52 (2H, q)	CH_2
	7·56—7·88 (4H, m)	2-, 3-, 6-, 7-H
	8·31—8·63 (4H, m)	1-, 8-, 12-, 13-H
	8·99 (1H, m [c])	10-H
	9·22—9·45 (2H, m)	4-, 5-H
(6)	7·51—7·83 (4H, m)	6-, 7-, 10-, 11-H
	8·33—8·60 (2H, m)	5-, 12-H
	8·78 (2H, s)	2-, 3-H
	8·97—9·23 (2H, m)	8-, 9-H
(7)	6·95—7·45 (14H, m)	
	7·65—7·90 (4H, m)	2′- 6′-, 2″-, 6″-H
(8)	6·93—7·51 (12H, m)	
	7·58—7·68 (2H, m)	Probably 10- and 17-H
	7·75—7·92 (2H, m)	1-, 8-H

[a] Becomes a doublet at slightly higher temperature. [b] Lit.,[2] δ 4·97. [c] On scale expansion.

The dibenzazepine part of structures (2) and (3) is twisted. The change to the rigid, planar structure found in (4)—(6) brings considerable change to the n.m.r. spectrum, in addition to that caused by replacement of an imidazole ring by a pyrazine ring. All three compounds show two very strongly deshielded protons at δ *ca.* 9·2 in addition to those in the δ 8·4—8·8 region; the latter owe their positions to proximity to nitrogen (see below). The former are considered to be 4- and 5-H [8- and 9-H in (6)], their chemical shifts being only a little greater than those of 4- and 5-H (δ 8·93) in phenanthrene.[6] Strong deshielding of protons in overcrowded positions is frequently observed.[7]

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[5] Sadtler N.M.R. Spectra Nos. 10891M–10894M.

[6] P. M. G. Bavin, K. D. Bartle, and J. A. S. Smith, *Tetrahedron*, 1965, **21**, 1087.

[7] L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, Oxford, 2nd edn., 1969, pp. 71, 204; C. W. Haigh, R. B. Mallion, and E. A. G. Armour, *Mol. Phys.*, 1970, **18**, 751 and references therein.

In dibenzo[*f,h*]quinoxaline (6) the two protons in the pyrazine ring (2- and 3-H) appear as a sharp singlet at δ 8·78 (*cf.* 8·5 in pyrazine[8] and 8·73 in quinoxaline[9]). 5- and 12-H (δ *ca.* 8·45) are deshielded by the nitrogen atom to a greater extent than 8-H (δ 7·8) in the non-planar compounds (2) and (3). The protons in the planar biphenyl part of the dibenzophenazines (4) and (5) have chemical shifts very similar to those of the corresponding protons in (6), the additional ring in (4) and (5) having a negligible effect on the chemical shifts of the remaining protons. Two of the protons in the additional ring in the phenazine (4) have δ *ca.* 8·4 (10- and 13-H); the other two are part of the 6H multiplet at δ *ca.* 7·8. In the phenazine (5) the ethoxycarbonyl group at C-11 brings its *ortho*-protons further downfield to δ 9·0 (10-H) and 8·4 (12-H) respectively.

The dibenzodiazocine (7) has a twisted 8-membered ring which is conformationally stable.[10,11] Four protons resonate in the δ 7·65—7·9 region and the rest in the δ 6·9—7·4 region. Presumably the twisted ring system and the rotation of the phenyl groups very much reduces the deshielding effect of the nitrogen which is so marked in the planar structures (4)—(6). Because of the twist, the protons in the 4,5-phenanthrene position (1- and 12-H) are not overcrowded and therefore show the shielding of normal aromatic protons. The four downfield protons are presumably the *ortho*-protons of the phenyl groups, deshielded by the adjacent C=N, which now functions as an unsaturated group and not as part of an aromatic ring (*cf.* 2′-, 6′-, 2″-, and 6″-H in 2,3-diphenylquinoxaline[12] with δ 7·43—7·8). The spectrum of the dibenzophenanthrodiazocine (8) is rather similar to that of (7): the protons fall into three groups with δ 7·8 (2H), 7·6 (2H), and 6·9—7·5 (12H). Only two protons are *ortho* to the C=N groups in this compound and appear at the same position (δ *ca.* 7·8) in the spectrum as the four *ortho*-protons in (7). The two at δ *ca.* 7·6 have not been unequivocally identified but are probably 10- and 17-H since a model shows some deshielding by 8- and 1-H respectively, avoided in (7) by rotation of the phenyl groups.

The most remarkable feature in the spectrum of (8) is the absence of signals at δ *ca.* 9·0, although 4- and 5-H are in the 4,5-phenanthrene positions and it might have been expected that this part of the structure would be planar and the protons therefore deshielded. Possibly the large twist in the diazocine ring causes sufficient departure from planarity in the phenanthrene system to reduce the proximity of these two protons. Only a small twist in the phenanthrene system is necessary, as shown by the fact that all the protons in 9,10-dihydrophenanthrene, where the dihedral angle[13,14] is *ca.* 15°, have chemical shifts of $\delta < 8$. It is, however, noteworthy that 4- and 5-H in 9,10-phenanthraquinone[15] are rather more shielded (δ 8·01) than are the similar protons in phenanthrene.

EXPERIMENTAL

N.m.r. spectra were determined at 60 or 100 MHz with tetramethylsilane as internal standard.

15H-*Dibenzo*[c,e]*benzimidazo*[1,2-a]*azepine* (2).—(a) *In methanol.* Biphenyl-2,2′-dicarbaldehyde[16] (1·05 g) and *o*-phenylenediamine (0·54 g) were dissolved separately in methanol (10 ml in all) and the solutions mixed and kept for a day at room temperature. Water was added to the clear solution and the pale yellow precipitate was dissolved in benzene, chromatographed on neutral alumina, and eluted with dry ether. Crystallisation from 65% aqueous ethanol gave the azepine (1·15 g, 82%), m.p. 192—193°.

(b) *In ethanol.* A similar reaction in ethanol (25 ml in all) gave a pale yellow solid, crystallising from the solution within a few minutes of mixing. Crystallisation from 65% aqueous ethanol, with or without chromatography, gave the azepine as prisms, m.p. 157—158°, in 66% yield. Recrystallisation, avoiding chance inoculation, gave m.p. 159—160°; recrystallisation with inoculation by the other form gave m.p. 192—193°.

(c) *In ethylene glycol.* A solution of the reactants in ethylene glycol was kept at 160° for 5 h. It was poured into water and the product extracted into ether and then into dilute acid. Reprecipitation with alkali and crystallisation from aqueous ethanol gave the azepine, m.p. 159—160°; picrate, m.p. 279—280° (decomp.) [lit.,[1] 278—280° (decomp.)].

Ethyl 15H-*Dibenzo*[c,e]*benzimidazo*[1,2-a]*azepine*-12-*carboxylate* (3).—Saturated ethanolic solutions of biphenyl-2,2′-dicarbaldehyde (0·84 g) and ethyl 3,4-diaminobenzoate[17] (0·72 g) were mixed and kept for a day at room temperature. Some solid separated and more was obtained by evaporating to dryness and chromatographing the residue. Crystallisation from ethanol gave the *ester* (50%), m.p. 228—229° (Found: C, 77·4; H, 5·3; N, 8·2. $C_{23}H_{18}N_2O_2$ requires C, 77·9; H, 5·1; N, 7·9%). Hydrolysis gave the *acid*, m.p. >360° (Found: C, 77·0; H, 4·3; N, 8·7. $C_{21}H_{14}N_2O_2$ requires C, 77·3; H, 4·3; N, 8·6%).

Dibenzo[a,c]*phenazine* (4).—This was prepared from *o*-phenylenediamine and phenanthraquinone and had m.p. 227—228° (from EtOAc) (lit.,[18] m.p. 223—224°).

Ethyl Dibenzo[a,c]*phenazine*-11-*carboxylate* (5).—This was prepared similarly from the diamino-ester and had m.p. 216—217° (from EtOH) (Found: C, 78·4; H, 4·6; N, 7·9; O, 8·9. $C_{23}H_{16}N_2O_2$ requires C, 78·4; H, 4·6; N, 7·95; O, 9·1%).

Dibenzo[*f,h*]quinoxaline (6) had m.p. 183—184° (white) (lit.,[19] m.p. 180·5°; pale yellow). 6,7-Diphenyldibenzo[*e,g*][1,4-diazocine (7) had m.p. 239—240° (lit.,[20] m.p. 238°).

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Dibenzo[*e*,*g*]phenanthro[9,10-*b*][1,4]diazocine (8) had m.p. 272—273° (lit.,[21] m.p. 268—269°).

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