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15*H*-DIBENZO[*c.e*]BENZIMIDAZO[1.2-*a*]AZEPINE

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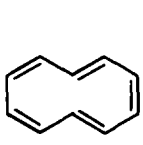
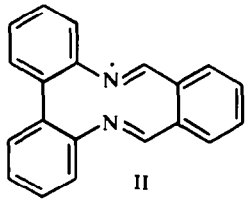
Abstract—The title compound V has been prepared by the condensation of biphenyl-2,2'-dialdehyde and *o*-phenylendiamine under a variety of conditions. The reaction is of considerable mechanistic interest as it has been shown to involve an intermolecular hydride shift, although in this system an intramolecular shift appears more likely.

[10]ANNULENE (I), the elusive monocyclic analogue of naphthalene has presented considerable difficulty in synthesis and in manipulation.[1] The stability of the cyclic 10 π-electron system is considerably enhanced by annelation,[2,4] but such derivatives still exhibit facile transannular rearrangements. The effect of hetero atoms on the properties of such ring systems is not known but would be of considerable interest.



I



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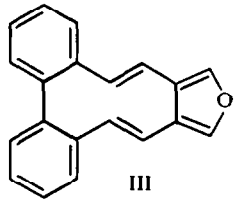

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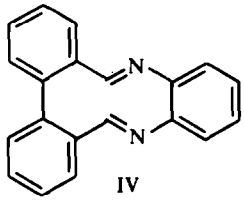
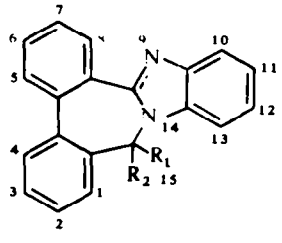


IV



V: $R_1 = R_2 = H$
XI: $R_1 = R_2 = D$
XIII: $R_1 = H, R_2 = D$

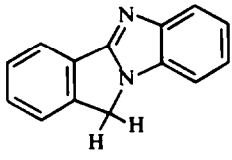
VIII: $R_1 = H, R_2 = OMe$
XII: $R_1 = D, R_2 = OMe$

An earlier attempt to prepare the annelated 1,6-diaza[10]annulene (II) through the condensation of 2,2'-diaminobiphenyl and *o*-phthalaldehyde failed to yield any identifiable products.[3]

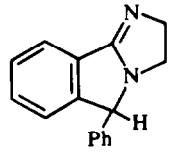
Since the success of such a synthesis may be dependent on the relative positions of the N atoms we attempted an analogous approach to the annelated 1,4-diaza[10]-annulene (IV). Hence the condensation of biphenyl-2,2'-dialdehyde and *o*-phenylene-diamine was investigated under a variety of conditions.

When the condensation was carried out in acetic acid (or benzene) solution, a single crystalline product (m.p. 160°) identified as 15H-dibenzo[*c.e*]benzimidazo-[1.2-*a*]azepine (V) was obtained. The structure of the azepine V follows from the analytical and spectral data. In particular, the molecular formula has been confirmed by accurate mass measurement, while the PMR spectrum (d_6-DMSO/D_2O) showed an AB double doublet due to the methylene protons centred at τ 3·42, 5·22 (2H). Obviously this eliminates IV as a possible structure for the condensation product. Furthermore, these signals remained virtually unaltered in the presence of D_2O and the IR spectrum confirmed the absence of any N—H group in the molecule.

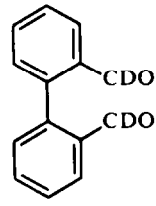
The related condensations of *o*-phthalaldehyde with *o*-phenylenediamine[5] and *o*-benzoylbenzaldehyde with ethylene diamine[6] give the polycyclic systems (VI and VII) respectively. Presumably these reactions involve a similar mechanism to that operating in the formation of the azepine V above.



VI



VII



X

On condensation in methanolic solution, biphenyl-2,2′-dialdehyde and *o*-phenylenediamine furnished the azepine V in excellent yield (90%) but it was contaminated with a small proportion (~20%) of 15-methoxydibenzo[*c,e*]benzimidazo[1.2-*a*]-azepine (VIII). Although the high resolution mass spectrum confirmed the presence of a compound $C_{21}H_{16}N_2O$ (i.e. VIII) and the PMR spectrum exhibited singlets at τ 3·56 (1H, proton 15) and 6·91 (3H, OMe protons) in addition to all the signals expected for V, the mixture could not be resolved by preparative TLC.

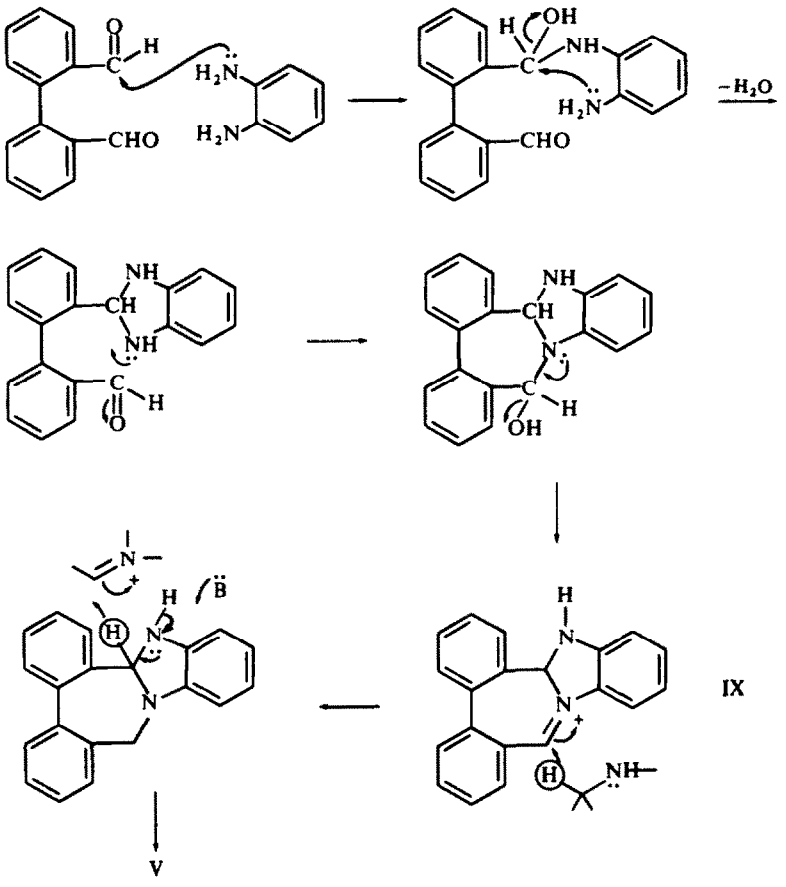
REACTION MECHANISM

The formation of the byproduct (VIII) led us to speculate on the reaction mechanism and one possibility is outlined in Scheme 1.

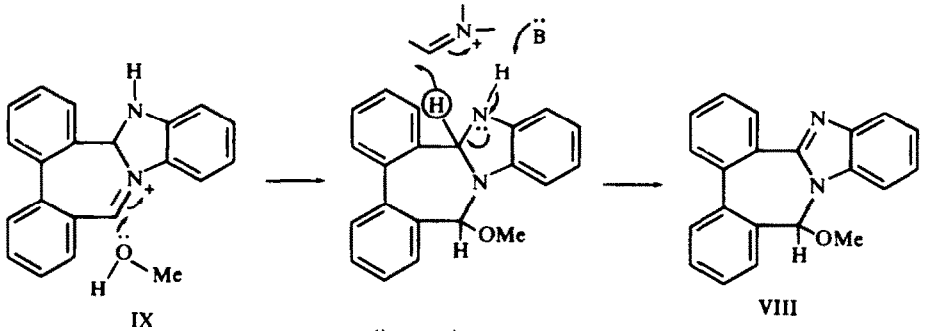
The key intermediate involved is the immonium salt (IX). Evidence for the hydride transfer has been obtained by deuterium labelling. Thus biphenyl-2,2′-dideutero-aldehyde (X) was prepared by the controlled reduction of 2,2′-diphenic acid-bis (N-methylanilide) with lithium aluminium deuteride at $-10°$.[7] The condensation of X with *o*-phenylenediamine in methanol yielded a mixture consisting mainly of the 15,15-dideuteroazepine (XI) together with a small amount of the 15-methoxy-15-deuteroazepine (XII).

Facile nucleophilic attack on immonium salts such as IX is well documented.[8] In the above scheme we propose that the major reaction pathway involves an intermolecular hydride shift, this being somewhat reminiscent of a Cannizzaro reaction.[9] In this case the driving force of the migration would be two-fold, since both aromatization of the benzimidazole ring system and neutralization of the charge on the electron

(A) MAJOR ROUTE



(B) MINOR ROUTE (IN METHANOL SOLUTION)



SCHEME 1

deficient N atom are energetically favourable processes. In view of the latter aspect, the above reaction can also be considered as being closely akin to the "disproportionation" of diaryl carbinols in acid solution, where hydride shift is promoted by migration to a carbonium ion.[10] The two-fold nature of the driving force probably

accounts for the fact that the hydride shift occurs equally well in acidic or weakly basic media.

Although the intermediate salt (IX) appears ideally constituted to undergo an intramolecular 1,3-hydride shift,[11] this mechanism has been invalidated. To confirm that this reaction did involve an *intermolecular* rather than intramolecular hydride shift, *o*-phenylenediamine was condensed with equimolar proportions of biphenyl-2,2'-dialdehyde and biphenyl-2,2'-dideuteroaldehyde. The major product (~40%) was shown to be the 15H,15-deuteroazepine (XIII), together with smaller quantities of the 15H-azepine V (~20%) and the 15,15-dideuteroazepine XI (~20%). In particular, the mass spectrum showed a base peak at *m/e* 283 due to the molecular ion of XIII.

When methanol is used as solvent the methoxyazepines VIII, XII are produced and must arise from competitive, intermolecular nucleophilic attack of methanol on the immonium salt IX. This has been confirmed by performing the condensation in the presence of a large excess of sodium methoxide. Intermolecular attack by methoxide ion predominates under such conditions and the major reaction product is the 15-methoxyazepine VIII. Even so a small quantity of the 15-*H*-azepine V is still obtained showing that the hydride shift still occurs to a small extent.

It seems probable that related condensation reactions, namely the condensation of *o*-phenylenediamine with *o*-phthalaldehyde and of *o*-benzoylbenzaldehyde with ethylene diamine, proceed via a similar pathway.

EXPERIMENTAL

IR spectra were recorded on a Unicam model S.P. 200G spectrometer and NMR spectra on a Perkin–Elmer R-10 spectrometer. Chemical shifts were measured on the τ-scale relative to TMS as internal standard (τ = 10·0). Mass spectra were recorded on a MS-9 spectrometer. M.ps are uncorrected. All chromatograms were carried out on thick layer plates (100 × 20 × 0·1 cm) using alumina (Merck G) as adsorbent.

Condensation of biphenyl-2,2'-dialdehyde with o-phenylenediamine

(i) *In glacial acetic acid*; 15H-*dibenzo*[c.e]*benzimidazo*[1.2-a]*azepine* (V). Biphenyl-2,2'-dialdehyde (0·21 g, 1·0 mmole) and *o*-phenylenediamine (0·11 g, 1·0 mmole) were dissolved in glacial AcOH (50 ml) and left at room temp (16 hr). The AcOH was removed under reduced press and the residue chromatographed using light petroleum (b.p. 60–80°)-CH_2Cl_2 (ratio 2:1) as eluent. The major yellow band was extracted and recrystallized from CCl_4 to give V (0·145 g, 51%) as a colourless crystals, m.p. 160°; UV $\lambda_{max}^{95\%EtOH}$ 230 nm (log ε 4·43), 260 (4·30), and 300 (4·28); NMR (d_6, DMSO-D_2O, 60 MHz) τ 1·70–1·93 (m, 1H), 2·00–2·75 (m, 11H) and an AB double doublet centred at 3·42, 5·22 (J = 15 Hz, 2H); mass spec. *m/e* 282·1168 (M^+), 281 (M^+ − H). (Found: C, 84·85; H, 5·20; N, 9·59. $C_{20}H_{14}N_2$ requires: C, 85·08; H, 5·60; N, 9·92% M282·1157).

(ii) *In methanol containing sodium methoxide*: 15-*methoxydibenzo*[c.e]*benzimidazo*[1.2-a]*azepine* (VIII). Biphenyl-2,2'-dialdehyde (0·21 g, 1·0 mmole) and *o*-phenylenediamine (0·11 g, 1·0 mmole) were dissolved in MeOH (200 ml) containing 5% NaOMe, and the reaction mixture was boiled under reflux (4 hr). The MeOH was then diluted with water and extracted with ether (3 × 100 ml). The combined ethereal extract was washed with water, dried (K_2CO_3), concentrated and the residue distilled at 140°/0·5 mm to yield VIII (0·105 g, 34%) as a pale yellow solid, m.p. 100°; UV $\lambda_{max}^{95\%EtOH}$ 230 nm (log ε 4·44), 260 (4·38) and 300 (4·35); NMR ($CDCl_3$, 60MHz) τ 1·56–1·80 (m, 1H), 2·10–2·80 (m, 11H), 3·56 (s, 1H) and 6·91 (s, 3H); mass spec *m/e* 312·1264 (M^+), 281 (M^+-OMe). Note that the NMR and mass spec shows that traces of the 15H-acepine V (~5%) were present as a contaminant in all samples of VIII prepared in the above manner.

(iii) *In methanol*; *mixture of* 15-H-*dibenzo*[c.e]*benzimidazo*[1.2-a]*azeptne* (V) *and* 15-*methoxydibenzo*-[1.2-a]*azepine* (VIII). Biphenyl-2,2'-dialdehyde (0·21 g, 1·0 mmole) and *o*-phenylenediamine (0·11 g, 1·0 mole) were dissolved in MeOH (50 ml) and the MeOH was evaporated on a water bath. The residue was

chromatographed as described (i) to give a mixture of V and VIII as a pale yellow solid (0·255 g, 90%), m.p. 155°; NMR and mass spec data showed that the mixture contained approximately 80% V and 20% VIII.

Biphenyl-2,2'-dideuteroaldehyde (X). This preparation was adapted from the method developed by Weygand *et al.*[7] Diphenic acid-bis-(N-methylanilide) (1·05 g, 2·5 mmoles) was dissolved in anhyd THF (100 ml) and the soln cooled in an ice-salt bath. A soln of LAD (0·11 g, 2·5 mmoles) in anhyd THF was then added dropwise with stirring over a period of 0·5 hr. The reaction mixture was cooled (in an ice–salt bath) and stirred for a further 8 hr, then hydrolysed with dil H_2SO_4 and extracted with ether. The ether extract was washed with water, dried (Na_2SO_4) and concentrated. The residue was chromatographed using light petroleum (b.p. 40–60°)–ether (6:4) as eluent, to furnish X (0·10 g, 19%) as a colourless solid, m.p. 63°; IR $\nu_{max}^{CCl_4}$ 1695 cm^{-1} (C=O); NMR ($CDCl_3$, 60MHz) τ 2·12–2·78 (m).

Condensation of biphenyl-2,2'-dideuteroaldehyde (X) *and o-phenylenediamine; mixture of* 15,15-*dideuterodibenzo*[c.e]*benzimidazo*[1.2-a]*azepine* (XI), 15-*methoxy*-15-*deuterodibenzo*[c.e]*benzimidazo*[1.2-a]-*azepine* (XII)

Biphenyl-2,2'-dideuteroaldehyde (0·085, 0·4 mmole) and *o*-phenylenediamine (0·043 g, 0·4 mmole) were condensed in MeOH (50 ml) as described in (iii) above. The mixture of XI and XII were obtained as a pale yellow solid (0·10 g, 90%), m.p. 153–155°; NMR ($CDCl_3$, 60MHz) τ 1·56–1·80 (m, area 1·8), 2·04–2·80 (m, 18·0) and 6·91 (s, 0·6); mass spec *m/e* 313 (M^+_{XII}), 286 (M^+_{XI}), 283 (M^+_{XI}—H) 282 (M^+_{XII}—OMe).

TABLE 1. MASS SPECTRAL DATA*
(*m/e* presented as % of base peaks)

m/e	Observed spectra			Calculated spectra	
	V	XI	Above mixture	Intermolecular XIII:V:XI 2:1:1	Intramolecular V:XI 1:1
285		22	11	11	16·5
284	2·5	100	58	57	77
283	20	34	100	100	41
282	100	33	90	91	100
281	64	7	51	45	53
280	10	5	12	11·5	11

* The samples utilised to obtain this mass spectral data were prepared in methanolic solution and as a result V contains ca. 20% VIII and XI contains ca. 20% XII. Hence these observed composite spectra were used to compute the calculated spectra expected from intermolecular or intramolecular reactions in methanol.

Condensation of o-phenylenediamine with equal proportions of biphenyl-2,2'-dialdehyde and biphenyl-2,2'-dideuteroaldehyde (X)

Biphenyl-2,2'-dialdehyde (0·105 g, 0·5 mmoles), biphenyl-2,2'-dideuteroaldehyde (0·106 g, 0·5 mmoles) and *o*-phenylenediamine (0·11 g, 1·0 mmole) were condensed in MeOH (50 ml) as described in (iii). The product (0·25 g, 90%) was obtained as a pale yellow solid, m.p. 153–156°; NMR and mass spec data confirmed that the major product was XIII, while V, XI and the methoxy compounds VIII and XII were present in smaller amounts. In particular, the NMR spectrum (d_6, DMSO—D_2O, 60MHz) did not exhibit a distinct AB double doublet as does pure V, but showed two broad peaks centred at τ 3·42, 5·22 (area 1H) due to the methylene protons of V, XIII. Furthermore, the mass spectrum of the mixture showed a base peak at *m/e* 283 due in the main, to the molecular ion of XIII. The overall mass spectrum of the mixture was consistent with complete intermolecular hydride transfer (see Table 1) but inconsistent with an intramolecular reaction.

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