An Approach To The Synthesis of a Cycloheptapyrazole (1,2-Diaza-azulene)

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2,6-Dihydro-5,7-dimethylcycloheptapyrazol-6-one was prepared by base-catalysed condensation of diethyl ketone with pyrazole-3,4-dicarbaldehyde. On treatment with phenyl-lithium, the tropone was converted into 2,6-dihydro-5,7-dimethyl-6-phenylcycloheptapyrazol-6-ol (IVb). This alcohol gave the perchlorate of a cyclic dimer of 5,7-dimethyl-6-phenylcycloheptapyrazole (I) with perchloric acid. Spectral data in support of this dimer are presented.

ALTHOUGH extensive work has been performed in azulene chemistry, only two monoaza-azulenes have been prepared.[1,2] In spite of various claims to a synthesis of a 1,2-diaza-azulene (cycloheptapyrazole), none of the reports [3,4] were supported by either descriptions of experimental procedures or presentations of any analytical data to authenticate the structures. The results of our efforts to synthesize a 1,2-diaza-azulene (I) are described in this report.

Pyrazole-3,4-dicarbaldehyde [5] (II) (see Scheme 1) and diethyl ketone condensed in the presence of sodium methoxide to afford 2,6-dihydro-5,7-dimethylcycloheptapyrazol-6-one (III).[6] This tropone (III) definitely did not exist in the enolic form but rather as the keto-tautomer as evidenced by spectral analysis (see the Table). The i.r. absorption for the carbonyl group was comparable to the frequency reported for 6,8-dimethylbenzocycloheptan-6-one (1597 cm^{-1}).[7] Similarly, the u.v. absorptions compared favourably with those of the benzocycloheptanone.[7] The n.m.r. signal of the tropone ring protons in the benzocycloheptanone appeared at δ 7·20 p.p.m.[8] With the keto-structure of tropone (III) confirmed, we attempted to convert it into the alcohol (IVa). However, all attempts to reduce (III) to (IVa) with such reagents as sodium borohydride, lithium aluminium hydride, or sodium bis-(2-methoxyethoxy)-aluminium hydride gave only near quantitative recovery of the tropone (III).

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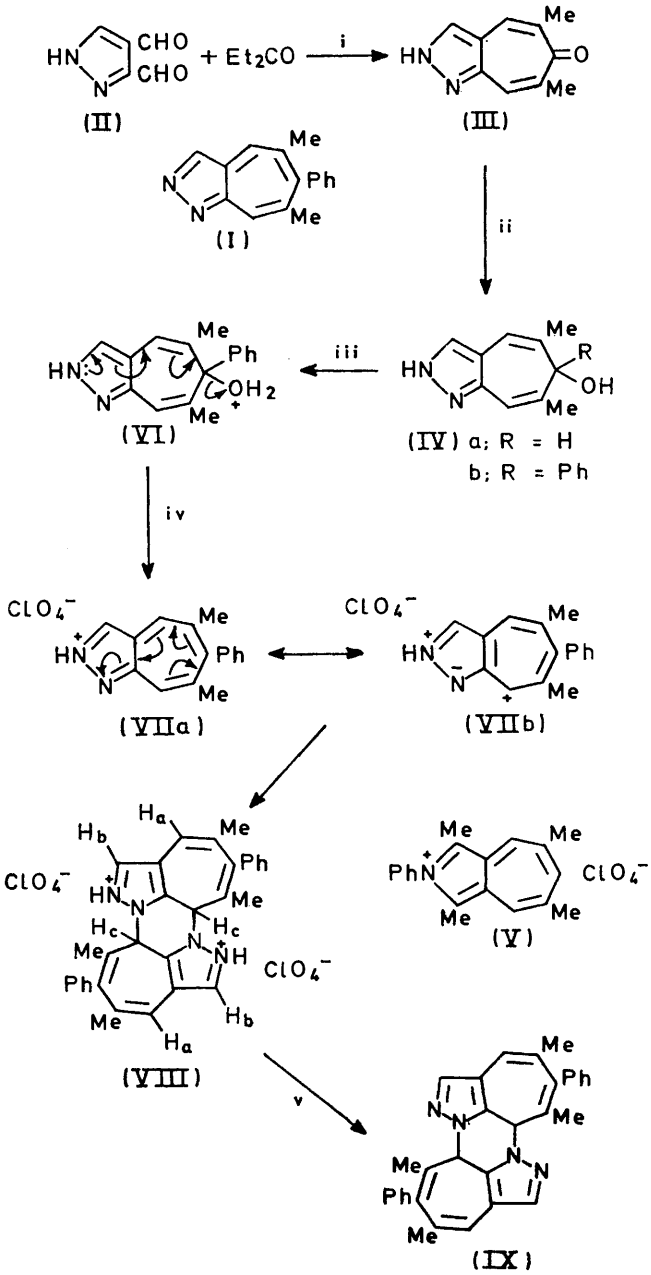
[7] D. Meuche, H. Strauss, and E. Heilbronner, *Helv. Chim. Acta*, 1958, **41**, 2220.
[8] F. G. Bordwell and M. Winn, *J. Org. Chem.*, 1967, **32**, 42.

In view of this resistance of (III) to reduction, we varied our approach to (I) in two ways compared with the method of El'tsov and his co-workers [2] in their



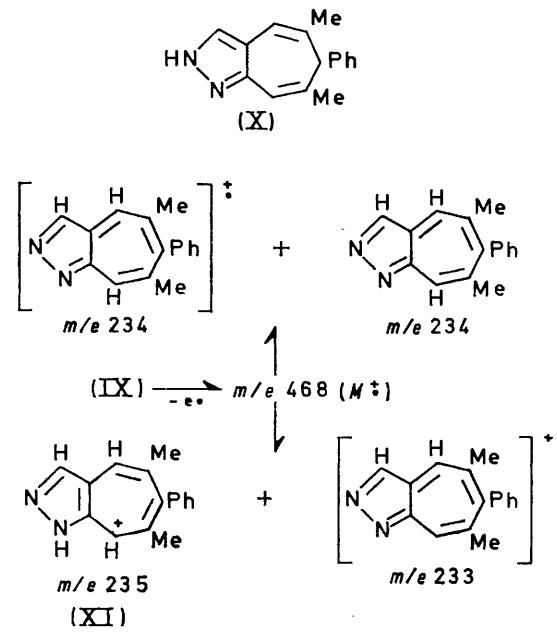
SCHEME 1

Reagents: i, MeONa–methanol; ii, PhLi–THF; iii, 70% $HClO_4$–ether; iv, loss of H_2O; v, 5% $NaHCO_3$–dichloromethane

synthesis of 1,3,5,7-tetramethyl-2-phenylcyclohepta[*c*]-pyrrolium perchlorate (V). First, there was no alkyl or aryl group substituent on either pyrazole ring nitrogen atom in (I) and secondly, it was necessary to treat the ketone (III) with a 2·5 molar excess of phenyl-lithium to obtain the alcohol (IVb) in 77% yield. The supporting spectral data is recorded in the Table.

We envisaged that treatment with perchloric acid would result in the sequence shown in Scheme 1 [*i.e.*, (IVb) → (VI) → (VII)]. However, the perchlorate (VIII) which did form was a cyclic dimer of 1,8-dihydro-5,7-dimethyl-6-phenylcycloheptapyrazole. Apparently, the loss of a molecule of water from (VI) formed the perchlorate (VIIa). As such, it underwent reaction with an identical cation in the 1,3-dipolar form (VIIb) to give the dimer diperchlorate (VIII). Neutralization of (VIII) with a 5% sodium hydrogen carbonate solution gave the dimer (IX), a white, high-melting crystalline compound which was insoluble in organic solvents. The spectral data for (VIII) is in the Table. Other attempts to obtain (I) from (IVb) such as heating under reflux in benzene or diglyme, or treatment with toluene-p-sulphonic acid gave only unchanged (IVb).

It is clear that this synthetic approach to aza- or diaza-azulenes, based on the method of Winn and Bordwell [9] for the preparation of 2-thia-azulenium perchlorates, fails as a result of the stability of the cation produced and the presence of a nucleophilic annular nitrogen atom.



SCHEME 2

In addition to the spectral evidence in support of (VIII), this product was subjected to mass spectral analysis. Considerable difficulty was encountered in obtaining and interpreting the mass spectrum. Hydrochloride salts usually liberate hydrogen chloride and then give the mass spectrum of the free base. It appears this salt (VIII) rapidly lost 2 molecules of perchloric acid to produce the parent ion *m/e* 468. This ion did not exist very long, being thermally degraded to the ion *m/e* 250, and a fragment of mass 236, the latter probably having the structure of the neutral compound (X) (see Scheme 2). The mass spectrum of (IX), however, clearly gave a

[9] M. Winn and F. G. Bordwell, *J. Org. Chem.*, 1967, **32**, 1610.

molecular weight of 468 in agreement with a dimer structure. The major fragmentations of (IX) consisted of fragments *m/e* 234 (*M* − 234) and 235 (*M* − 233), which are accounted for in Scheme 2. The degradation of (IX) to (XI) is consistent with our proposed sequence for the formation of (VIII).

EXPERIMENTAL

I.r. spectra were measured on a Perkin-Elmer Infracord model 137, u.v. spectra were obtained with a Bausch and Lomb 505 Spectrophotometer, and the n.m.r. spectra were recorded on a Varian A60A with tetramethylsilane as an internal standard. Mass spectral analyses were performed by Morgan–Schaeffer of Montreal, Canada (70 eV). Microanalyses were determined by Schwarzkopf Microanalytical Laboratories, Woodside, New York or Childers Microanalytical Laboratory, Milford, New York.

Diazomethane was prepared according to the procedure of Eistert,[10] assayed as described by Fieser,[11] and used in the preparation of pyrazole-3,4-dicarbaldehyde (82% yield, m.p. 202—203°; lit.,[5] 203—205°) by reacting with acetylenedialdehyde bis(diethyl acetal)[12] according to the procedure of Henkel and Weygand.[5]

2,6-Dihydro-5,7-dimethylcycloheptapyrazol-6-one (III).—To a solution of sodium (4·1 g) in methanol (120 ml), diethyl ketone (5 g) in methanol (30 ml) was added dropwise with stirring (10 min). The orange solution was stirred 24 h at room temperature, heated under reflux for 0·75 h, and evaporated to a gum. This was dissolved in water (130 ml), acidified with hydrochloric acid, and cooled in an ice bath. The precipitate was filtered off, washed with water until neutral to litmus, and air-dried to afford the *tropone* (III) as a white powder (4·5 g), m.p. 187—188° (from chloroform). In seven preparations the yields ranged from 15·2—64·3%. The tropone (III) did not react with 2,4-dinitrophenylhydrazine (Found: C, 69·0; H, 5·7; N, 16·1. $C_{10}H_{10}N_2O$ requires C, 68·95; H, 5·75; N, 16·1%).

2,6-Dihydro-5,7-dimethyl-6-phenylcycloheptapyrazol-6-ol (IVb).—To a solution of the tropone (III) (1·0 g) in tetrahydrofuran (20 ml), phenyl-lithium (8 ml, 1·43M) was added in one portion. The orange suspension was heated under reflux for 30 min and more phenyl-lithium (3 ml) was added. This solution was stirred for 30 min at room temperature, heated under reflux for 10 min and decomposed with water (20 ml). The aqueous layer was extracted with ether (2 × 25 ml) and the combined ether and tetrahydrofuran solutions were dried ($MgSO_4$). The filtered solution was evaporated to a yellow solid, which was triturated with benzene and filtered again to afford (IVb) (1·1 g), m.p. 248—249° (from chloroform). Seven preparations gave yields between 60 and 69% (Found: C, 76·05; H, 6·55; N, 10·8. $C_{16}H_{16}N_2O$ requires C, 76·15; H, 6·3; N, 11·1%).

Spectral data

Compound	$\nu_{max.}$ (KBr)/cm^{-1}	$\lambda_{max.}$/nm (log ε)	δ/p.p.m.
(III)	3205 (NH) 1592 (C=O) 1610 (C=C) 1515 (C=N)	222 (4·15) [a] 254 (4·15) 334 (3·79)	2·20 (6H, d, 5- and 7-Me) [b] 7·76 (2H, s, 4- and 8-H_2) 8·08 (1H, s, 3-H) 13·68 (1H, s, NH)
(IVb)	3226 (NH) and (OH) 776, 707 (monosubstituted benzene)	212 (3·47) [a] 222 (3·55)	1·98 (6H, d, 5- and 7-Me) [b] 5·70 (1H, s, OH) [c] 6·25 (2H, d, 4- and 8-H_2) 7·01—7·50 (6H, m, 3-H and ArH) 12·40 (1H, s, NH) [c]
(VIII)	3000—2800 (broad NH) 1099 (perchlorate band) [d] 766, 704 (phenyl)	266 (4·81) [e] 330 (3·82) 380 (4·01) 450 (3·34)	2·60 (12H, s, 4 × Me) 6·90—7·20 (2H, s, 2 × NH^+) 7·40 (6H, m, *o*-ArH) 7·64 (4H, m, *m*-and-*p*-ArH) 9·20 (2H, s, 2 × H_a) [g] 9·40 (2H, s, 2 × H_b) [g] 9·80 (2H, s, 2 × H_c)
(IX)	Absence of NH, 762, 699 (phenyl)	*h*	*h*

[a] In methanol. [b] In dimethyl sulphoxide. [c] Absorptions disappear in presence of D_2O. [d] See ref. 13. [e] Solvent 95% sulphuric acid. [f] Solvent $(CD_3)_2CO$. [g] These *peri*-hydrogens showed a slight splitting of the singlet peaks. [h] Insoluble in all solvents: spectra could not be obtained.

Diperchlorate Salt of the Cyclic Dimer (VIII) *of 5,7-Dimethyl-6-phenylcycloheptapyrazole* (I).—To a solution of the foregoing alcohol (IVb) (0·25 g) in ethyl acetate–ether (40 ml; 1 : 3 v/v) was added a solution of 70% perchloric acid (0·12 g) in ether (30 ml). The precipitate was filtered off to give the *dimer* (VIII) (0·2 g) as light yellow crystals, m.p. 192—194° [from chloroform–light petroleum (b.p. 30—60°)] (Found: C, 57·1; H, 4·7; N, 8·55. $C_{32}H_{30}Cl_2N_4O_8$ requires C, 57·4; H, 4·5; N, 8·3%).

Cyclic Dimer (IX) *of 5,7-Dimethyl-6-phenylcycloheptapyrazole* (I).—A solution of the perchlorate salt (VIII) (0·35 g) in dichloromethane (20 ml) was adjusted to pH 6 with 5% sodium hydrogen carbonate. The dried ($MgSO_4$) dichloromethane layer afforded a yellow solid upon evaporation which after trituration with ethyl acetate gave the *dimer* (IX) (0·15 g) as white plates, m.p. 329—331° (Found: C, 82·15; H, 6·1; N, 11·9. $C_{32}H_{28}N_4$ requires C, 82·05; H, 6·0; N, 12·0%).

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