Rationale for Predominance of 1,3-Dipolar Cycloreversion in Thermolysis of 3,4-Dihydropyrazole from Ethano-bridged Diphenyldiazomethane and 2,5-Dimethyl-1,4-benzoquinone. An X-Ray Study

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The X-ray crystal structure of the title dihydropyrazole indicates that the steric and π-conjugative effects associated with the conformational locking of the two phenyl rings are the crucial factors in the predominance of 1,3-dipolar cycloreversion rather than nitrogen extrusion to give the cyclopropane derivative.

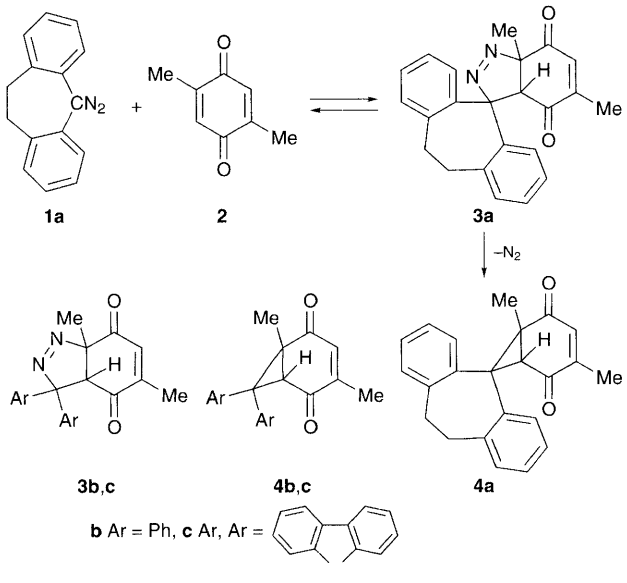
In a previous paper, we reported that thermolysis of the dihydropyrazole **3a** from 5-diazo-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cycloheptene **1a** and 2,5-dimethyl-1,4-benzoquinone **2** preferentially gives rise to the diazoalkane and quinone *via* 1,3-dipolar cycloreversion in competition with nitrogen extrusion to provide the cyclopropane derivative **4a** (Scheme 1).[1] This type of true cycloreversion regenerating the component dipole and dipolarophile is seldom seen in the extensive field of dihydropyrazole chemistry,[2] mainly because of the unfavourable thermodynamic energy balance between the reactants and the products; *i.e.* the free energy difference must be very small for the practical attainment of equilibrium. Another requisite for cycloreversion is the resistance of dihydropyrazoles to subsequent degradation such as nitrogen extrusion[3] and [1,3] H shift.[4] Five-membered rings with an N=N double bond can easily eliminate molecular nitrogen on activation by only a small amount of thermal energy.[3]

We now report that based on the X-ray structure analysis of the dihydropyrazole **3a**, the steric and π-conjugative effects of the two ethano-bridged aromatic nuclei play a decisive role in the occurrence of 1,3-dipolar cycloreversion in preference to nitrogen extrusion. We also report the thermolysis of the structurally analogous dihydropyrazoles **3b**,**c** derived from the reaction of diphenyldiazomethane (DDM) and 9-diazofluorene (9-DF) with **2**.

As noted previously, diazoalkane **1a** and quinone **2** had an equilibrium constant K of 2.02 dm^3 mol^{-1} (50 °C, C_6D_6) with the dipolar adduct **3a**.[1] The formation of **3a** is therefore favoured by only ΔG = 1.86 kJ mol^{-1}, satisfying the thermodynamic requirement mentioned above. From kinetic studies of the thermolysis of **3a**, the activation free energy ($\Delta G^{\ddagger}$) for the cycloreversion is calculated to be 105.1 kJ mol^{-1}, slightly smaller than that for nitrogen extrusion (107.3 kJ mol^{-1}, 50 °C, C_6D_6).† Thus, the energy profile of the overall process **1a** + **2** ⇌ **3a** → **4a** satisfies the thermodynamic requirement for cycloreversion.

In contrast with **3a**, **3b** derived from DDM did not revert to the starting materials but exclusively extruded nitrogen to afford the cyclopropane derivative **4b**, although nitrogen extrusion has a $\Delta G^{\ddagger}$ value (104.7 kJ mol^{-1}) appreciably larger than that for the formation of **3b** (101.3 kJ mol^{-1}).‡ This means the possible foregoing equilibrium, DDM + **2** ⇌ **3b**, is completely shifted towards the dihydropyrazole **3b**; *i.e.* cycloreversion of **3b** has a much higher energy barrier in this case. An attempt to obtain the dihydropyrazole **3c** from 9-DF failed; only the cyclopropane derivative was obtained with no detection of the intermediate **3c** (by NMR). Therefore, this reaction can be represented by the second-order sequence, 9-DF + **2** ⇌ **3c** → **4c**, with a $\Delta G^{\ddagger}$ value (104.1 kJ mol^{-1})§ which is 2.8 kJ mol^{-1} larger than that of the DDM reaction, although the question of which step is rate-determining remains open.

These thermodynamic data show that the dihydropyrazole **3a** is characterized by its high potential energy comparable to that of the reactant system. Furthermore, the rate of nitrogen extrusion of dihydropyrazoles **3a–c** increases in the order **3a** < **3b** < **3c**. The thermal behaviour of **3a–c** may be rationalized in



Scheme 1

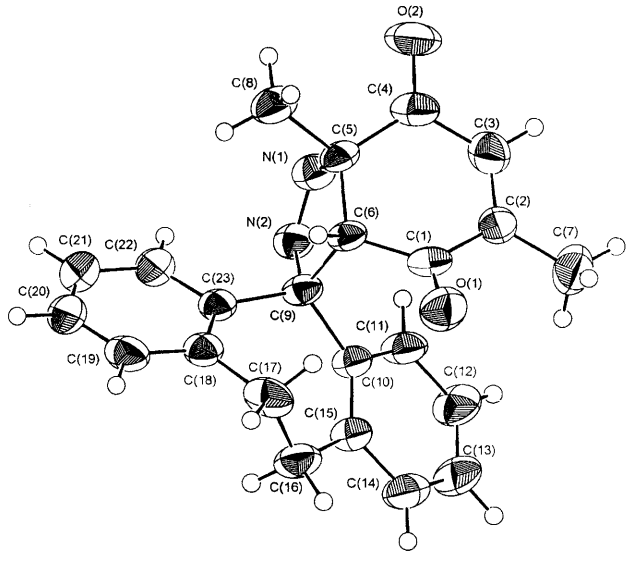


Fig. 1 Molecular structure and atom labelling scheme of **3a**. Selected bond lengths (Å) and angles (°): O(2)–C(4), 1.217(9); O(1)–C(1), 1.218(9); N(1)–N(2), 1.247(8); N(1)–C(5), 1.515(9); N(2)–C(9), 1.511(8); C(5)–C(6), 1.519(9); C(6)–C(9), 1.580(9); C(9)–C(10), 1.546(9); C(9)–C(23), 1.539(9); C(10)–C(15), 1.380(9); C(15)–C(16), 1.514(10); C(16)–C(17), 1.540(11); C(17)–C(18), 1.519(10); C(18)–C(23), 1.401(9); N(2)–N(1)–C(5), 112.6(6); N(1)–N(2)–C(9), 112.9(6); N(1)–C(5)–C(6), 105.6(5); C(5)–C(6)–C(9), 102.5(5); N(2)–C(9)–C(10), 106.0(5); N(2)–C(9)–C(23), 105.3(5); C(9)–C(10)–C(15), 126.4(6); C(9)–C(23)–C(18), 120.9(6); C(10)–C(15)–C(16), 126.8(6); C(15)–C(16)–C(17), 116.2(6); C(16)–C(17)–C(18), 110.3(6); C(17)–C(18)–C(23), 120.7(6).

terms of the structural nature of the substituted two aromatic rings.

The X-ray crystal structure analysis of **3a** shows in particular that the quinone oxygen O(1) occupies a crowded position nearly touching the C(9), C(10), C(15) and C(17) atoms of the diaryl substituent with almost van der Waals distances of 3.257, 3.163, 3.331 and 3.344 Å, respectively (Fig. 1).¶ In accordance with this, the bond length of the cleaved C(6)–C(9) is notably longer: 1.580(9) Å. Hence, the potential energy of **3a** will increase owing to the steric congestion coupled with the conformational rigidity of the ethano-bridged two phenyl ring moiety. The dihydropyrazoles **3b** and **3c** are expected to be free from such a steric hindrance.

In nitrogen extrusion giving cyclopropane derivatives, a simultaneous homolytic cleavage of two C–N bonds is generally argued for dihydropyrazoles like **3** with less polar substituents, and a 1,3-biradical-like transition state is envisaged.[3] In Fig. 1, each of the aromatic rings of **3a** is unfavourably located in such a way that the breaking C(9)–N(2) bond can not fully benefit from π-conjugative stabilisation, as judged from the relevant torsion angles; N(2)–C(9)–C(10)–C(15) 25.5°, N(2)–C(9)–C(23)–C(22) 8.7°. By contrast, the enhanced π-conjugation associated with increasing flexibility of the twisted phenyl groups of **3b** seems to be responsible for the decrease in $\Delta G^{\ddagger}$ by 2.6 kJ mol^{-1} compared to **3a**. The high lability of **3c** may be ascribed to the planar π-system which is approximately perpendicular to the breaking C(9)–N(2) bond.

Thus, in the thermolysis of the ethano-bridged diphenyl-substituted dihydropyrazole **3a** the unusual 1,3-dipolar cycloreversion may prevail over the more common nitrogen extrusion to give the cyclopropane as a result of the conformational locking of the aromatic nuclei, raising the potential energy of **3a** and leading to less favourable π-conjugation for nitrogen elimination.

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Footnotes

† All the kinetic runs were performed in NMR tubes at 50 °C in C_6D_6; see ref. 1. The rate constants, k, for cycloreversion and nitrogen extrusion were 6.75×10^{-5} s^{-1} and 2.96×10^{-5} s^{-1}, respectively.

‡ Pure **3b** could not be isolated because of its greater thermal lability to give the cyclopropane derivative so kinetic measurements were made on a mixture of **3b** and the cyclopropane (9 : 1). The rate constants k, for cycloreversion and formation of **3b** were 8.15×10^{-5} s^{-1} and 2.85×10^{-4} dm^3 mol^{-1} s^{-1}, respectively.

§ A value of 1.01×10^{-4} dm^3 mol^{-1} s^{-1} was obtained.

¶ *Crystal data* **3a**: $C_{23}H_{20}N_2O_2$, M = 356.40, triclinic, space group $P\bar{1}$, a = 7.620(3), b = 9.76(1), c = 12.47(1) Å, α = 100.22(7), β = 99.48(5), γ = 95.25(6)°, V = 893(1) Å^3, Z = 2, D_c = 1.33 g cm^{-3}, μ(Mo-Kα) = 0.797 cm^{-1}. Data were collected on a Mac Science MXC3 diffractometer at 20 °C by using the ω–2θ scan method with 2θ in the range $3 \leqslant 2\theta \leqslant 40°$. Of the 1682 unique data collected, 1380 with $I > 3\sigma(I)$ were used for refinement on F. The structure was solved by SHELX-86 and subsequent Fourier maps, and submitted to full-matrix least-squares refinement with the non-hydrogen atoms treated anisotropically, and the hydrogen atoms placed at their geometrically calculated positions (C–H 0.96 Å). The final agreement factors were R = 0.0618 and R_w = 0.0663 for 264 variables. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallograpic Data Centre. See Information for Authors, Issue No. 1.

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