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1,3-DIPOLAR CYCLOADDITIONS OF AROMATIC AZOXY COMPOUNDS TO STRAINED CYCLOALKENES

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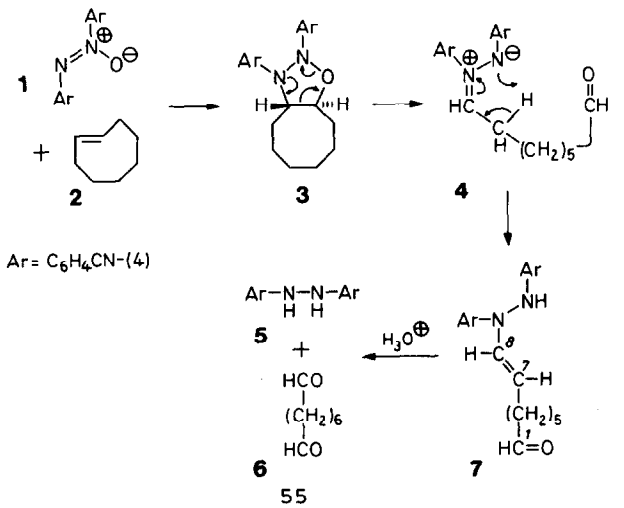
Summary The 1,2,3-oxadiazolidines resulting from the addition of 4,4'-dicyanoazoxybenzene to *trans*-cyclooctene or *cis,trans*-cycloocta-1,5-diene are not stable, but suffer 1,3-dipolar cycloreversion to give an azomethine imine; this intermediate is either captured by a second molecule of the strained cycloalkene to give 1:2 adducts in high yields or it tautomerizes to an enehydrazine. 4,4'-Dinitroazoxybenzene and benzo[c]cinnoline N-oxide react analogously.

In the classification of 1,3-dipoles,[1] azoxy compounds appear amongst those of the allyl type. In 1973, Challand, Rees, and Storr [2] reacted benzo[c]cinnoline N-oxide and its 3,8-dimethoxy derivative with dimethyl acetylenedicarboxylate and isolated 1:1 adducts in 2 and 7% yield; not the initially formed 1,2,3-oxadiazolines, but the azomethine imines originating from electrocyclic ring opening were obtained.

Azoxy compounds possess low-lying π MO's and the addition to an electron-rich dipolarophile should overcome the activation barrier easy as long as sufficient thermodynamic driving force is provided. The high ring strain of *trans*-cyclooctene and *cis,trans*-cycloocta-1,5-diene is released during the cyc-

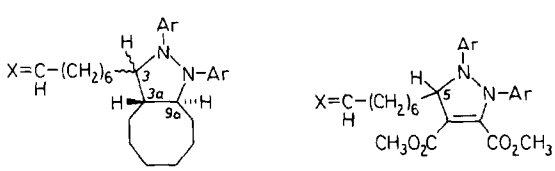


loaddition; 6 and 18 kcal mol^{-1},[3] respectively, should contribute to the reaction enthalpy. Leitich [3] reported on the first thermal cycloadditions of aromatic nitro compounds to the mentioned strained cycloalkenes.

4,4'-Dicyanoazoxybenzene (1, 2.0 mmol) and (*E*)-cyclooctene (2, 2.2 mmol) [4] in 6 ml dry glyme were refluxed under nitrogen for 36 h; 8% 1 was reisolated. Thick-layer chromatography (TLC) on silicagel (ether/benzene 7:3, R_F 0.55) furnished 8-(N,N'-di-p-cyanophenylhydrazino)-oct-7-enal (7) as a yellow resin [5] in 81% yield. ^1H NMR ($CDCl_3$, 100 MHz) δ 9.70 (t, 1-H, J = 1.7 Hz), 8.45 (s, NH), 7.03 (dt, $J_{7,8}$ = 13.3 Hz, $J_{6,8}$ = 1.0 Hz, 8-H), 5.15 (dt, $J_{7,8}$ = 13.3 Hz, $J_{6,7}$ = 7.2 Hz, 7-H); the assignments were secured by double resonance. ^{13}C NMR ($CDCl_3$, 25.2 MHz) δ 202.3 (d, C-1), 126.5 (d, C-8), 111.1 (d, C-7), 119.3 and 112.0 (2 s, 2 CN), all further signals specified. IR ($CHCl_3$) 3360 (N-H), 1723 cm^{-1} (C=O). MS (70 eV, 200°C) m/e 358 (M^+, 1%), 118 (p-cyanoanilinium, 100%).

Treatment of 7 in chloroform with 2 N H_2SO_4 afforded suberaldehyde (6, bp 60°C/0.001, 85% yield, NMR identical with an authentic specimen) and 4,4'-dicyanohydrazobenzene (5, mp 196 - 97°C, 85% yield); 6 was characterized as bis-2,4-dinitrophenylhydrazone, mp 177 - 79°C.

The weakness of the NO bond of 3 is mainly responsible for the 1,3-dipolar cycloreversion which gives rise to the azomethine imine 4. Its stabilization through sigmatropic 1,4 H-shift should give rise to the *cis*-enehydrazine; $J_{7,8}$ = 13.3 Hz indicates the trans double bond in 7. Cis,trans isomerization in enehydrazines is probably as fast as in enamines.[6] Is it possible to trap the transient azomethine imine ?



8 X = O **10**

9 X = N–N–$C_6H_3(NO_2)_2$ **11**
H

Ar = C_6H_4CN-(4)

The suspension of 2.0 mmol of 1 and 4.2 mmol of 2 in 1.0 ml glyme was heated 2 d to 60°C in the course of which 1 slowly dissolved; the molar concentration of the dipolarophile 2 was increased ∿ 7-fold compared with the first experiment. TLC separated the oily 1:2 adduct 8 (R_F 0.78, 70% yield) from the 1:1 adduct 7 (R_F 0.55, 6%).

The spectroscopic properties of the bis-adduct are in accordance with

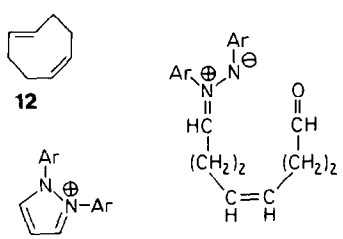
the structure of the cyclooctapyrazole derivative 8. The NMR signal of the aldehydic H suggests a mixture of diastereomers; their separation by repeated TLC or HPLC failed. The ^{1}H NMR will be discussed for the analogous 15. IR ($CHCl_3$) 2217 (C≡N), 1718 (C=O). MS (70 eV, 220°C) m/e 468 (M^+, 100%), 440 (M^+ - CO, 11%), 355 (M^+ - $(CH_2)_6CHO$, 44%), 102 ($C_6H_4CN^+$, 90%).

The 2,4-dinitrophenylhydrazone 9 (viscous orange oil after TLC, 87% yield) likewise failed to crystallize, but provided like 8 correct CH and N analyses.

The enehydrazine 7 does not react with 2 (6 d at 70°C), *i.e.*, 7 is not an intermediate on the pathway to 8. The 1,3-dipolar cycloaddition of the azomethine imine 4 to a second molecule of *trans*-cyclooctene to give 8 competes with the 1,4 H-shift, 4 → 7.

The azoxy compound 1 and to some extent the strained cyclooctene 2 are inert to dimethyl acetylenedicarboxylate (DMAD) at room temperature. When 2.2 mmol 2 were added in 3 h to the stirred suspension of 2.0 mmol 1 in 10 mmol DMAD and 5 ml THF, the solution was clear 4 h later. After two days TLC afforded 75% of 10 (R_F 0.50), the 1:1:1 adduct of the three reactants. Thus, DMAD won in the competition for intermediate 4.

The 3-pyrazoline 10 was not obtained pure, but the 2,4-dinitrophenylhydrazone (85% yield after TLC, orange resin) analyzed correctly for 11. ^{1}H NMR ($CDCl_3$, 60 MHz) δ 11.06 (s, NH); 9.09, 8.31 and 7.92 (d, dd and d, ABC of C_6H_3), 6.95 - 7.73 (2 AA'BB', 2 C_6H_4), 4.00 and 3.72 (2 s, 2 OCH_3), 4.51 (m, 5-H). ^{13}C NMR ($CDCl_3$) δ 162.3 and 161.7 (2 s, 2 CO), 152.2 (d, CH=N), 141.2 (s, C-3), 107.1 (s, C-4), 73.8 (d, C-5), 53.9 and 52.2 (2 q, 2 OCH_3).



12

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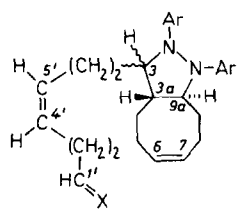
14



15 X = O

16 X = N-N-$C_6H_3(NO_2)_2$ (H)

Ar = C_6H_4CN-(4)

The higher dipolarophilic activity of (*E*,*Z*)-cycloocta-1,5-diene (12) compared with 2 is revealed by the lower temperature for the reaction with 1 as well as by the exclusive formation of the 1:2 product 15. Enehydrazine formation from the intermediate azomethine imine 14 is suppressed in favor of the interception by a second molecule of 12 even under the conditions which provi-

ded 81% of 7 from 2.

The mixture of 2.0 mmol 1 and 4.2 mmol 12 in 5 ml dry THF was stirred 1 d at 45°C under nitrogen. TLC (SiO_2, hexane/acetone 2:1) provided the resinous bisadduct 15 (R_F 0.40, 85% yield) [5] which consists of a 76:24 mixture of diastereomers I and II. ^{1}H-NMR ($CDCl_3$, 100 MHz) δ 9.71 and 9.64 (2 t, $J_{1',2'}$ = 1.3 Hz, 1'-H of I and II, 76:24), 3.81 and 3.31 (2 m, 3-H and 9a-H); irradiation at δ 2.5 (CH_2 region) permitted the analysis of the vinyl-H: 5.82 and 5.75 (AB, J = 10.2 Hz, 6-H and 7-H for both diastereomers), 5.55 (s, A_2, 4'-H + 5'-H of I), 5.46 (s, A_2, 4'-H and 5'-H of II). IR ($CHCl_3$) 2220 (C≡N), 1725 cm^{-1} (C=O). MS (70 eV, 220°C) m/e 464 (M^+, 90%), 436 (M^+- CO, 10%), 353 (M^+- $C_6H_{10}CHO$, 100%), 271 ($C_{17}H_{11}N_4^+$, 13, 15%). The conversion to 16 (82% yield after TLC, orange resin) contributed to the chemical characterization of the aldehyde 15.

The trans fusion of 5- and 8-membered ring in 8 and 15 was not experimentally established, but rests on the analogy with the retention of dipolarophile configuration in various 1,3-dipolar cycloadditions of 2.[7]

Corresponding 1:2 adducts of 4,4'-dinitroazoxybenzene and benzo[c]cinnoline N-oxide with (*E*)-cyclooctene (yield 75%, 83%) and (*E*,*Z*)-cycloocta-1,5-diene (84%, 89%) were similarly prepared and structurally elucidated by their spectra.

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Dedicated to Leopold Horner on the Occasion of His Seventieth Birthday

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