

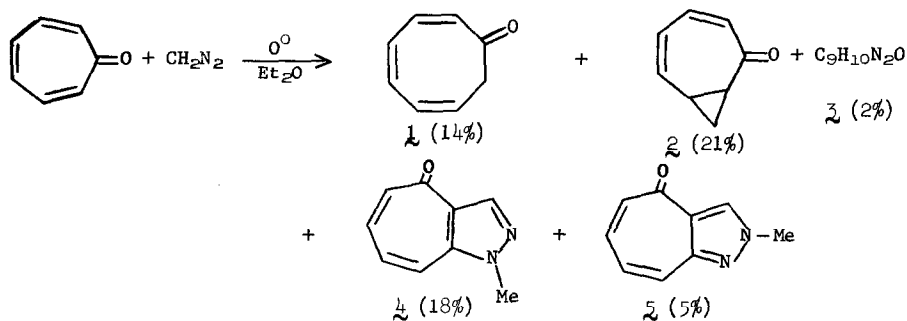
PYRAZOLOTROPONES FROM THE CYCLOADDITION OF DIAZOMETHANE TO TROPONE

L.J. Luskus and K.N. Houk<sup>1</sup>  
 Department of Chemistry, Louisiana State University  
 Baton Rouge, Louisiana 70803 U.S.A.

(Received in USA 12 December 1971; received in UK for publication 5 April 1972)

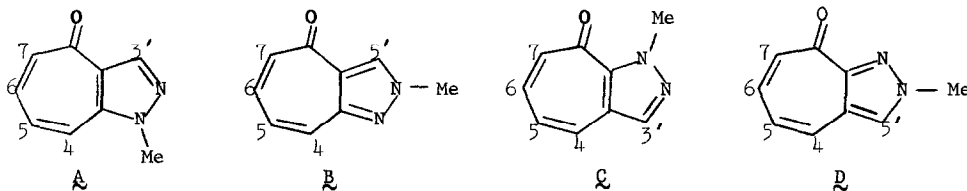
The reactions of diazoalkanes with tropone have been reported to produce 2,4,6-cyclooctatrienones as the only products.<sup>2</sup> However, in the course of our studies of periselectivity in 1,3-dipolar cycloadditions to trienes,<sup>3,4</sup> we have found that cyclooctatrienone is but one of many products formed upon reaction of diazomethane with tropone. In particular, 2,3-homotropone and pyrazolotropones are the major products of this reaction. Pyrazolotropones have been isolated previously from diazomethane additions to troponoids,<sup>5</sup> but our use of the Eu(dpm)<sub>3</sub> shift reagent has made possible proofs of two pyrazolotropone structures for the first time.

Tropone (10 mmoles) and diazomethane (from 14 mmole Diazald) were allowed to react at 0° in ether solution for 4 days. Thick layer chromatography gave products 1-5 in the approximate yields shown based on tropone.



2,4,6-Cyclooctatrienone, 1, had spectral properties identical to those of an authentic sample prepared by the method of Cope.<sup>6</sup> The ir, nmr, and mass spectra of 2 were the same as those reported for 2,3-homotropone<sup>7</sup> and differed significantly from those reported for 4,5-homotropone.<sup>8</sup> Although the molecular formula of 3 has been obtained from spectral data, the structure of 3 has not been determined.

The structures of the N-methyl pyrazolotropones were determined from spectral data. The major pyrazolotropone,  $\underline{4}$ ,<sup>9</sup> mp. 137.5° had a typical troponeid carbonyl stretch at 6.24 $\mu$  in the ir. Catalytic hydrogenation (5% Pd/C, 1 atm.) gave a tetrahydro-derivative with a carbonyl stretch at 6.01 $\mu$ , establishing the location of the aromatic pyrazole ring  $\alpha,\beta$ - to the carbonyl. Similar results were obtained for  $\underline{5}$ . Structures A through D for  $\underline{4}$  and  $\underline{5}$  are compatible with this evidence. To distinguish between these structures, nmr spectra of  $\underline{4}$  and  $\underline{5}$  were recorded during incremental addition of Eu(dpm)<sub>3</sub>. Exemplary shifts are tabulated below.



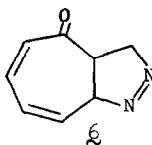
Chemical Shifts and Eu(dpm)<sub>3</sub> Induced Shifts

$\underline{4}$							$\underline{5}$				
H	3'	4	5	6	7	Me	H	5'	4,5,6	7	Me
$\delta$ (ppm)	7.90	~7.3	~6.2	~6.6	~6.7	3.33	$\delta$ (ppm)	8.23	7.1-7.4	7.1	4.09
$\Delta^{\text{Eu}}$ (Hz)	+ 61	~+23	~+24	~+24	+105	+ 12	$\Delta^{\text{Eu}}$ (Hz)	+ 52	~+11 to + 18	+69	+ 18

The assignment of protons 4-7 in  $\underline{4}$  could be made by analysis of the spectrum with Eu(dpm)<sub>3</sub> added. The observed coupling constants ( $J_{67} = 12.5\text{Hz}$ ,  $J_{56} = 8\text{Hz}$ ;  $J_{45} = 11\text{Hz}$ ) are nearly identical to those reported for tropone and simple derivatives.<sup>10</sup> In addition, the largest paramagnetic shift is observed for proton 7, establishing its location nearest the carbonyl group, the assumed site of complexation of the paramagnetic Europium ion (*vide infra*). The fact that the pyrazole proton displays the next largest shift indicates that  $\underline{4}$  must possess either structure  $\underline{A}$  or  $\underline{B}$ . Similar shifts indicate that  $\underline{5}$  must be either structure  $\underline{B}$  or  $\underline{A}$ . The shift in N-methyl resonances can be used to distinguish between these alternatives. Thus, the magnitude of the N-methyl hydrogen shift in structure  $\underline{A}$  should be smaller than the magnitude of the hydrogen 4-6 shifts, due to both the greater distance of the former protons from the complexed Eu and the greater O-Eu-H angle for the former protons.<sup>11,12</sup> In  $\underline{B}$ , the N-methyl protons are closer to Eu than hydrogens 4 and 5, but this proximity effect is damped by the much larger O-Eu-H angle. The observed relative shifts are compatible only with

structures  $\underline{A}$  and  $\underline{B}$  for  $\underline{4}$  and  $\underline{5}$ , respectively. Although aromatic nitrogen lone pairs can coordinate with  $\text{Eu}(\text{dpm})_3$ ,<sup>12</sup> the observed relative shifts are not compatible with any of the structures  $\underline{A-D}$  if the pyrazole N-2' lone pair coordinates with Eu. The preference for O coordination may be attributed to the unusually high basicity of troponoid carbonyl groups.<sup>10</sup> The inherent assumption that only pseudocontact shifts are important in these experiments is reinforced by the similarity of the couplings of the complexed  $\underline{4}$  and  $\underline{5}$  to those in uncomplexed troponone models.<sup>10</sup>

All the products  $\underline{4-5}$  could arise, in principle, from intermediate  $\underline{6}$ . The presence of  $\underline{4}$  and  $\underline{5}$  in our reactions and their absence in an earlier report<sup>2</sup> could be the result of adventitious base and/or  $\text{O}_2$  in our experiments which rapidly cause(s) rearrangement and oxidation of  $\underline{6}$ .



The regiochemistry of  $\underline{6}$  is the reverse of that commonly observed in the cycloadditions of diazoalkanes to  $\alpha,\beta$ -unsaturated carbonyls.<sup>13</sup> The differing regiochemistries are compatible with the differing relative magnitudes of the  $\alpha$  and  $\beta$  coefficients in the LUMOs of  $\alpha,\beta$ -unsaturated ketones and troponone, implying that the regiochemistry of addition is determined by the HOMO of diazomethane and LUMO of the dipolarophile.<sup>14</sup>

Nozoe and Itô et.al. have isolated pyrazolotropones analogous to  $\underline{6}$  and  $\underline{7}$  from the reaction of diazomethane with halotropones.<sup>5</sup> In light of the appearance of the N-methyl resonance at  $\sim 4.5\delta$  in these adducts, the original structural assignments are probably correct, indicating that  $\beta$ -halogens may reverse the cycloaddition regiochemistry.

Acknowledgement is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this research.

1. Author to whom correspondence should be addressed.
2. M. Franck-Neumann, Tetrahedron Lett., 2143 (1970).
3. K.N. Houk and C.R. Watts, ibid., 4025 (1970).
4. K.N. Houk and L.J. Luskus, ibid., 4029 (1970).

5. T. Nozoe, unpublished results; S. Itô, K. Takase, N. Kawabe, and H. Sugiyama, Bull. Chem. Soc. Japan, 39, 253 (1966); T. Nozoe, T. Asao, E. Takahashi, and K. Takahashi, ibid., 39, 1310 (1966). Synthesis of the isomeric 4,5-c(d)-pyrazolotropone has recently been reported: C.V. Greco and M. Pesce, J. Org. Chem., 37, 676 (1972).
6. A.C. Cope and B.D. Tiffany, J. Amer. Chem. Soc., 73, 4158 (1951); C. Ganter, S.M. Pokras, and J.D. Roberts, ibid., 88, 4235 (1966).
7. J.D. Holmes and R. Pettit, ibid., 85, 2531 (1963); L.A. Paquette and O. Cox, ibid., 89, 5634 (1967).
8. O.L. Chapman and R.A. Fugiel, ibid., 91, 215 (1969).
9. Anal., Calcd. for  $C_9H_6N_2O$ : C, 67.48; H, 5.03; N, 17.49; Fnd.: C, 67.36; H, 4.97; N, 17.45,  $\lambda_{EtOH}^{233}$  ( $\epsilon = 2.0 \times 10^4$ ), sh 240 ( $\epsilon = 1.8 \times 10^4$ ), sh 248 ( $\epsilon = 1.1 \times 10^4$ ), 273  $\lambda_{Max}$  ( $\epsilon = 3.8 \times 10^3$ ), 286 ( $\epsilon = 3.4 \times 10^3$ ), 355 ( $\epsilon = 6.2 \times 10^3$ ).  $\zeta$  Was not obtained entirely free of  $\zeta$  in sufficient amounts for elemental analysis.
10. D.J. Bertelli, T.A. Andrews, Jr. and P.O. Crews, J. Amer. Chem. Soc., 91, 5286 (1969).
11. H.H. McConnell and R.E. Robertson, J. Chem. Phys., 29, 1361 (1958).
12. J.K.M. Sanders and D.H. Williams, J. Amer. Chem. Soc., 93, 641 (1971).
13. G.W. Cowell and A. Ledwith, Quart. Rev., 24, 119 (1970).
14. Hückel MO coefficients ( $\alpha_o = \alpha_c + \beta_{cc}$ ) of the LUMOs (acrolein<sup>15</sup>:  $C_\alpha = -.23$ ,  $C_\beta = +.66$ ; tropone<sup>16</sup>:  $C_\alpha = .52$ ,  $C_\beta = -.23$ ) exaggerate the differences, but these trends are retained in SCF calculations; K.N. Houk, unpublished results.
15. C.A. Coulson and A. Streitwieser, Jr., "Dictionary of  $\pi$  Electron Calculations," W.H. Freeman, San Francisco, 1965, p. 227.
16. L. Salem, J. Amer. Chem. Soc., 90, 553 (1968).