Anal. Calcd for $C_{41}H_{45}NO_7S$: C, 70.77; H, 6.52; N, 2.01. Found: C, 70.89; H, 6.44; N, 1.97.

Thiazole D-*galacto*-D-*glycero*-hepto-1,5-pyranose **9c**: mp 98–100 °C (*n*-hexane–dichloromethane); ^{1}H NMR ($CDCl_3$–D_2O) δ 1.31 (s, 3 H), 1.38 (s, 3 H), 1.5 (s, 3 H), 1.53 (s, 3 H), 4.1–4.75 (m, 4 H), 5.36 (d, 1 H, J = 5.0 Hz), 5.61 (d, 1 H, J = 4.8 Hz), 7.36 (d, 1 H, J = 3.2 Hz), 7.81 (d, 1 H, J = 3.2 Hz).

Anal. Calcd for $C_{15}H_{21}NO_6S$: C, 52.47; H, 6.17; N, 4.08. Found: C, 52.44; H, 6.20; N, 4.05.

Thiazole L-*ido*-1,4-furanose **10c**: oil; ^{1}H NMR ($CDCl_3$–D_2O) δ 1.32 (s, 3 H), 1.45 (s, 3 H), 4.13–4.76 (m, 5 H), 5.32 (d, 1 H, J = 4.4 Hz), 5.96 (d, 1 H, J = 3.4 Hz), 7.22 (m, 6 H), 7.67 (d, 1 H, J = 3.2 Hz).

Anal. Calcd for $C_{18}H_{21}NO_5S$: C, 59.49; H, 5.83; N, 3.86. Found: C, 59.58; H, 5.76; N, 3.81.

Thiazole D-*gluco*-L-*glycero*-1,4-furanose **11c**:[2] syrup; ^{1}H NMR ($CDCl_3$–D_2O) δ 1.32 (s, 3 H), 1.48 (s, 3 H), 3.97–4.76 (m, 8 H), 5.32 (d, 1 H, J = 1.1 Hz), 5.96 (d, 1 H, J = 3.7 Hz), 7.26 (m, 11 H), 7.78 (d, 1 H, J = 3.2 Hz).

Anal. Calcd for $C_{26}H_{29}NO_6S$: C, 64.58; H, 6.05; N, 2.90. Found: C, 64.49; H, 6.11; N, 2.85.

Acknowledgment. Financial support by CNR (Rome) is greatly appreciated.

Supplementary Material Available: Crystal data, tables of bond distances, positional parameters, and bond angles, and an ORTEP drawing of **5c** (8 pages). Ordering information is given on any current masthead page.

Electron-Deficient Isoxazoles: 1,3-Dipolar Cycloadditions of Ethyl 4-Nitro-3-phenylisoxazole-5-carboxylate with Diazoalkanes[1]

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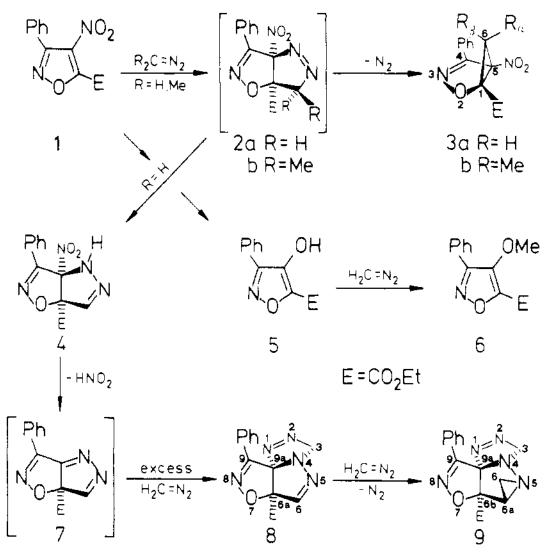
In an earlier note we reported that ethyl 4-nitro-3-phenylisoxazole-5-carboxylate (**1**) reacts with diazoalkanes as dipolarophile to give adducts that lose nitrogen, leading to the 2-oxa-3-azabicyclo[3.1.0]hex-3-enes **3**.[1] Both nitro and ester groups are required for the cycloaddition. We have now found that the reaction of **1** with excess diazomethane gives rise to the unusual tricyclic and tetracyclic products **8** and **9** (Scheme I).

Results and Discussion

When the nitro ester **1** was allowed to react with diazomethane, the reaction course strongly depended on the relative proportions of the two reagents; thus, in the presence of an equimolecular amount of the dipole, a partial conversion of **1** was achieved, affording the bicyclic derivatives **3a** and **4** as the largely predominant reaction products.

Scheme I



The structure of **3a**, isolated by flash chromatography, followed from analytical and spectral evidence. In particular, the cyclopropane moiety was recognized by an IR absorption at 3115 cm^{-1} for the methylene at position 6; on the other hand, the ^{1}H NMR spectrum characteristically displayed an AX system at δ 1.60 and 3.33, attributable to the strongly diastereotopic protons of the same group, which, in turn, gave rise to a doublet of doublets at δ 19.8 in the proton-coupled ^{13}C NMR pattern.

Although repeated efforts to isolate ethyl (3a*R**,6a*S**)-3a,6a-dihydro-3a-nitro-3-phenyl-4*H*-pyrazolo[3,4-*d*]isoxazole-6a-carboxylate (**4**) were completely unsuccessful, its presence in the original reaction mixture was firmly established spectroscopically: careful comparison of the rapidly taken spectra of the crude product with those of compounds **1** and **3a** enabled us to detect all the most diagnostic signals of **4**.

Among these, an IR absorption was observed at 3380 cm^{-1} for the NH group, which gave rise to an exchangeable peak at δ 7.90 in the ^{1}H NMR spectrum; on the other hand, the latter was also characterized by a singlet at δ 6.99 for the H-6 proton, whereas the off-resonance ^{13}C pattern clearly showed, besides a doublet at δ 139.0 (CH), four singlets at δ 161.8, 152.2, 117.0, and 104.0 for the CO, C-3, C-3a, and C-6a carbons, respectively. Furthermore, on the basis of the relative intensities of the proton singlets of **4** with respect to those of the doublets at higher field of **3a**, it could be easily ascertained that the crude product contained nearly equimolecular quantities of these compounds.

After chromatographic workup, we isolated a small amount of the isoxazole derivative **5**, at first absent in the reaction mixture; the structure of this compound, which probably arises from the unreacted **1** through an acid-catalyzed Michael addition of water to the C(4)–C(5) double bond of the latter, followed by elimination of nitrous acid, was determined by spectral data and conversion into the corresponding methoxy derivative **6** with diazomethane.

Failure to isolate **4** can be imputed to its tendency to lose nitrous acid, affording the isopyrazole system **7**, which is unstable, probably due to the presence of a strained exocyclic C=N double bond. This explanation was strongly supported by the behavior of **1** with an excess (molar ratio 1:3) of diazomethane: under these conditions,

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[1] For a preliminary communication on a part of this work, see: Nesi, R.; Giomi, D.; Quartara, L.; Bracci, S.; Papaleo, S. *J. Chem. Soc., Chem. Commun.* **1987**, 1077.

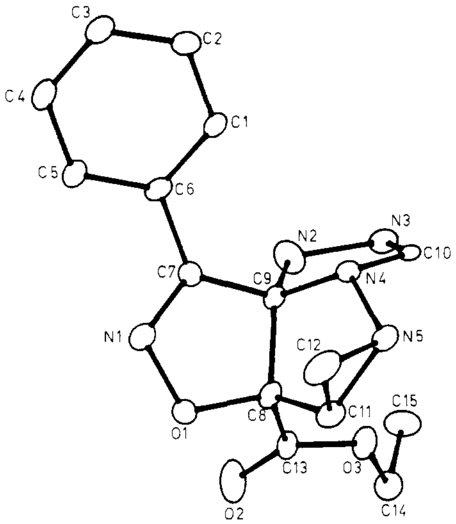

Figure 1. A computer-generated drawing of **9** derived from the X-ray coordinates with hydrogens omitted for clarity.

the starting material was completely consumed, but compound **4** was absent in the crude product, which now contained, besides a very small amount of **9**, compounds **3a** and **8** as the predominant components (^{1}H NMR). The last derivative was also detected to a small extent in the reaction of **1** with 1 equiv of the dipole (Experimental Section). Further increases of the dipolar agent (molar ratio 1:5) sensibly favored the tetracyclic system **9** with respect to **8**, and these compounds were isolated together with **3a**, in 11%, 27%, and 25% yields, respectively.

These findings can again be rationalized, starting from the key intermediate **4**: as noted above, this compound gives rise easily to elimination of nitrous acid, but the resulting unstable **7** can now be trapped by the excess diazomethane with formation of **8** through a regio- and diastereoselective cycloaddition on the exocyclic C=N double bond. Further reaction of the same reagent on the Δ^2-pyrazoline moiety of **8** finally affords **9** with concomitant loss of nitrogen.

The spectral data of the polycyclic compounds **8** and **9** (Experimental Section) were in agreement with the assigned structures.

The relative stereochemistry of **9**, presented in Figure 1, was elucidated by an X-ray structure determination.[2] This result, of course, allowed us to establish unambiguously the configuration of the direct precursor **8** and to confirm the regiochemistry of the above compounds. Likewise, it demonstrated that, according to the behavior of other nitroheterocycles[3] and variously substituted nitroalkenes[4] with the same diazoalkanes, the NO_2 group at position 4 exerts a complete regiochemical control in the primary cycloaddition process of the dipole on the activated C(4)–C(5) isoxazole double bond. It is noteworthy that the reaction of **7** with diazomethane, affording selectively the 1,2,4-triazole derivative **8**, exhibits an *anomalous* regiochemistry,[5] probably due to the peculiar nature of the isopyrazole C(3a)–N(4) double bond.

In summary, this study shows a new feature of the isoxazole chemistry that can be of interest from a mechanistic viewpoint and for synthetic purposes; particularly, although a few 2-oxa-3-azabicyclo[3.1.0]hex-3-enes have easily been obtained by other strategies,[6,7] the reaction of **1** with the above diazoalkanes represents a valuable entry into the first 1,5-difunctionalized derivatives of this attractive bicyclic ring system.

Experimental Section

Melting points were taken on a Büchi 510 apparatus and are uncorrected. Except where otherwise indicated, infrared spectra were measured for dispersions in KBr with a Perkin-Elmer 283 spectrometer, while ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solutions on a Perkin-Elmer R32 (90 MHz) and a Varian FT-80A (20 MHz) instrument, respectively. Silica gel plates (Merck F_{254}) and silica gel 60 (Merck; 230–400 mesh) were used for analytical and flash chromatographies, respectively. Ethereal solutions of diazomethane (ca. 0.5 M) and 2-diazopropane (ca. 2 M), freshly prepared by known procedures from *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide[8] and acetone hydrazone,[9] respectively, were employed.

Reactions of the Nitro Ester 1 with Diazomethane. Preparation of Compounds 3a, 5, 8, and 9. A. Ethereal diazomethane (4 mL, 2 mmol) was added to a solution of **1**[10] (0.524 g, 2 mmol) in the same solvent (20 mL), and the mixture was set aside overnight at room temperature. Removal of the solvent left a gummy orange residue (0.57 g), which was subjected to flash chromatography with 40–70 °C petroleum ether/ethyl acetate (5:1 v/v) as eluent. The first fraction gave the unreacted **1** (0.214 g), whereas the second one afforded ethyl 5-nitro-4-phenyl-2-oxa-3-azabicyclo[3.1.0]hex-3-ene-1-carboxylate (**3a**) as a pale yellow solid (0.132 g, 40% yield based on the recovered **1**) that was crystallized from petroleum ether as colorless needles: mp 74–75 °C; IR 3115 (cyclopropane CH_2), 1735 (CO), 1545, and 1370 cm^{-1} (NO_2); ^{1}H NMR δ 1.32 (t, J = 7 Hz, 3 H, OCH_2CH_3), 1.60 (d, J = 7.5 Hz, 1 H, Hβ-6), 3.33 (d, J = 7.5 Hz, 1 H, Hα-6), 4.35 (q, J = 7 Hz, 2 H, OCH_2CH_3), 7.40–7.78 (m, 5 H, Ph); ^{13}C NMR [CD_2Cl_2 + Cr (acac)$_3$] δ 13.75 (q, OCH_2CH_3), 19.8 (dd, C-6), 63.5 (t, OCH_2CH_3), 76.9 (s, C-1), 78.8 (s br s, C-5), 125.7 (s), 127.0 (d), 129.4 (d), 131.9 (d) (Ph), 156.6 (s, C-4), 162.3 (s, CO). Anal. Calcd for $C_{13}H_{12}N_2O_5$: C, 56.52; H, 4.38; N, 10.14. Found: C, 56.47; H, 4.31; N, 9.86.

After a slower small fraction (ca. 0.05 g), containing **8** as the predominant product (^{1}H NMR), was separated, the column was eluted with ether (2 × 150 mL) and the combined solutions were evaporated to dryness; the semisolid residue was mixed with sand and sublimed at 50 °C (10^{-2} Torr) to give ethyl 4-hydroxy-3-phenylisoxazole-5-carboxylate (**5**) (0.05 g, 18% yield based on the recovered **1**) as an ivory-colored solid: mp 101.5–102.5 °C (from ether); IR (CCl_4) 3390 (br, OH) and 1690 cm^{-1} (CO); ^{1}H NMR δ 1.46 (t, J = 7 Hz, 3 H, OCH_2CH_3), 4.51 (q, J = 7 Hz, 2 H, OCH_2CH_3), 7.40–7.60 (m, 4 H, Ar H_3 and OH), 8.0–8.15 (m, 2 H, Ar H_2); ^{13}C NMR δ 13.95 (q, OCH_2CH_3), 62.0 (t, OCH_2CH_3), 126.9 (s and d), 128.6 (d), 130.1 (d) (Ph), 140.8 (s, C-4/C-5), 145.2 (s, C-5/C-4), 153.5 (s, C-3), 159.5 (s, CO). Anal. Calcd for $C_{12}H_{11}NO_4$: C, 61.80;, H, 4.75; N, 6.01. Found: C, 62.02; H, 4.76; N, 6.27.

B. Treatment of **1** (0.524 g, 2 mmol) with an excess of diazomethane (10 mmol) in ether (40 mL) under the same conditions gave a crude product (ca. 0.6 g), which was resolved into three components by flash chromatography with 40–70 °C petroleum ether/ethyl acetate (3:1 v/v) as eluent. After the fastest running fractions, containing small amounts of sticky products, were discarded, the first band afforded the bicyclic derivative **3a** (0.138 g, 25%), identical (IR and ^{1}H NMR) with the material obtained as above. The second one yielded ethyl (6a*R**,9a*S**)-9-phenyl-

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[2] Attempts to obtain crystals of 8 suitable for an X-ray analysis failed.

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3H,6aH-isoxazolo[4′,5′:3,4]pyrazolo[3,2-c]-1,2,4-triazole-6a-carboxylate (**8**) (0.16 g, 27%) that was crystallized from ether as colorless needles: mp 107–108 °C dec (with foaming); IR 1730 cm^{-1} (CO); ^{1}H NMR δ 1.35 (t, J = 7 Hz, 3 H, OCH$_2$CH_3), 4.36 (q, J = 7 Hz, 2 H, OCH_2CH$_3$), 4.74 (AB system, J_{AB} = 19 Hz, 2 H, 3-CH$_2$), 7.30 (s, 1 H, H-6), 7.51 (br s, 5 H, Ph); ^{13}C NMR δ 13.9 (q, OCH$_2$CH$_3$), 63.6 (t, OCH$_2$CH$_3$), 71.9 (t, C-3), 83.6 (s, C-6a), 100.9 (s, C-9a), 125.3 (s), 127.2 (d), 129.2 (d), 131.3 (d) (Ph), 145.8 (d, C-6), 154.2 (s, C-9), 164.1 (s, CO). Anal. Calcd for $C_{14}H_{13}N_5O_3$: C, 56.18; H, 4.38; N, 23.40. Found: C, 56.07; H, 4.48; N, 23.09.

Finally, the slowest running band gave ethyl (6aR*,6bS*,9aR*)-6a,6b-dihydro-9-phenyl-3H,6H-azirino-[1′,2′:2,3]isoxazolo[4′,5′:3,4]pyrazolo[3,2-c]-1,2,4-triazole-6b-carboxylate (**9**) (0.069 g, 11%) as a colorless crystalline solid: mp 117–118 °C dec (with foaming) (from ether); IR 1747 cm^{-1} (CO); ^{1}H NMR δ 1.34 (t, J = 7 Hz, 3 H, OCH$_2$CH_3), 2.0–2.30 (m, 2 H, 6-CH$_2$), 3.40 (dd, J = 4.4 and 6.4 Hz, 1 H, H-6a), 4.37 (q, J = 7 Hz, 2 H, OCH_2CH$_3$), 4.61 (s br s, 2 H, 3-CH$_2$), 7.40–7.75 (m, 5 H, Ph); ^{13}C NMR δ 13.8 (q, OCH$_2$CH$_3$), 29.8 (dd, C-6), 46.5 (d, C-6a), 63.1 (t, OCH$_2$CH$_3$), 74.9 (t, C-3), 90.0 (s, C-6b/C-9a), 97.0 (s, C-9a/C-6b), 125.5 (s), 127.1 (d), 129.1 (d), 131.1 (d) (Ph), 155.1 (s, C-9), 166.4 (s, CO). Anal. Calcd for $C_{15}H_{15}N_5O_3$: C, 57.50; H, 4.83; N, 22.35. Found: C, 57.38; H, 4.62; N, 22.58.

X-ray Crystal Structure Determination for 9. Crystals **9** were grown from 75–120 °C ligroin/ethyl acetate (1:1 v/v). Data were collected at room temperature on an Enraf-Nonius CAD4 diffractometer. No loss of intensity of three standard reflections was observed. Computer programs were those of SHELX76. Absorption corrections were not applied. Crystal data: orthorhombic; space group $Pcab$, determined by the conditions $hk0$, $k = 2n$, $h0l$, $h = 2n$, $0kl$, $l = 2n$; M = 313.31; a = 7.982 (1) Å, b = 10.605 (4) Å, c = 34.351 (4) Å; cell vol = 2907.9 (7) Å^3; Z = 8; d = 1.43 g cm^{-3}; abs coeff μ = 7.66 cm^{-1}; Cu Kα radiation (λ = 1.5418 Å), graphite monochromator. Intensity data were collected to $2\theta_{\max}$ of 100° in the octant $+h,+k,+l$ by using a $\omega - 2\theta$ scan of (0.70 + 0.14 tg ω)° width, with a rate scan of 0.07°/s. A total of 1571 unique reflections were collected of which 449 were suppressed as unobserved ($I < 3\sigma(I)$), leaving 1122 for solution and refinement of the structure. The structure was solved by direct methods. The hydrogen atoms were introduced in calculated positions, with an overall isotropic temperature factor U of 0.05. Anisotropic temperature parameters were assigned to the other atoms. The final difference map showed no significant features. A weighting scheme of $w = 1/\sigma^2(F)$ was used. Final agreement factors were R = 0.079 and R_w = 0.071 (209 parameters).

Ethyl 6,6-Dimethyl-5-nitro-4-phenyl-2-oxa-3-azabicyclo-[3.1.0]hex-3-ene-1-carboxylate (3b). Compound **1** (0.262 g, 1 mmol) was allowed to react with an excess of 2-diazopropane (2 mmol) in ether (10 mL) at room temperature for 4 h; after a further amount of the same reagent (1 mmol) was added, the reaction mixture was set aside overnight. Removal of the solvent left a semisolid residue largely consisting (^{1}H and ^{13}C NMR) of the dimethyl derivative **3b**, which was obtained as a pure product (0.222 g, 73%) by flash chromatography with toluene as eluent: white crystals; mp 84–85 °C (from petroleum ether/ether); IR 1730 (CO), 1552, and 1350 cm^{-1} (NO$_2$); ^{1}H NMR δ 1.14 (s, 3 H, 6-βCH$_3$), 1.32 (t, J = 7 Hz, 3 H, OCH$_2$CH_3), 1.81 (s, 3 H, 6-αCH$_3$), 4.34 (q, J = 7 Hz, 2 H, OCH_2CH$_3$), 7.40–7.73 (m, 5 H, Ph); ^{13}C NMR δ 13.7 (q, OCH$_2$CH$_3$), 15.7 (q, 6-CH$_3$), 16.0 (q, 6-CH$_3$), 29.4 (s, C-6), 62.7 (t, OCH$_2$CH$_3$), 82.9 (s, C-1), 86.2 (s br s, C-5), 125.8 (s), 126.75 (d), 129.1 (d), 131.5 (d) (Ph), 154.9 (s, C-4), 162.4 (s, CO). Anal. Calcd for $C_{15}H_{16}N_2O_5$: C, 59.21; H, 5.30; N, 9.21. Found: C, 59.01; H, 5.40; N, 9.10.

Ethyl 4-Methoxy-3-phenylisoxazole-5-carboxylate (6). Treatment of the hydroxy ester **5** (0.047 g, 0.2 mmol) with diazomethane (0.5 mmol) in ether (10 mL) at room temperature gave, after the usual workup, compound **6** (0.049 g, quantitative yield) as a pale yellow oil that solidified by prolonged cooling; an analytical sample was obtained as white crystals by sublimation at 35–40 °C (10^{-2} Torr): mp 56.5–58 °C; IR 1730 cm^{-1} (CO); ^{1}H NMR δ 1.45 (t, J = 7 Hz, 3 H, OCH$_2$CH_3), 4.08 (s, 3 H, OCH$_3$), 4.49 (q, J = 7 Hz, 2 H, OCH_2CH$_3$), 7.45–7.60 (m, 3 H, Ar H$_3$), 7.95–8.10 (m, 2 H, Ar H$_2$); ^{13}C NMR δ 14.0 (q, OCH$_2$CH$_3$), 61.8 (t, OCH$_2$CH$_3$), 62.65 (q, OCH$_3$), 127.3 (s and d), 128.7 (d), 130.2 (d) (Ph), 144.9 (s, C-4/C-5), 146.6 (s, C-5/C-4), 156.7 (s, C-3/CO), 156.9 (s, CO/C-3). Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.66. Found: C, 63.07; H, 5.17; N, 5.55.

Acknowledgment. We wish to thank Brunella Innocenti for the analytical data.

Registry No. **1a**, 99934-18-6; **3a**, 117607-35-9; **3b**, 117607-34-8; **4**, 117607-36-0; **5**, 117607-37-1; **6**, 117607-38-2; **8**, 117607-39-3; **9**, 117607-40-6.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond lengths, and bond angles for **9** (4 pages). Ordering information is given on any current masthead page.

On the Photochemistry of Tropone in Acidic Media

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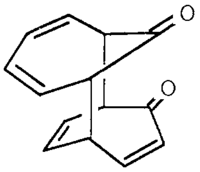
Received August 23, 1988

Substituted tropones normally isomerize to bicyclo[3.2.0]heptadienones upon irradiation.[3] In contrast, tropone itself has been reported to undergo dimerization when irradiated in either organic or aqueous solution. Kende has reported that irradiation of tropone in acetonitrile produces dimers **1–3**, with the stereochemistry of **2** and **3** unspecified.[4] Mukai et al. obtained **1** and **3** upon irradiation in ether and determined the stereochemistry of **3** to be trans, as shown.[5] On the other hand, the same authors found that in aqueous solution dimer **4** was obtained to the exclusion of the other three dimers;[6] they obtained a "low yield" in neutral water and a 7.5% yield in 10% sulfuric acid.



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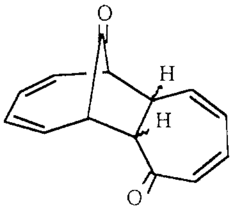

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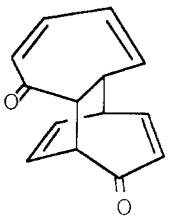

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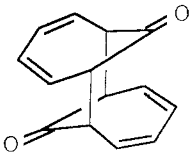

4

For several years we have been trying to prepare **4** for synthetic purposes. In the process we have accumulated a good deal of data concerning the photochemistry of tropone in various acidic media, and we report our observations herein.

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