3*H*,6a*H*-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, $\mathrm{OCH_2C}H_3$), 4.36 (q, J = 7 Hz, 2 H, $\mathrm{OC}H_2\mathrm{CH_3}$), 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-3*H*,6*H*-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, $\mathrm{OCH_2C}H_3$), 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, $\mathrm{OC}H_2\mathrm{CH_3}$), 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, $\mathrm{OCH_2C}H_3$), 1.81 (s, 3 H, 6-αCH$_3$), 4.34 (q, J = 7 Hz, 2 H, $\mathrm{OC}H_2\mathrm{CH_3}$), 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, $\mathrm{OCH_2C}H_3$), 4.08 (s, 3 H, OCH$_3$), 4.49 (q, J = 7 Hz, 2 H, $\mathrm{OC}H_2\mathrm{CH_3}$), 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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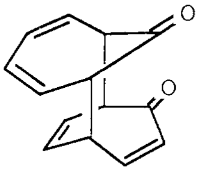
Received August 23, 1988

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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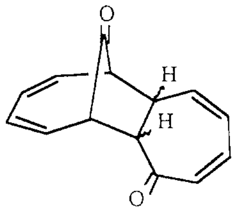

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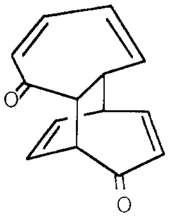

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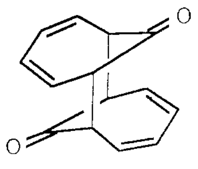

4

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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[1] Current address: Department of Chemistry, Juniata College, Huntingdon, PA 16652.

[2] Middlebury College, Middlebury, VT 05753.

[3] Chapman, O. L. *Adv. Photochem.* **1963**, *1*, 323.

[4] Kende, A. S. *J. Am. Chem. Soc.* **1966**, *88*, 5026.

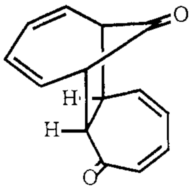
[5] Tezuka, T.; Akasaki, Y.; Mukai, T. *Tetrahedron Lett.* **1967**, 1397.

[6] Mukai, T.; Tezuka, T.; Akasaki, Y. *J. Am. Chem. Soc.* **1966**, *88*, 5025.

0022-3263/89/1954-0708$01.50/0 © 1989 American Chemical Society

When tropone[7] was irradiated in 10% sulfuric acid in an immersion well for 6 days, according to Mukai et al.,[5] a mere 1–2% yield of 4 was obtained, along with large quantities of polymer, making isolation of the product extremely time-consuming. We have now succeeded in improving the efficiency of this process. The important changes in conditions were the use of an Ace "thin-film reactor"[8] in conjunction with a phase-transfer method, wherein a constant extraction through dichloromethane was performed in an external reservoir and an aqueous layer (20% sulfuric acid) pumped through the apparatus. In this way acceptable yields of 4–6% of 4 were obtained. Significantly, these yields could be obtained with only 2–3 days of irradiation, and a single passage through silica gel cleanly separated the reaction products.

The identity of the reaction products proved quite interesting. In addition to **4**, two other dimers were obtained. These were shown to be **2** and **3**, never previously obtained in aqueous medium. Dimer **3**, obtained in about 17% yield, was identified by its melting point[4] and the similarity of its NMR spectrum to that published by Tezuka, Akasaki, and Mukai.[5] Dimer **2**, obtained in about 12% yield, was identified by melting point[4] and by detailed analysis of its 300-MHz NMR spectrum. In particular, J_{2-8} was determined to be 12.8 Hz, J_{1-2} was 4.9 Hz, and J_{8-9} was ~6 Hz. Kende had already shown that the cis-exo structure **2a** was unlikely, based on chemical evidence;[3] of the remaining three stereochemistries, these coupling constants are best accommodated by trans structure **2b**. On the other hand, protons 10 and 13 have significantly different chemical shifts (5.6 vs 6.0 ppm), as would be expected if the cycloheptadienone ring were held beneath the C-10 to C-13 diene system as in **2c**. The nuclear Overhauser effect readily distinguished between these possibilities: presaturation of H-12 resulted in a small but significant enhancement at H-2, while presaturation of H-10 enhanced H-7. These results are accommodated only by structure **2b**; models show this far more clearly than the accompanying drawings.



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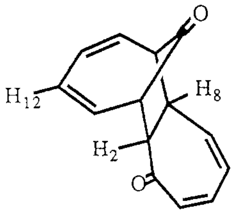

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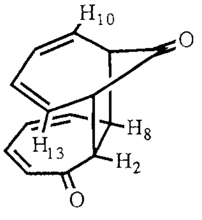
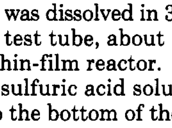


2c

In addition to these three dimers, another product was observed on a few occasions when the concentration of tropone was particularly low. This proved to be bicyclo[3.2.0]hepta-3,6-dien-2-one (**5**). Although Childs has shown that protonated **5** is one of the products when protonated tropone is irradiated in an NMR tube,[9] **5** has never previously been isolated as a product of tropone irradiation. While the yield of this product was quite low under these conditions, it was determined that when tropone is irradiated in acidic *organic* solutions, **5** can be the major isolated product if the solution is not too concentrated. The best results were obtained in trifluoroacetic acid: after a week of irradiation of 1 g of tropone in 35 mL of this acid, NMR analysis indicated that one-third of the tropone had been converted into **5**, with no other noticeable products being formed. Presumably longer irradiation would lead to highly efficient conversion. Previously **5** has been available only by a several-step sequence starting with norbornadienol.[10] The isolation of **5** brings tropone into line with its derivatives in that it isomerizes to the bicyclic structure photochemically.



5

Further investigations in nonaqueous acids led to another novel result. When the concentration of tropone was sufficiently high, (6 + 6) dimerization occurred. In 1:1 acetonitrile–methanesulfonic acid, dimer **4** was the only recognizable product. However, the yield was dismally low and the reaction mixture quite difficult to work with: after 5 days, 1 g of tropone in 7 mL of this solvent mixture produced only 1% of **4** plus 40–50% of recovered tropone. Better results were obtained with trifluoroacetic acid: 2 of tropone in 2 mL of trifluoroacetic acid gave 4% of **4** after 5 days of irradiation, with about 90% recovered tropone. Whether or not this solvent will replace aqueous acid as the medium of choice for the synthesis of the (6 + 6) dimer remains to be seen, but these results do represent the first time **4** has been produced in nonaqueous solution.

Experimental Section

Photolyses were done in a traditional immersion well, in an Ace thin-film reactor, or, on a small scale, in Pyrex collar designed to fit around the outside of a cooling jacket. All irradiations were done with a Hanovia 450-W lamp or a homemade lamp consisting of a mercury vapor street lamp with the outer glass casing cut away connected to a street lamp power supply. This gives virtually the same output as a Hanovia lamp.[11] Reactions were worked up by partition between chloroform and water, removal of the chloroform, and chromatography on silica gel using benzene–ethyl acetate mixtures. NMR spectra were acquired on a General Electric QE300 spectrometer.

Dimerization of Tropone. In a typical experiment, 10.0 g of tropone (0.094 mol) was dissolved in 30 mL of dichloromethane and placed in a large test tube, about 100 mL, which served as the reservoir for the thin-film reactor. The reactor was charged with 150 mL of 20% sulfuric acid solution, which was pumped through the reactor to the bottom of the reservoir, then from the top of the reservoir back through the reactor. The reservoir was immersed in an ice bath to minimize evaporation of the dichloromethane, and the mixture was irradiated for 3 days, with occasional replenishment of solvents as needed. The reactor was rinsed well with chloroform, the aqueous layer was extracted thoroughly with chloroform, and the organic layer was dried over magnesium sulfate and concentrated. The crude product was purified by flash chromatography on 500 mL of silica gel using 1 L each of 2%, 5%, 8%, and 25% ethyl acetate in benzene, to give 0.543 g (5.43%) of **4**, 1.181 g (11.81%) of **2**, 1.693 g (16.93%) of **3**, and 1.827 g (18.27%) of recovered tropone. After several

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(7) Reingold, I. D.; DiNardo, L. *J. Org. Chem.* **1982**, *47*, 3544.

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recrystallizations, the dimers had mp 216-8 °C (from ethyl acetate, lit.[6] mp 220 °C), 122-4 °C (from 2-propanol, lit.[4] mp 124-5 °C), and 115-7 °C (from 2-propanol, lit.[4] mp 118-9 °C), respectively.

Acknowledgment. This research was supported by a grant from the National Science Foundation under the Research in Undergraduate Institutions Program.

Registry No. 2, 118041-56-8; 3, 118101-04-5; 4, 14637-55-9; 5, 35826-08-5; tropone, 539-80-0.

Diels-Alder Reactions of Cycloalkenones. 16. Endo Diastereoselectivity of Some Cycloalkenones in Reactions with 1,3-Cyclohexadiene[1]

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Ferdinando Pizzo,[2a] Aldo Taticchi,*,[2a] and Ernest Wenkert*,[2b]

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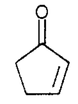
Received September 27, 1988

As part of a broad study of Diels-Alder reactions of 2-cycloalkenones the interaction of 2-cyclohexenones with cyclopentadiene was investigated recently.[3] Whereas this constituted the first use of a cyclic diene in the extended experimental series, the diene was a Diels-Alder substrate of high reactivity.[4] In order to complete the picture, a set of experiments involving a cyclic diene of low reactivity had to be executed. For this reason 1,3-cyclohexdiene (1)[4] was chosen as a Diels-Alder diene component and its cycloaddition with the following dienophiles pursued: 2-cyclopentenone (2), 2-cyclohexenone (3a), 4,4-dimethyl-2-cyclohexenone (3b), 5,5-dimethyl-2-cyclohexenone (3c), and 2-cycloheptenone (4).

1



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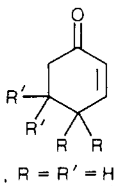
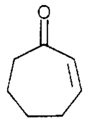


3a, R = R' = H
b, R = Me; R' = H
c, R = H; R' = Me



4

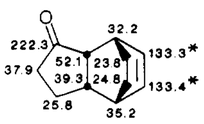
Diels-Alder Reaction Products

The cycloadditions were performed with various diene-dienophile combinations under aluminum trichloride catalysis in toluene solutions at 40 °C and led to 70-95% yields of adducts (Table I). The reactions were highly endo-diastereoselective. In view of the isolated material accounting for at least 97% of the product mixture, no more than 3% exo adducts may have been present. As in the earlier cyclopentadiene study[3] the Diels-Alder adducts were kinetically based, no exo-endo isomerization being observed throughout the course of the GC-monitored reactions nor such isomerization taking place on exposure of the pure adducts to the reaction conditions of the cycloadditions. Tricycles 5 and 6 were the products of the reactions of cyclopentenone (2) and the cyclohexenones 3, respectively. The 1-4 reaction led to a 1.2:1 mixture of tricyles 7 and 8, the primary product 7 having undergone acid-induced, α-keto bridgehead isomerization.

Table I. Reaction Conditions of the Diels-Alder Reactions of 1,3-Cyclohexadiene (1) and Cycloalkenones 2-4[a]

enone[b]	diene/ketone[c]	product yield,[d] %
2	12	85
3a	6	80
3b	6	70
3c	6	80
4[e]	12	95

[a] Complexation time,[11] 40 min; complexation temperature,[11] 22 °C; reaction time, 144 h; reaction temperature, 40 °C; $AlCl_3$/ketone equivalents ratio, 0.5. [b] Ketone concentration, 0.1 M. [c] Ratio of equivalents. [d] GC-based; >96% of the reaction products isolated. [e] Reaction time: 24 h.



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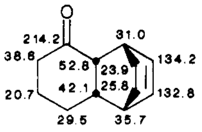

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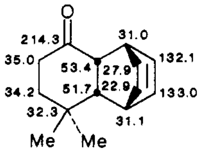

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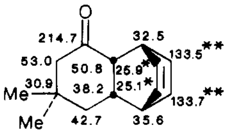

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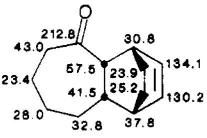

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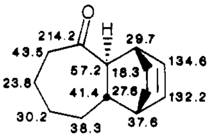

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The structures of the cycloadducts 5-8 were determined by ^1H and ^{13}C NMR specroscopy as well as by 2-D NMR (COSY and ^1H-^{13}C correlation) experiments. The ^1H shifts and coupling characteristics are listed in the Experimental Section and the ^{13}C shifts are depicted on the formulas 5-8. The stereochemistry assignment was aided greatly by NMR data on exo and endo adducts of cyclopentadiene and 2-cyclohexenones.[3]

The δ values of the hydrogens of the saturated two-carbon bridge of adducts 6 were diagnostic of the stereochemistry of these compounds. The hydrogens facing the olefinic π bond revealed a 1.29 ± 0.03 ppm shift, reminiscent of the 1.30 ± 0.06 ppm shift of the sterically identical hydrogen of the methylene bridge of the *exo*- and *endo*-3-cyclopentadiene adducts.[3] The chemical shift of the hydrogen of the one-carbon bridge of the cyclopentadiene adducts facing away from the olefinic π bond is stereochemistry-dependent, i.e., shielded (1.21 ± 0.04 ppm) in the exo compounds (presumably because of the anisotropy of the carbonyl group) and deshielded (1.45 ± 0.03 ppm) in the endo substances (because of the removal of the anisotropy of the carbon-carbon double bond). Adducts 6 show the hydrogens of the saturated two-carbon bridge facing away from the olefinic π bond to be deshielded (1.54 ± 0.07 ppm), in consonance with an endo adduct configuration. The latter conclusion is aided by the strong shift similarity of the vicinal hydrogens (the $\Delta\delta$ value averaging 0.05 ppm). Hydrogen shift comparison between adducts 6 and 5 and 7 indicate the latter two compounds to belong also to the endo series.

Comparison of the methylene carbon shifts (24-26 ppm) of the saturated two-carbon bridge of the Diels-Alder adducts 5, 6a, 6c, and 7 with those of bicyclo[2.2.2]octene models, i.e., *exo*- and *endo*-1-acrolein cycloaddition products (endo adduct equivalent $\delta(CH_2)$ = 25 ppm),[5]

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[1] For the previous paper, see: Angell, E. C.; Fringuelli, F.; Pizzo, F.; Minuti, L.; Taticchi, A.; Wenkert, E. *J. Org. Chem.*, in press.

[2] (a) University of California. (b) Università di Perugia.

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