Thermal Cycloaddition Reaction of Tropone to 1,1-Diethoxyethene. Structure Revision of Cantrell's Diels–Alder Adduct

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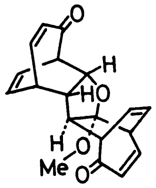
Synopsis. A reinvestigation of Cantrell's thermal cycloaddition of tropone to 1,1-diethoxyethene has led to the isolation of three products: [4+2], [6+2], and [8+2] cycloadducts. The structure of the [4+2] cycloadduct was revised on the basis of an NMR analysis of the hydrolyzed diketone, and newly identified was a superficial *anti*-Woodward-Hoffmann [6+2] cycloadduct. These adducts did not cause mutual isomerization by heating under formation conditions.

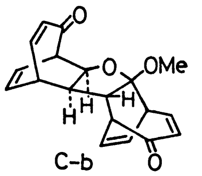
In connection to our continuing interest on the cycloadditions of tropones, we have recently carried out the reaction of tropone (**1**) with 2-methoxyfuran (**A**) to give 1 : 1- (**B**) and 2 : 1-cycloadducts (**C**), for which, the second step of the reaction should fall into a category of the cycloaddition of **1** to a 1,1-dialkoxyethene.[1)]

After analyzing the interconversions of these adducts, we noticed a different regioselectivity between the [4+2] cycloadducts found in the **C**-type products and the Cantrell's [4+2] cycloadduct **2a** prepared from **1** and 1,1-diethoxyethene (**3**).[2)] This superficial discrepancy prompted us to reinvestigate the Cantrell's experiment. The findings will be described herein.

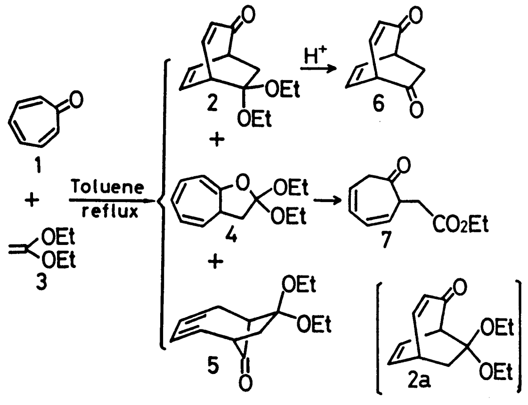
When a toluene solution of **1** and **3** was refluxed under a nitrogen atmosphere for 17 h, the formation of two products (**2** and **4**) was recognized as being consistent with Cantrell's result;[2)] they seemed to be identical with his [4+2] and [8+2] cycloadducts, respectively. Furthermore, the presence of a third cycloadduct (**5**) was recognized. However, when the reaction was carried out under aerial conditions at 90 °C, the mixture became dark-colored and showed an inferior material balance (Table 1).



C-a



C-b



Scheme 1.

Under 3000 bar, the yeilds of **2** and **4** showed considerable improvement (Table 2).

In view of the variable yields depending on the conditions, oxygen-susceptible **5** might be a non-electrocyclic, radical product. On the other hand, an increase in the yields of **2** and **4** by an increase in the pressure shows that **2** and **4** are electrocyclic, concerted reaction products.

The ^{1}H NMR spectrum of **2** disclosed four vinylic protons, as well as two signals due to ethoxyl groups, suggesting that it is the [4+2] cycloadduct. Therefore, the only point to be clarified was the regiochemistry: between two possibilities, Cantrell's proposal, **2a**, and the isomer, **2**. However, we could not discriminate one from the other, since its 100- and 270-MHz ^{1}H NMR spectra showed still overlapped bridge-head protons underneath the methylene signal. A mild hydrolysis of **2** by dil hydrochloric acid yielded a diketone **6**, whose ^{1}H NMR spectrum[3)] disclosed, together with four vinyl proton signals, well-separated methylene proton signals with a large vic-coupling (J=19 Hz), and doubly-allylic methine proton signal at δ=3.91. The spin-coupling pattern of this signal had only two large vic-couplings, J=9 and 7 Hz, indicating that the newly-generated carbonyl group is adjacent to the doubly allylic carbon. Thus, **6** is bicyclo[3.2.2]nona-3,8-diene-2,6-dione, and **2** is the corresponding diethyl acetal. The regiochemistry of **2** was in accord to our [4+2]-[4+2] cycloadducts (**C-a** and **C-b**), whose second step of formation could reasonably be explained in terms of a HOMO–LUMO interaction; however, it did

Table 1. The Cycloaddition of **1** to **2**

Condition	Yield/% of product [8+2]	[6+2]	[4+2]	Recovered **1**
90 °C, 48 h/sealed tube	9.2	0.7	1.9	38
110 °C, 17 h, N_2/reflux	47	5.2	15	9.2

Table 2. Change of Product Distributions and Pressure Effect

Condition	Yield/% [8+2]	[6+2]	[4+2]	Recovery **1**
120 °C, 10 h, 1 bar	9.1	3.1	1.1	70
120 °C, 10 h, 3000 bar	17	—	13	84

not follow Cantrell's formula **2a**. Although his structure argument seemed to depend on the ^{1}H NMR criteria, the disclosed evidence alone did not allow any conclusion to be drawn.

The **4** was quantitatively converted to the keto ester **7**, even in chloroform at 50 °C. The ^{1}H NMR spectrum of **4** was identical with the reported figures by Cantrell,[2)] and **4** is undoubtedly the [8+2] cycloadduct. The ^{13}C NMR spectrum of **4** disclosed a characteristic signal due to the ortho ester carbon at δ 124.6.

The structure of **5** was again elucidated by the NMR spectroscopy; its ^{1}H NMR revealed AA'BB'-type four vinylic proton signals and its IR showed a peak due to an unconjugated carbonyl stretching frequency at 1750 cm^{-1} and it is the [6+2] cycloadduct. Noteworthy was the occurrence of such a Woodward-Hoffmann-Rule-disallowed process.[4)] However, the [6+2] cycloadduct, **5**, might not be a secondary product since its formation could not be explained by symmetry-allowed sigmatropic reactions from **2** or **4**. This was verified when we carried out thermal isomerizations of the adducts; all the cycloadducts were surprisingly stable up to 130 °C, higher than the formation conditions, and recovered the starting materials quantitatively. Therefore, **5** must be formed directly from **1** and **3**.

Experimental

Thermal Cycloaddition of 1 to 3.[2)] a) An anhydrous toluene solution (4 cm^3) of **1** (97 mg) and **3** (1.0 g) was refluxed under an N_2 atmosphere for 17 h. After evaporation of the solvent in vacuo, the residue was chromatographed on a silica-gel column to give **4** [a yellow oil, 88 mg; 48%. Found: m/z 222.1257 (M$^+$).[5)] Calcd for $C_{13}H_{18}O_3$: M, 222.1255. ^{1}H NMR δ=1.21 (3H, t, J=7 Hz), 1.23 (3H, t, J=7 Hz), 2.23 (1H, dd, J=13, 6 Hz), 2.64 (1H, dd, J=13, 10 Hz), 2.8—2.9 (1H, m), 3.67 (2H, q, J=7 Hz), 3.68 (2H, q, J=7 Hz), 5.00 (1H, dd, J=10, 4 Hz), 5.68 (1H, d, J=6.5 Hz), 6.07 (1H, ddd, J=9.5, 6, 1.5 Hz), 6.22 (1H, dd, J=11, 6 Hz), and 6.37 (1H, dd, J=11, 6.5 Hz). ^{13}C NMR[6)] δ=15.2 (2C, q), 38.5 (d), 39.6 (t), 58.3 (t), 59.0 (t), 97.0 (s), 123.0 (d), 124.3 (d), 124.6 (d), 126.7 (d), 128.6 (d), and 150.7 (s). IR ν: 3000 and 1640 cm^{-1}], **2** [a yellow oil, 28 mg; 15%. Found: m/z 222.1256 (M$^+$). ^{1}H NMR δ=1.16 (6H, t, J=7 Hz), 2.16 (2H, overlapped s), 3.3—3.6 (6H, m), 5.79 (1H, dd, J=11, 2 Hz), 6.12 (1H, ddd, J=8.5, 7.5, 1.5 Hz), 6.44 (1H, ddd, J=8.5, 7.5, 1.5 Hz), and 6.88 (1H, dd, J=11, 9 Hz). ^{13}C NMR δ=15.2 (2C, q), 33.9 (t), 45.1 (d), 51.4 (d), 56.4 (t), 57.0 (t), 107.8 (s), 126.5 (d), 129.6 (d), 136.2 (d), 149.1 (d), and 197.2 (s). IR ν: 2980 and 1660 cm^{-1}], and **5** [a yellow oil, 10 mg; 5.4%. Found: m/z 222.1251 (M$^+$). ^{1}H NMR δ=1.14 (3H, t, J=7 Hz), 1.21 (3H, t, J=7 Hz), 2.49 (2H, d, J=6.5 Hz), 2.8—2.9 (1H, m), 3.19 (1H, d, J=7.5 Hz), 3.4—3.5 (4H, m), 5.37 (1H, dd, J=11.5, 7.5 Hz), 5.84 (1H, dd, J=10, 7.5 Hz), and 5.9—6.0 (2H, m). ^{13}C NMR δ=15.2 (2C, q), 40.3 (t), 46.4 (d), 56.8 (d), 58.8 (t), 59.6 (t), 112.5 (s), 123.3 (d), 125.5 (d), 125.9 (d), 129.8 (d), and 210.5 (s). IR ν: 3000 and 1750 cm^{-1}]. Recovery of **1** was only 9 mg (9.3%).

Thermal Cycloaddition of 1 to 3 under High-Pressure Conditions. A mixture of **1** (151 mg) and **3** (539 mg) in toluene (2 cm^3) was heated at 120 °C under 3000 bar for 10 h. The product distribution is compiled in Table 2. A careful inspection of every chromatographic fraction assured the absence of **5**.

Attempted Thermal Rearrangement of 2 and 4. Each toluene-d_8 solution (O_2 was carefully removed, 0.4 cm^3) of **2** (25 mg) and **4** (45 mg) was heated in a sealed glass tube at 130 °C for 6 to 7 h. Occasional NMR monitoring of the mixture indicated no occurrence of the reaction.

Hydrolysis of 2. A THF solution (10 cm^3) of **2** (40 mg) and conc HCl (0.5 cm^3) was refluxed for 10 min. The mixture was then diluted with water, and extracted with ether. Silica-gel column chromatography of the extract afforded **6** [a colorless oil, 17 mg; 64%. Found: m/z 148.0519 (M$^+$). Calcd for $C_9H_8O_2$: 148.0524. ^{1}H NMR δ=2.53 (1H, ddd, J=19, 5.5, 1.5 Hz), 2.65 (1H, dd, J=19, 1.5 Hz), 3.59 (1H, m), 3.91 (1H, ddd, J=9, 7, 1 Hz), 6.04 (1H, ddd, J=11, 2, 1 Hz), 6.34 (1H, td, J=8, 1 Hz), 6.59 (1H, ddd, J=8, 7, 1.5 Hz), and 6.91 (1H, dd, J=11, 9 Hz). ^{13}C NMR δ=32.1 (t), 50.1 (d), 55.8 (d), 128.6 (d), 132.2 (d), 134.5 (d), 143.9 (d), 193.2 (s), and 202.8 (s). IR ν: 1730 and 1670 cm^{-1}].

References

1) S. Sugiyama, T. Tsuda, A. Mori, H. Takeshita, and M. Kodama, *Bull. Chem. Soc. Jpn.*, **60**, 2695 (1987).

2) T. S. Cantrell, *Tetrahedron Lett.*, **1975**, 907.

3) The NMR spectra were measured in $CDCl_3$ solutions by an FX 100 Model or a GSX 270H Model Spectrometer, JEOL, and the chemical shifts were from the internal Me_4Si in ppm scale.

4) R. B. Woodward and R. Hoffmann, "Conservation of Orbital Symmetry," Verlag Chemie, Weinheim (1975), p. 142.

5) This series of compounds were considerably hygroscopic, and their precise weighing was difficult to obtain acceptable figures from the combustion analyses. However, every new compound described was homogeneous in respect of high-pressure liquid chromatograms (Microporasil column with AcOEt-hexane).

6) Multiplicities of the ^{13}C NMR signals were identified by off-resonance experiments.