Temperature Effect of the High-Pressure Diels-Alder Reaction of Tropone with Acrylonitrile

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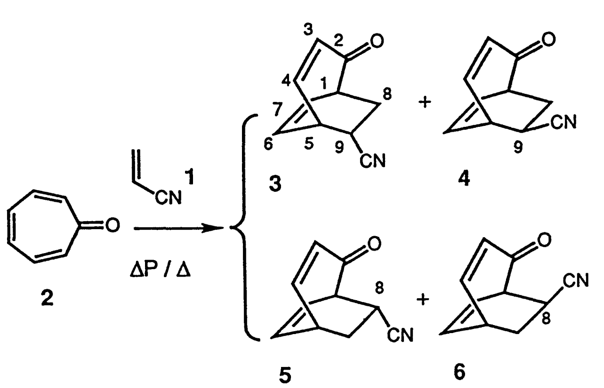
Synopsis. The high-pressure (to 10000 bar) Diels-Alder reaction of tropone with acrylonitrile showed temperature-dependent product distributions: at 80 °C, the product distribution was very similar to that obtained under atmospheric pressure to give four products, among which 9-*endo*-cyanobicyclo[3.2.2]nona-3,6-dien-2-one, in 38% yield, was the major product, while at room temperature there were only three products, i.e., 8-*endo*-, 9-*endo*-, and 9-*exo*-cyano derivatives. The absence of the 8-*exo*-cyano derivative might be due to an electrostatic repulsive interaction of cyano and carbonyl groups in the transition state geometry.

Synthetic utility of the Diels-Alder adducts of tropones has recently been the focus of attention; we reported1) an improved synthesis of homobarrelenones (**A**)2) by means of the high-pressure Diels-Alder reaction of tropones to 2,3-bis(methoxycarbonyl)-7-oxabicyclo[2.2.1]heptadiene, subsequent fragmentation, and further photochemical isomerization of **A** to functionalized dihydroindenones as well as related tricyclic derivatives.3) We now reinvestigated the Diels-Alder reaction of acrylonitrile (**1**) with tropone (**2**)4) under high-pressure conditions to furnish 9- or 8-cyanobicyclo[3.2.2]nona-3,6-dien-2-ones.

Results and Discussion

Thermal High-Pressure Cycloaddition. When **1** and **2** were heated at 80 °C under 10000 bar (1 bar=10^5 Pa) for 10 h, 91% of **2** was consumed to give 1 : 1-adducts (**3**, **4**, **5**, and **6**).

Their structures were identified by ^{1}H NMR comparisons with authentic compounds.



Scheme 1.

Table 1. Product Distributions of the Diels-Alder Reaction of **1** and **2** under Various Pressures

Pressure	8-*endo*	9-*endo*	8-*exo*	9-*exo*	Conv.
bar	**5**	**3**	**6**	**4**	%
1[a)]	12	70	9	9	91
6000[b)]	8	67	5	20	31
8000[b)]	9	66	6	19	52
10000[b)]	8	66	7	19	90
10000[c)]	8	68	0	24	16

a) At 140 °C. b) At 80 °C. c) At 20 °C.

Table 2. Temperature Effect of the Product Distributions of the Diels-Alder Reaction of **1** and **2** under 10000 Bar

Temp	8-*endo*	9-*endo*	8-*exo*	9-*exo*	Conv.
°C	**5**	**3**	**6**	**4**	%
20[a)]	8	68	0	24	16
50[b)]	7	71	3	19	19
80[c)]	8	66	7	19	86
140[c)]	6	74	7	13	100

a) For 185 h in dichloromethane. b) For 50 h in dichloromethane. c) For 12 h in toluene.

From the results, the similarity of the product distributions with those under atmospheric pressure was obvious: they revealed a predominant formation of 9-cyano derivatives, **3** and **4**.4) The pressure effect of the reaction is summarized in Table 1.

As expected, the rate enhancement under high-pressure was quite significant; under 1 bar, 43% of **2** was consumed in ca. 100 h-period at 100 °C, but under 10000 bar, 93% of **2** was consumed within 12 h at 80 °C.

The product distribution was not pressure-dependent, but rather, temperature-dependent; the product distributions at 80 °C were almost same under the range of 6000 to 10000 bar (Table 1); although the yields of 8-*endo*-(**5**), 8-*exo*-(**6**), and 9-*endo*-(**3**) were not much different, the yields of 9-*exo*-(**4**) increased upon decreasing the reaction temperature (Table 2). Moreover, the 8-*exo*-(**6**) was undetectable when the reaction was carried out at low temperature, such as at 20 °C.

In general, the Diels-Alder reaction of tropones predicts the endo selectivity controlled by the secondary orbital interactions; particularly with such acyclic dienophiles as acrylonitrile4) and methyl methacrylate5) it became less effective. Also, the predominant formation of 9-cyano derivatives from **1** and **2** could be explained by the MO considerations.6) While the 9-*exo*-(**4**) showed an increase in the yield, the absence of 8-*exo*-(**6**) at 20 °C was noticed. This was probably due to an electrostatic repulsive interaction between the strongly electronegative carbonyl and cyano groups for the transition state geometry leading to **6**.

Table 3. ^{13}C NMR Chemical Shifts Data of Cyanobicyclo[3.2.2]nona-3,6-dien-2-ones

No.	8-*endo*-CN	8-*exo*-CN	$\Delta\delta_{\text{en-ex}}$	9-*endo*-CN	9-*exo*-CN	$\Delta\delta_{\text{en-ex}}$
1	55.1	54.5	+0.6	51.0	50.9	+0.1
2	195.8	193.5	+2.3	195.7	195.8	−0.1
3	129.8	130.6	−0.8	131.4	132.1	−0.7
4	152.3	152.6	−0.3	148.3	147.5	+0.8
5	35.6	35.7	−0.1	39.4	38.9	+0.5
6	140.1	139.5	+0.6	135.6	137.0	−1.4
7	124.3	125.3	−1.0	128.5	127.2	+1.3
8	24.3	24.4	−0.1	26.8	25.9	+0.9
9	32.6	32.3	+0.3	29.1	29.7	−0.6
CN	121.5	120.9	+0.6	121.9	121.0	+0.9

Table 4. ^{13}C NMR Chemical Shift Comparisons of Cyano- and Ethoxybicyclo[3.2.2]nonadienones

No.	8-*endo*-$\Delta\delta$	8-*exo*-$\Delta\delta$	9-*endo*-$\Delta\delta$	9-*exo*-$\Delta\delta$
1	−3.4	−3.2	−0.1	−0.8
2	+0.1	−2.2	−1.6	−1.8
3	+0.4	−0.4	+0.5	+1.1
4	−1.6	−0.9	−0.9	−2.1
5	+0.1	−1.0	−2.7	−3.0
6	+1.7	−0.3	+0.5	+0.5
7	−0.5	0.0	+0.9	0.0
8	−51.4	−50.7	−3.9	−2.7
9	−2.2	−4.1	−48.7	−49.8

The ^{13}C NMR Chemical Shifts of the Cyanobicyclo[3.2.2]nona-3,6-dien-2-ones. In a previous paper[7] we showed the usefulness of ^{13}C NMR chemical shift data of 8- and 9-ethoxybicyclo[3.2.2]nona-3,6-dien-2-ones regarding structure elucidation.[7] The ^{13}C NMR spectra again provided a sound basis for a structure identification of the 8- and 9-cyanobicyclo[3.2.2]nona-3,6-dien-2-ones (Table 3).

Though the ^{13}C NMR spectra of epimeric pairs were similar, the strong electron-withdrawing effect of the cyano group revealed a chemical shift difference ($\Delta\delta$) in the proximity. As can be seen in Table 4, a close parallelism in ^{13}C chemical shifts was also observed between the cyano- and the ethoxy derivatives;[7] each pair of compounds having the same stereochemistry shows very similar chemical shifts. For example, though in 8-substituted derivatives, the $\Delta\delta$ for C-1 were −3.4 and −3.2, those of C-5, the other bridgehead carbon atom, were +0.1 and −1.0, and in 9-substituted derivatives; the $\Delta\delta$ for C-5 were −2.7 and −3.0 and the $\Delta\delta$ for C-1 were −0.1 and −0.8.

Experimental

High-Pressure Diels-Alder Reaction of 1 and 2. A toluene solution (4 cm^3) of **1** (590 mg), **2** (424 mg), and hydroquinone (20 mg) was heated at 80 °C under 10000 bar for 12 h. The mixture was then separated by means of silica-gel column and high-pressure liquid (Microporasil, EtOAc, and hexane) chromatography to give the following products:

3:[4] Colorless crystals, mp 118—120 °C, 270 mg; 37.9%. ^{1}H NMR δ[8]=2.30 (1H, ddd, J=14.7, 6.4, 3.6 Hz), 2.38 (1H, dm, J=14.7, 9.9 Hz), 3.26 (1H, ddd, J=9.9, 3.6, 2.0 Hz), 3.64 (1H, dddd, J=7.5, 6.4, 2.4, 2.0 Hz), 3.68 (1H, dd, J=8.7, 7.9 Hz), 5.84 (1H, dd, J=11.1, 2.4 Hz), 6.34 (1H, dd, J=7.7, 7.5 Hz), 6.64 (1H, dd, J=7.9, 7.7 Hz), and 6.98 (1H, dd, J=11.1, 8.7 Hz). MS m/z (%): 159 (74), 132 (25), 131 (42), 130 (100), 117 (21), 116 (32), 104 (38), 103 (25), 91 (19), 78 (35), 77 (22), 65 (12), 55 (13), 52 (17), 39 (21), and 26 (19). IR (KBr) 3036, 2950, 2238, 1734, 1670, 1634, 1386, 1253, 1162, 851, 729, and 682 cm^{-1}. UV $\lambda_{\max}^{\text{MeOH}}$=237 nm ($\varepsilon$=4400) and 342 (130).

4:[4] A colorless oil, 200 mg; 28.1%. ^{1}H NMR δ=2.18 (1H, dd, J=14.3, 7.0 Hz), 2.49 (1H, ddd, J=14.3, 10.6, 8.6 Hz), 2.97 (1H, ddd, J=10.6, 7.0, 4.7 Hz), 3.56 (1H, ddd, J=8.6, 7.3, 2.2 Hz), 3.68 (1H, ddd, J=8.4, 7.7, 4.7 Hz), 6.00 (1H, dd, J=11.1, 2.2 Hz), 6.17 (1H, dd, J=8.4, 7.3 Hz), 6.55 (1H, dd, J=8.4, 7.7 Hz), and 7.05 (1H, dd, J=11.0, 8.4 Hz). MS m/z (%): 159 (M$^+$, 48), 131 (40), 130 (100), 116 (25), 104 (68), 78 (34), and 51 (22). IR (oil) 3050, 2948, 2236, 1670, 1635, 1384, 1264, 1169, 831, and 714 cm^{-1}.

5:[4] Colorless crystals, mp 91—92 °C, 14 mg; 2.0%. ^{1}H NMR δ=2.06 (1H, ddd, J=13.2, 6.2, 4.4 Hz), 2.52 (1H, dd, J=13.2, 9.9 Hz), 3.20 (1H, dd, J=9.9, 6.2 Hz), 3.46 (1H, ddd, J=8.8, 7.3, 4.4 Hz), 3.82 (1H, dd, J=7.3, 2.0 Hz), 5.80 (1H, dd, J=11.0, 2.0 Hz), 6.21 (1H, dd, J=8.4, 7.3 Hz), 6.76 (1H, dd, J=8.4, 7.3 Hz), and 7.09 (1H, dd, J=11.0, 8.8 Hz). MS m/z (%): 159 (M$^+$, 34), 131 (38), 130 (100), 116 (26), 104 (35), 78 (49), 77 (25), 51 (32), and 39 (30). IR (KBr) 2960, 2232, 1667, 1634, 1387, 1263, 829, and 713 cm^{-1}.

6:[4] A colorless oil, 28 mg; 3.9%. ^{1}H NMR δ=2.26 (1H, ddd, J=13.5, 10.7, 4.8 Hz), 2.34 (1H, ddd, J=13.5, 4.0, 2.0 Hz), 3.22 (1H, ddd, J=10.7, 5.6, 4.0 Hz), 3.46 (1H, dddd, J=8.7, 8.0, 4.8, 2.0 Hz), 3.80 (1H, ddd, J=7.5, 5.6, 2.0 Hz), 5.94 (1H, dd, J=11.1, 2.0 Hz), 6.12 (1H, dd, J=8.4, 7.5 Hz), 6.65 (1H, dd, J=8.4, 8.0 Hz), and 7.19 (1H, dd, J=11.1, 8.7 Hz). MS m/z (%): 160 (12), 159 (100), 158 (20), 132 (36), 131 (57), 130 (94), 117 (34), 116 (43), 104 (43), 103 (33), 91 (19), 78 (40), 77 (26), 65 (14), 55 (14), 52 (27), 51 (30), 50 (15), 43 (14), 39 (24), and 26 (25). IR (oil) 2946, 2236, 1667, 1636, 1387, 1161, 842, 727, and 683 cm^{-1}.

Diels-Alder Reaction of 2 with 1 under Atmospheric Pressure. A toluene solution (4 cm^3) of **1** (590 mg) and **2** (424 mg) was heated in a sealed tube at 100 °C for 100 h. The mixture was chromatographed on a silica-gel column to give a mixture of **3**, **4**, **5**, and **6** (117 mg; 16.5%) together with the recovered **2** (242 mg; 57%). Further fractionation was carried out by means of high-pressure liquid chromatography to show very similar results to those of Ref. 4 in Table 1.

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8) All the NMR spectra were measured with JEOL FX 100 and GSX 270H spectrometers in $CDCl_3$ through out.