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Thermodynamic *vs.* Kinetic Control in the Diels-Alder Cycloaddition of Cyclopentadiene to 2,3-Dicyano-*p*-benzoquinone: Kinetic Control Revisited

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Abstract. Diels-Alder cycloaddition of cyclopentadiene (**1**) to 2,3-dicyano-*p*-benzoquinone (**2**), when performed in methanol solvent at ambient temperature (kinetic control), gave **3b**. Reduction of **3b**, carried out under mild conditions by using $CeCl_3$-$NaBH_4$, proceeded stereospecifically to afford diol **5**. Subsequently, **5** was converted into the corresponding bis(*O*-acetyl) derivative, **6**, whose structure was established unequivocally via application of X-ray crystallographic methods. An earlier suggestion that **3a** results via kinetic control of Diels-Alder cycloaddition of **1** to **2** is thereby shown to be erroneous. © 1998 Elsevier Science Ltd. All rights reserved.

Introduction. Recently, we reported the results of a study of thermodynamic *vs.* kinetic control of the Diels-Alder cycloaddition of cyclopentadiene (CPD, **1**) to 2,3-dicyano-*p*-benzo-quinone (**2**).[1] It was shown that the *exo*/*endo* stereochemistry of the resulting [4 + 2] cycloadduct depends strikingly upon the reaction conditions employed (see Scheme 1).

When a benzene solution of **1** and **2** was refluxed for 3 h (i.e., conditions that resulted in thermodynamic control of the resulting Diels-Alder cycloaddition), a single [4 + 2] cycloadduct was obtained. Subsequently, this cycloadduct was demonstrated unequivocally to possess structure **4a** (Scheme 1) via application of X-ray crystallographic methods.[1]

Since the corresponding product of kinetic control, i.e., **3a**, had been reported previously by other investigators,[2] no additional effort was made to characterize this material at the time of our study.[1] However, it should be noted that characterization of the product of kinetic control (assigned structrure **3a**)[2] was based solely upon its observed behavior during melting and *not* upon compelling spectral evidence or other physical or chemical properties of this cycloadduct.

Our respective research groups have had a long-standing interest in studies of Diels-Alder reactions of cyclopentadienes with a wide variety of substituted *p*-benzoquinones. In the past, we have performed detailed analyses of the ^1H and ^{13}C NMR spectra of the resulting [4 + 2] cycloadducts and their derivatives.[3] In addition,

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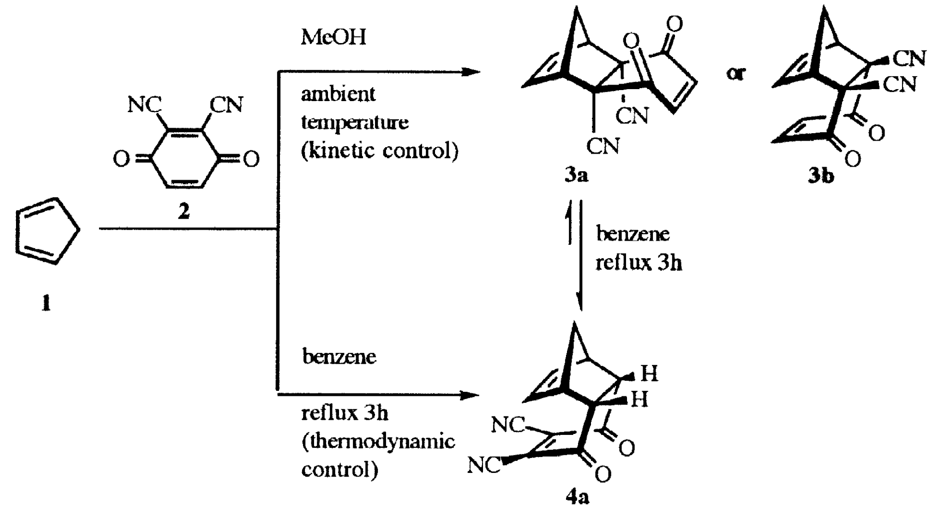
Diels-Alder cycloadducts of this type are of interest as immediate precursors to functionalized pentacyclo-$[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]$undecane-8,11-diones, which can be obtained from them simply via intramolecular [2 + 2] photocyclization.[4,5]

Scheme 1



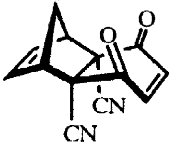
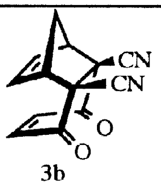
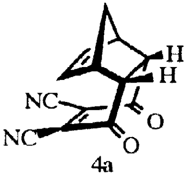
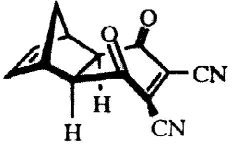
Results and Discsussion. Pursuant to ongoing interest in the mechanism of the Diels-Alder reaction, we have recently utilized advanced theoretical (computational) methods in an effort to improve our understanding of the detailed nature of Diels-Alder transition states.[6] In this connection, the four possible *exo/endo* ground and transition states for Diels-Alder cycloaddition of **1** to **2** have been computed at the HF/3-21G* level of theory. The results thereby obtained are shown in Table 1.

The results of ground state calculations clearly predict **4a** to be the preferred product of thermodynamic control of the Diels-Alder cycloaddition of **1** to **2**, in agreement with experiment.[1] Importantly, the results of the corresponding transition state calculations indicate that the transition state leading to **3b** should be preferred, and, hence, **3b** (rather than **3a**) is predicted to be the product formed via kinetic control of this Diels-Alder cycloaddition. This result stands in stark contrast with previously published conclusions.[2]

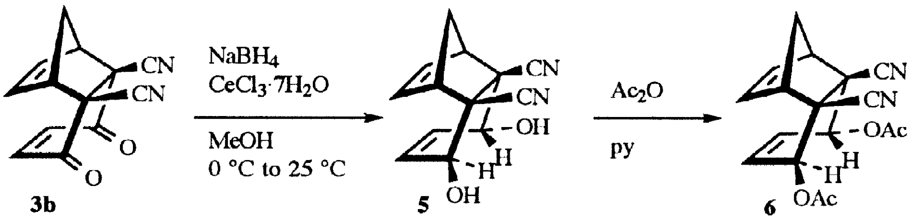
In order to resolve the discrepancy noted above, we repeated the Diels-Alder reaction of **1** with **2** under conditions that have been reported[2] to afford the product of kinetic control. Then, in order to prevent its thermal isomerization of the configuration of the kinetic product to **4a**, the resulting cycloadduct was reduced under mild conditions with $NaBH_4$-$CeCl_3$,[7] thereby affording the corresponding *exo*-8,*exo*-11 diol, **5** (Scheme 2), which is configurationally stable. This diol subsequently was converted into the corresponding bis(*O*-acetyl) derivative, **6**.[8] A suitable single crystal of **6** was obtained, and its structure was determined via X-ray crystallographic methods. An X-ray structure drawing of **6** is shown in Figure 1 (see the Experimental Section).

Summary and Conclusions. An earlier report[2] regarding the structure of the cycloadduct formed via Diels-Alder cycloaddition of **1** to **2** under conditions of kinetic control stands in conflict with the corresponding prediction based upon our analysis of the results of ab initio HF/3-21G* calculations. This conflict has been resolved by synthesizing the cycloadduct and by converting it into a stable, crystalline derivative whose structure subsequently was established unequivocally via application of X-ray crystallographic methods. The structure thereby determined is consistent with the prediction based upon the results of ab initio calculations, i..e., that the kinetic product of Diels-Alder cycloaddition of **1** to **2** possesses structure **3b** rather than **3a**.

Table 1. Calculated ground state and transition state energies for the four possible modes of Diels-Alder cycloaddition of **1** to **2**.

	 3a	 3b	 4a	 4b
Calculated absolute ground state energy RHF/3-21G* (hartrees)	-751.27837	-751.27947	-751.28364	-751.28253
Relative energy, ΔH° (kcal-mol^{-1})	(3.3)	(2.6)	(0.0)	(0.7)
Calculated absolute transition state energy RHF/3-21G* (hartrees)	-751.20561	-751.21028	-751.20731	-751.20236
Relative energy, ΔH$^{\neq}$ (kcal-mol^{-1})	(3.0)	(0.0)	(1.9)	(5.0)

Scheme 2



Experimental Section

Melting points are uncorrected. Elemental microanalyses were performed by M-H-W Laboratories, Phoenix, AZ. Ab initio calculations were performed by using Gaussian'94.[9] on an SGI INDIGO2 platform.

1α,4α,4aβ,8aβ–Tetrahydro-5,8-dioxo-1,4-methanonaphthalene-4aα,8aα-dicarbonitrile (3b). A solution of 2,3-dicyano-1,4-benzoquinone[2,10] (**2**, 500 mg, 3.16 mmol) in MeOH (5 mL) was cooled to 0 °C via application of an external ice-water bath. To this cooled solution was added dropwise with vigorous stirring freshly cracked cyclopentadiene[11] (**1**, 230 mg, 3.48 mmol). After all of the diene had been added, the reaction mixture was filtered, and the filtrate was allowed to air-dry. The resulting solid was recrystallized from EtOAc, thereby affording pure **3b** (490 mg, 70%) as a pale yellow microcrystalline solid: mp 135-136 °C, dec. at T > 190 °C (lit.[2] "double mp" 135-136 °C, 256 °C); IR (KBr) 2980 (w), 2253 (s), 1660 cm^{-1} (m); ^{1}H NMR (DMSO-d_6) δ 1.81 (*AB*, J_{AB} = 10.2 Hz, 1 H), 2.12 (A*B*, J_{AB} = 10.2 Hz, 1 H), 4.02 (m, 2 H), 6.22 (br s, 2 H), 6.84 (s, 2 H).

1α,4α,4aβ,8aβ–Tetrahydro-5,8-dihydroxy-1,4-methanonaphthalene-4aα,8aα-dicarbonitrile (5). To a suspension of **3b** (900 mg, 3.94 mmol) in MeOH (30 mL) was added $CeCl_3 \cdot 7H_2O$ (2.93 g, 7.88 mmol), and the resulting mixture was cooled to 5 °C via application of an external ice-water bath. To the cooled mixture was added in four equal portions with stirring $NaBH_4$ (300mg, 7.9 mmol) during 0.5 h. The external cold bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature with stirring during 4 h. Water (40 mL) was added, and the resulting aqueous suspension was extracted with EtOAc (4 x 25 mL). The organic layer was washed with water (10 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated *in vaccuo*. The residue was recrystallized from EtOAc-hexane, thereby affording pure **5** (700 mg, 77%) as a colorless microcrystalline solid: mp 185-186 °C; IR (KBr) 3422 (s), 2238 (m), 1703 cm^{-1} (w); ^{1}H NMR (DMSO-d_6) δ 1.55 (*AB*, J_{AB} = 9.8 Hz, 1 H), 1.84 (A*B*, J_{AB} = 9.8 Hz, 1 H), 4.60 (s, 2 H), 5.24 (s, 2 H), 5.86 (s, 2 H), 6.13 (s, 2 H); ^{13}C NMR (DMSO-d_6) δ 46.9 (s), 52.2 (t), 52.6 (s), 67.7 (t), 123.6 (s), 129.6 (d), 136.3 (d). Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H 5.30. Found: C, 68.50; H, 5.46.

1α,4α,4aβ,8aβ–Tetrahydro-5,8-diacetoxy-1,4-methanonaphthalene-4aα,8aα-dicarbonitrile (6). To a solution of **5** (700 mg, 2.91 mmol) in pyridine (15 mL) under argon was added Ac_2O (18.5 g, excess), and the resulting solution was stirred at ambient temperature for 30 h. The reaction mixture then was acidified via careful addition of 10% aqueous HCl (40 mL), and the resulting aqueous suspension was extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were washed sequentially with water (10 mL), 10% aqueous $NaHCO_3$ (10 mL) and water (10 mL). The organic layer was dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified via column chromatography on silica gel by eluting with 30% EtOAc-hexane. The eluate was concentrated *in vacuo*, and the residue was recrystallized from EtOAc-hexane. Pure **6** (400 mg, 57%) was thereby obtained as a colorless microcrystalline solid: mp 155-156 °C; IR ($CHCl_3$) 2237 (w), 1753 (s), 1657 (w), 1223 cm^{-1} (m); ^{1}H NMR ($CDCl_3$) δ 1.75 (*AB*, J_{AB} = 10.0 Hz, 1 H), 2.16 (A*B*, J_{AB} = 10.0 Hz, 1 H), 2.17 (s, 3 H), 3.56 (m, 2 H), 5.32 (d, J =1.2 Hz, 2 H), 5.78 (d, 2 H), 5.94 (t, J = 1.7 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.7 (q), 47.9 (t), 49.8 (s), 53.7 (d), 69.4 (d), 121.2 (s), 127.4 (d), 136.8 (d), 169.1 (s). Anal. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16. Found: C, 65.44; H, 5.13.

X-ray Structure of 6. All data were collected at ambient temperature on a Rigaku AFC6S diffractometer with graphite monochromated Mo Kα radiation (λ = 0.71073 Å) by using the ω–2θ scan technique with multiple scans for weak reflections. Pertinent X-ray data are given in Table 2. Data were corrected for Lorentz and polarization effects. Azimuthal scans of several reflections indicated that absorption corrections were negligible. The structures were solved by direct methods[12] and were refined and analyzed by using TEXSAN[13] and PLATON.[14] Hydrogen atoms were located in a difference map and were allowed to ride at a fixed distance from the attached heavy atom. The structure contains two independent molecules of **6** per unit cell.

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Table 2. X-ray data collection and processing parameters for **6**.

Compound	**6**	Z-value	8
		D_{calc} (g-cm^{-3})	1.255
Formula	$C_{17}H_{16}N_2O_4$	μ (cm^{-1})	0.90
Size (mm)	0.40 x 0.50 x 0.70	T (K)	296
Space Group	$P2_1/n$	$2\theta_{max}$ (°)	55.0
a (Å)	15.340 (4)	Total reflections	5075
b (Å)	13.714 (4)	Unique reflections	4786
c (Å)	15.814 (2)	Observed Reflections I $\geq 3\sigma$(I)	1550
α (°)	90	Parameters	415
β (°)	91.31 (2)	R, R_w	0.059; 0.054
γ (°)	90	$(\Delta/\sigma)_{max}$	0.05
V (Å^3)	3325 (1)	ρ_{max}; ρ_{min} (eÅ^{-3})	0.21; -0.23

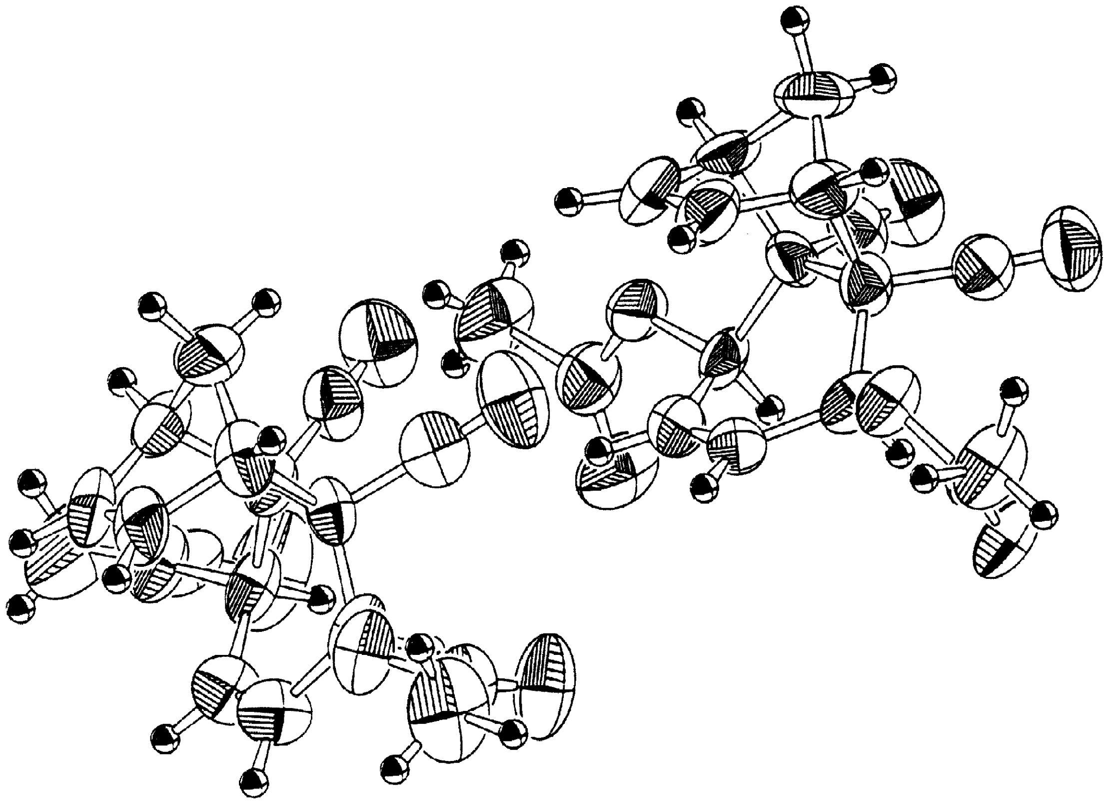

Figure 1. X-ray structure drawing of **6**

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