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Stereoselective $[2\pi+4\pi]$-Type Addition Reactions of Benzocyclobutadiene with 2-Substituted Tropones and 8,8-Dicyanoheptafulvene

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Thermal addition reactions of 2-substituted tropones and 8,8-dicyanoheptafulvene with benzocyclobutadiene proceeded stereoselectively to produce *endo*-$[2\pi+4\pi]$-type cyclo adducts, where the troponoid compounds acted as 4π components. Molecular orbital calculations were employed to explain the selectivity.

Keywords 2-substituted tropone; 8,8-dicyanoheptafulvene; benzocyclobutadiene; $[2\pi+4\pi]$-type cycloaddition; stereoselective

From the early stages of research related to the Woodward–Hoffmann rule, tropone and its derivatives have provided many opportunities for experimental and theoretical investigations. In studies of pericyclic reactions, it has been revealed that tropones react as 2π, 6π, and 8π electrons units in $[2\pi+4\pi]$-, $[6\pi+4\pi]$-, and $[8\pi+2\pi]$-type cycloaddition reactions.[1]

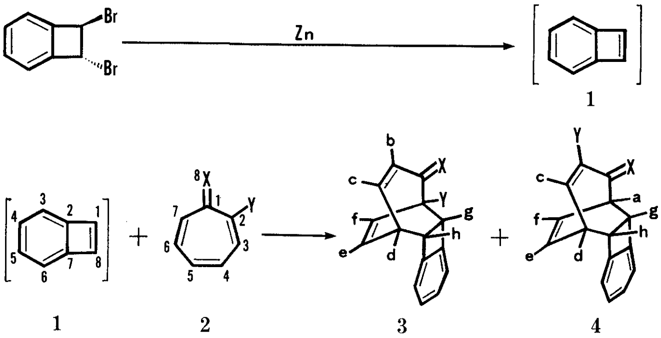
Cyclobutadienes, typical 4π electron anti-aromatic compounds, are very unstable and their reactions have not been investigated in great detail.[2] Benzocyclobutadiene (**1**) is still too unstable to be isolated, but its reactivities can be studied more easily because its formation is straightforward. However, except for dimerization or cycloadditions to some kinds of unsaturated hydrocarbons, little work has been reported on the reactivities of **1**.[3] We have studied reactions of **1** with several kinds of 2-substituted tropones (**2a**—**f**) and 8,8-dicyanoheptafulvene (**2g**), and the results are presented here.

Results and Discussion

Benzocyclobutadiene (**1**) was generated *in situ* by reaction of *trans*-1,2-dibromo-1,2-dihydrobenzocyclobutene and zinc dust.[4] An excess of zinc dust was added to a solution of tropone (**2a**) and 3 molar eq of *trans*-1,2-dibromo-1,2-dihydrobenzocyclobutene in tetrahydrofuran (THF). After the exothermic reaction, the reaction mixture was further stirred at room temperature for 2 h to give the cycloadduct (**3a**) in 29% yield. A similar reaction using 2-chlorotropone (**2b**) gave two isomers (**3b** and **4b**) in 18 and 6% yields, respectively. The analogous isomers (**3c** and **4c**) were obtained in 16 and 12% yields, respectively, in the reaction with 2-methyl-tropone (**2c**), but only **3d** (6%) was formed in the reaction with 2-methoxytropone (**2d**). The 4,7-position type adducts were major products in the reaction with 2-phenyltropone derivatives. The reaction of 2-phenyltropone (**2e**) gave **3e** and **4e** in 6 and 31% yields, respectively. Analogously, **4f** was the major product (15%), compared to **3f** (7%), in the reaction with 2-(*p*-methoxyphenyl)tropone (**2f**). The reaction of 8,8-dicyano-heptafulvene (**2g**) afforded **3g** in 13% yield.

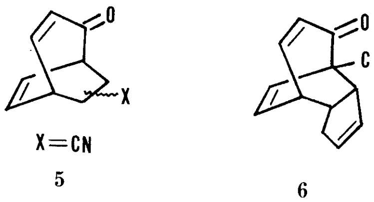
No interconversion between **3** and **4** was observed under the reaction conditions, thus showing that these adducts were primary products.

The structures of **3** and **4** were deduced based on their spectral, especially NMR spectral, properties and confirmed by comparisons of these properties with those of analogous compounds such as **5** and **6**.[5] The *endo* structures of **3** and **4** were decided on the basis of the chemical shifts of the signals of H_e (6.18—6.40 ppm) and H_f (5.40—6.13 ppm), which appeared at higher field compared to those of the corresponding protons of **5** and **6** (H_e: 6.39—6.75 ppm, H_f: 6.05—6.32 ppm). This fact could only be rationalized in terms of anisotropic effects caused by the phenyl ring in the *endo*-form. The coupling constants between the bridgehead protons (J_{ag} and/or J_{dh}) also supported the *endo*



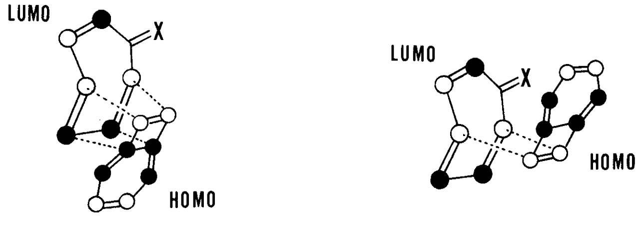
	2	3	4
a	X=O, Y=H	29%	—
b	X=O, Y=Cl	18%	6%
c	X=O, Y=Me	16%	12%
d	X=O, Y=OMe	6%	0%
e	X=O, Y=Ph	6%	31%
f	X=O, Y=*p*-MeO-Ph	7%	15%
g	X=C(CN)$_2$, Y=H	13%	—

Fig. 1



5 6

Fig. 2



endo-type *exo*-type

Fig. 3

Table I. Coefficients and Orbital Energies of LUMO and HOMO of **1** and **2**

	Coefficients Positions[a]								Energies (eV)
	1	2	3	4	5	6	7	8	
LUMO									
1	0.431	0.380	−0.186	−0.368	0.368	0.186	−0.380	−0.431	−0.295
2a	0.000	0.452	−0.274	−0.470	0.470	0.274	−0.452	0.000	−0.815
2b	0.030	0.483	−0.352	−0.424	0.480	0.220	−0.417	−0.029	−1.186
2c	0.013	0.469	−0.311	−0.449	0.473	0.245	−0.432	−0.012	−0.862
2d	0.014	0.479	−0.304	−0.445	0.463	0.248	−0.428	−0.013	−0.941
2e	0.009	0.457	−0.298	−0.442	0.459	0.248	−0.428	−0.008	−0.821
2f	0.004	0.456	−0.298	−0.441	0.459	0.253	−0.429	−0.002	−0.872
2g	0.541	0.117	−0.385	0.150	0.150	−0.385	0.117	−0.481	−1.467
HOMO									
1	0.428	−0.373	−0.200	0.371	0.371	−0.200	−0.373	0.428	−8.361
2a	0.009	0.433	0.251	−0.441	−0.442	0.250	0.433	−0.330	−9.253
2b	0.010	0.438	0.266	−0.426	−0.432	0.233	0.413	−0.312	−9.473
2c	0.016	0.450	0.280	−0.422	−0.439	0.229	0.414	−0.319	−9.171
2d	0.020	0.448	0.318	−0.400	−0.447	0.202	0.399	−0.306	−9.158
2e	0.010	0.429	0.264	−0.408	−0.415	0.227	0.399	−0.308	−9.191
2f	0.004	0.186	0.130	−0.177	−0.177	0.097	0.168	−0.138	−9.173
2g	−0.216	0.341	0.259	−0.324	−0.324	0.259	0.341	−0.535	−8.852

a) Numbering of the positions is shown in Fig. 1.

configurations of the adducts.[6]

Clearly the reactions proceeded stereoselectively to form *endo*-type adducts. Molecular orbital calculations by the modified neglect of diatomic overlap (MNDO) method[7] were carried out on **1** and **2**. The coefficients of the wave functions and the orbital energies of LUMO and HOMO of **1** and **2** are summarized in Table I.

The energy differences between the HOMO of **1** and the LUMO of **2** were smaller than those of the opposite combinations, suggesting that the reactions were determined by interactions between the HOMO of **1** and the LUMO of **2**. Figure 3 shows bonding-type secondary orbital interactions in the *endo*-type transition states between the HOMO of **1** and the LUMO of **2**.[8] On the other hand no such stabilizations could be found in the *exo*-type transition states. As a result the *endo* additions proceeded predominantly.[9]

Experimental

NMR spectra were measured with a Varian XL-200 spectrometer with deuterio chloroform as a solvent and tetramethylsilane as an internal standard. IR and MS spectra were measured with JASCO FT/IR 3100 and Hitachi M-2000S spectrometers, respectively.

Only a typical reaction is described below.

Reaction of 1 with 2a Activated zinc (1.5 g) was added to a solution of *trans*-1,2-dibromo-1,2-dihydrobenzocyclobutene (790 mg, 3.0 mmol) and **2a** (120 mg, 1.1 mmol) in THF (7 ml). The mixture was stirred at room temperature for 2 h, then the zinc was filtered off. The filtrate was evaporated and the residue was chromatographed on silica gel using hexane–ethyl acetate (9 : 1) to give a yellow oil **3a** (70 mg, 29%).

3a: High resolution MS (HRMS): *m*/*z* 208.0886. Calcd for $C_{15}H_{12}O$: *m*/*z* 208.0886. MS *m*/*z* (rel. intensity): 208 (M^{+}, 43), 128 (100). IR (oil): 1661 cm^{-1}. ^{1}H-NMR $\delta=3.54$ (ddd, $\mathrm{H_d}$), 3.75 (ddd, $\mathrm{H_a}$), 3.83 (dd, $\mathrm{H_g}$), 3.92 (dd, $\mathrm{H_h}$), 5.73—5.83 (2H, m, $\mathrm{H_b}$, $\mathrm{H_f}$), 6.19 (dd, $\mathrm{H_e}$), 7.02—7.28 (5H, m, $\mathrm{H_c}$, Ph). Coupling constants in Hz: $J_{ab}=2.3$, $J_{af}=7.6$, $J_{ag}=2.3$, $J_{bc}=11.2$, $J_{cd}=8.6$, $J_{de}=8.6$, $J_{dh}=2.5$, $J_{ef}=9.1$, $J_{gh}=5.6$.

3b: HRMS: *m*/*z* 242.0497. Calcd for $C_{15}H_{11}ClO$: *m*/*z* 242.0497. MS *m*/*z* (rel. intensity): 242 (M^{+}, 6), 179 (100). IR (oil); 1680 cm^{-1}. ^{1}H-NMR $\delta=3.58$ (m, $\mathrm{H_d}$), 3.95 (dd, $\mathrm{H_h}$), 4.02 (d, $\mathrm{H_g}$), 5.78 (d, $\mathrm{H_f}$), 6.04 (d, $\mathrm{H_b}$), 6.18 (m, $\mathrm{H_e}$), 7.04—7.46 (5H, m, $\mathrm{H_c}$, Ph). Coupling constants in Hz: $J_{bc}=11.2$, $J_{cd}=8.6$, $J_{de}=7.5$, $J_{dh}=2.4$, $J_{ef}=9.1$, $J_{gh}=5.0$.

4b: mp 67—69 °C. HRMS: *m*/*z* 242.0499. Calcd for $C_{15}H_{11}ClO$: *m*/*z* 242.0498. MS *m*/*z* (rel. intensity): 242 (M^{+}, 8), 102 (100). IR (KBr): 1682 cm^{-1}. ^{1}H-NMR $\delta=3.66$ (m, $\mathrm{H_d}$), 3.88 (dd, $\mathrm{H_g}$), 3.98 (dd, $\mathrm{H_h}$), 4.06 (dd, $\mathrm{H_a}$), 5.85 (dd, $\mathrm{H_f}$), 6.26 (dd, $\mathrm{H_e}$), 7.04—7.35 (4H, m, Ph), 7.56 (dd, $\mathrm{H_c}$). Coupling constants in Hz: $J_{af}=7.8$, $J_{ag}=2.2$, $J_{cd}=9.1$, $J_{de}=7.8$, $J_{dh}=2.6$, $J_{ef}=8.4$, $J_{gh}=5.0$.

3c: HRMS: *m*/*z* 222.1028. Calcd for $C_{16}H_{14}O$: *m*/*z* 222.1043. MS *m*/*z* (rel. intensity): 222 (M^{+}, 30), 142 (100). IR (oil): 1663 cm^{-1}. ^{1}H-NMR $\delta=1.46$ (3H, s, Me), 3.52 (m, $\mathrm{H_d}$), 3.65 (d, $\mathrm{H_g}$), 3.81 (dd, $\mathrm{H_h}$), 5.40 (d, $\mathrm{H_f}$), 5.88 (d, $\mathrm{H_b}$), 6.19 (dd, $\mathrm{H_e}$), 7.05—7.35 (5H, m, $\mathrm{H_c}$, Ph). Coupling constants in Hz: $J_{bc}=11.2$, $J_{cd}=8.2$, $J_{de}=7.8$, $J_{dh}=2.5$, $J_{ef}=8.4$, $J_{gh}=4.7$.

4c: HRMS: *m*/*z* 222.1043. Calcd for $C_{16}H_{14}O$: *m*/*z* 222.1043. MS *m*/*z* (rel. intensity): 222 (M^{+}, 67), 128 (100). IR (oil): 1663 cm^{-1}. ^{1}H-NMR $\delta=1.80$ (3H, s, Me), 3.48 (m, $\mathrm{H_d}$), 3.80 (2H, m, $\mathrm{H_a}$, $\mathrm{H_g}$), 3.88 (dd, $\mathrm{H_h}$), 5.79 (dd, $\mathrm{H_f}$), 6.28 (dd, $\mathrm{H_e}$), 7.00—7.30 (5H, m, $\mathrm{H_c}$, Ph). Coupling constants in Hz: $J_{af}=8.6$, $J_{cd}=8.6$, $J_{de}=7.3$, $J_{dh}=2.6$, $J_{ef}=8.6$, $J_{gh}=4.9$.

3d: HRMS: *m*/*z* 238.0994. Calcd for $C_{16}H_{14}O_2$: *m*/*z* 238.0993. MS *m*/*z* (rel. intensity): 238 (M^{+}, 55), 158 (100). IR (oil): 1676 cm^{-1}. ^{1}H-NMR $\delta=3.58$ (m, $\mathrm{H_d}$), 3.70 (3H, s, OMe), 3.92 (dd, $\mathrm{H_h}$), 4.04 (d, $\mathrm{H_g}$), 5.71 (d, $\mathrm{H_f}$), 5.92 (d, $\mathrm{H_b}$), 6.12 (dd, $\mathrm{H_e}$), 7.05—7.35 (5H, m, $\mathrm{H_c}$, Ph). Coupling constants in Hz: $J_{bc}=10.3$, $J_{cd}=7.4$, $J_{de}=7.6$, $J_{dh}=2.0$, $J_{ef}=8.2$, $J_{gh}=4.6$.

3e: mp 135—137 °C. HRMS: *m*/*z* 284.1203. Calcd for $C_{21}H_{16}O$: *m*/*z* 284.1200. MS *m*/*z* (rel. intensity): 284 (M^{+}, 43), 204 (100). IR (KBr): 1655 cm^{-1}. ^{1}H NMR $\delta=3.59$ (m, $\mathrm{H_d}$), 4.10 (dd, $\mathrm{H_h}$), 4.34 (d, $\mathrm{H_g}$), 5.94 (d, $\mathrm{H_b}$), 6.15 (d, $\mathrm{H_f}$), 6.40 (2H, m, $\mathrm{H_e}$, Ph), 7.24 (dd, $\mathrm{H_c}$), 7.00—7.55 (8H, m, Ph). Coupling constants in Hz: $J_{bc}=11.2$, $J_{cd}=8.3$, $J_{de}=7.6$, $J_{dh}=2.5$, $J_{ef}=8.1$, $J_{gh}=5.0$.

4e: mp 146.5—147.8 °C. HRMS: *m*/*z* 284.1195. Calcd for $C_{21}H_{16}O$: *m*/*z* 284.1199. MS *m*/*z* (rel. intensity): 284 (M^{+}, 30), 128 (100). IR (KBr): 1658 cm^{-1}. ^{1}H-NMR $\delta=3.66$ (m, $\mathrm{H_d}$), 3.94 (2H, m, $\mathrm{H_a}$, $\mathrm{H_g}$), 4.00 (dd, $\mathrm{H_h}$), 5.87 (dd, $\mathrm{H_f}$), 6.25 (dd, $\mathrm{H_e}$), 7.00—7.40 (10H, m, $\mathrm{H_c}$, Ph). Coupling constants in Hz: $J_{af}=8.3$, $J_{cd}=8.1$, $J_{de}=7.3$, $J_{dh}=2.4$, $J_{ef}=8.3$, $J_{gh}=5.5$.

3f: mp 149—151 °C. HRMS: *m*/*z* 314.1304. Calcd for $C_{22}H_{18}O_2$: *m*/*z* 314.1305. MS *m*/*z* (rel. intensity): 314 (M^{+}, 100). IR (KBr): 1649 cm^{-1}. ^{1}H-NMR $\delta=3.60$ (ddd, $\mathrm{H_d}$), 3.90 (3H, s, OMe), 4.11 (dd, $\mathrm{H_h}$), 4.30 (d, $\mathrm{H_g}$), 5.95 (d, $\mathrm{H_b}$), 6.13 (d, $\mathrm{H_f}$), 6.40 (2H, m, $\mathrm{H_e}$, Ph), 7.20—7.40 (8H, m, $\mathrm{H_c}$, Ph). Coupling constants in Hz: $J_{bc}=11.2$, $J_{cd}=8.2$, $J_{de}=7.3$, $J_{dh}=2.1$, $J_{ef}=8.8$, $J_{gh}=5.1$.

4f: mp 156—158 °C. HRMS: *m*/*z* 314.1314. Calcd for $C_{22}H_{18}O_2$: *m*/*z* 314.1306. MS *m*/*z* (rel. intensity): 314 (M^{+}, 71), 133 (100). IR (KBr): 1665 cm^{-1}. ^{1}H-NMR $\delta=3.66$ (m, $\mathrm{H_d}$), 3.81 (3H, s, OMe), 3.94 (2H, m, $\mathrm{H_a}$, $\mathrm{H_g}$), 4.00 (dd, $\mathrm{H_h}$), 5.88 (dd, $\mathrm{H_f}$), 6.25 (dd, $\mathrm{H_e}$), 7.23 (d, $\mathrm{H_c}$), 6.90—7.30 (8H, m, Ph). Coupling constants in Hz: $J_{af}=7.3$, $J_{cd}=9.0$, $J_{de}=7.4$, $J_{dh}=2.5$, $J_{ef}=8.5$, $J_{gh}=4.8$.

3g: HRMS: *m*/*z* 256.1001. Calcd for $C_{18}H_{10}N_2$: *m*/*z* 256.1001. MS *m*/*z* (rel. intensity): 256 (M^{+}, 97), 242 (100). IR (oil); 2224 cm^{-1}. ^{1}H-NMR $\delta=3.61$ (m, $\mathrm{H_d}$), 3.74 (dd, $\mathrm{H_g}$), 3.94 (dd, $\mathrm{H_h}$), 4.26 (dd, $\mathrm{H_a}$), 5.79 (dd, $\mathrm{H_f}$), 6.61 (dd, $\mathrm{H_b}$), 6.19 (dd, $\mathrm{H_e}$), 7.00—7.35 (5H, m, $\mathrm{H_c}$, Ph). Coupling constants in Hz: $J_{ab}=2.2$, $J_{af}=7.5$, $J_{ag}=2.1$, $J_{bc}=10.9$, $J_{cd}=8.6$, $J_{de}=7.5$, $J_{dh}=2.8$,

$J_{ef}=8.3$, $J_{gh}=4.7$.

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9) The unequal yields of **3** and **4** suggested the possibility of regioselective reactions. It is known that the values calculated by the following equation

$$((C_r \cdot C_s)^2/(E_r - E_s)) \qquad (1)$$

explain the regioselectivities of cycloaddition reactions.

Table II. Values Calculated According to Eq. 1 ($\times 10^{-2}$)

	2a	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**
2,5-Position	1.032	1.184	1.084	1.096	1.019	1.024	0.962
4,7-Position		0.903	0.948	0.941	0.920	0.926	

Table II shows these values calculated for each tropone derivative using the MO data of the HOMO of **1** and the LUMO of **2**. These values seem to explain the regioselectivity in favor of the 2,5-position adducts in the reactions of **2b**—**2d**. However, the regioselectivity of the reactions of 2-aryltropones (**2e, f**) is opposite. The reason for this discrepancy is not clear, but one possible explanation is the steric repulsions at the reaction points caused by the bulky aryl groups. G. R. Tian, S. Sugiyama, A. Mori, H. Takeshita, M. Higashi, and H. Yamaguchi, *Chem. Lett.*, **1988**, 941.