Diels-Alder Reaction of 2-Substituted Tropones with Ethylene. HMO Level Aspect of the Regioselectivity

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2-Chloro-, 2-methoxy-, 2-phenyl-, and 2-methyltropones (2,4,6-cycloheptatrien-1-ones) and benzoate of tropolone (2-hydroxy-2,4,6-cycloheptatrien-1-one) reacted with ethylene affording Diels-Alder type 1,4-addition products, bicyclo[3.2.2]nona-3,6-dien-2-ones. The regioselectivities of the cycloaddition are quite random, while they are reproduced by the calculated interaction energies based on Salem's PMO equation which includes the closed-shell repulsion term.

Recently we have reported that tropone (2,4,6-cycloheptatrien-1-one, **1**) reacts relatively easily with alternant hydrocarbons (neutral olefins), such as ethylene, styrene and acenaphthylene giving Diels-Alder type 1,4-addition products.[1)] The HOMO-LUMO orbital arrangements of the reactions indicate that the interaction between $\mathrm{HOMO}_{\text{dienophile}}$—$\mathrm{LUMO}_{\text{tropne}}$ is dominant in each case. On the basis of Sustmann's classification,[2)] those reactions are of the "inverse electron demand" type.

From a theoretical point of view, a diene synthesis utilizing ethylene as the dienophile is of interest. We can treat the Diels-Alder reaction quantitatively because of absence of complicated secondary interactions. We now like to describe the regioselectivities of the Diels-Alder reaction of 2-substituted tropones with ethylene and perturbational MO (PMO) approach to the selectivities based on Eqs. 1 and 2.

The stabilization energy through the interconjugation between a diene and a dienphile at the transition state is evaluated by Eq. 1, based on which the frontier orbital approach was derived.[3)]

$$\Delta E = 2\left(\sum_{\mathrm{i}}^{\mathrm{occ}}\sum_{\mathrm{j}}^{\mathrm{unocc}} - \sum_{\mathrm{i}}^{\mathrm{unocc}}\sum_{\mathrm{j}}^{\mathrm{occ}}\right)\frac{(C_{1\mathrm{r}}^{\mathrm{i}}C_{2\mathrm{r}}^{\mathrm{j}}+C_{1\mathrm{s}}^{\mathrm{i}}C_{2\mathrm{s}}^{\mathrm{j}})^2}{E_{1\mathrm{i}}-E_{2\mathrm{j}}}\gamma^2 \tag{1}$$

Equation 2, derived by Salem,[4)] consists of the closed-shell repulsion term (the first term, E_{rep}) and the overlap stabilization terms (E_{stab}) which are similar to Eq. 1. Here subscripts r and r′ refer to a pair

$$\left.\begin{aligned} E_{\mathrm{int}} = & -k\sum_{\mathrm{rr'}}(q_{\mathrm{r}}+q_{\mathrm{r'}})S_{\mathrm{rr'}}^2 \\ & -2\sum_{\mathrm{j}}^{\mathrm{occ}}\sum_{\mathrm{k'}}^{\mathrm{unocc}}\Big(\sum_{\mathrm{rr'}}C_{\mathrm{jr}}C_{\mathrm{k'r'}}S_{\mathrm{rr'}}\Big)^2[k^2/(E_{\mathrm{k'}}-E_{\mathrm{j}}) \\ & \qquad\qquad + (E_{\mathrm{k'}}-E_{\mathrm{j}})/4] \\ & -2\sum_{\mathrm{j'}}^{\mathrm{occ}}\sum_{\mathrm{k}}^{\mathrm{unocc}}\Big(\sum_{\mathrm{rr'}}C_{\mathrm{kr}}C_{\mathrm{j'r'}}S_{\mathrm{rr'}}\Big)^2[k^2/(E_{\mathrm{k}}-E_{\mathrm{j'}}) \\ & \qquad\qquad + (E_{\mathrm{k}}-E_{\mathrm{j'}})/4] \end{aligned}\right\} \tag{2}$$

of atoms in a diene and a dienophile at which a bond is formed. q is the charge density and S denotes the overlap integral. k is the value of the ratio of interaction integral to overlap integral.

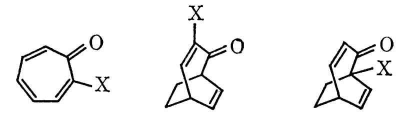
Results and Discussion

The dienophile, ethylene, is able to add to the 4- and 7-positions of 2-substituted tropones giving 3-substituted bicyclo[3.2.2]nona-3,6-dien-2-ones (A-type adducts) and to the 2- and 5-positions affording 1-substituted ones (B-type adducts). A reaction of 2-substituted tropones (**2**—**6**) with ethylene was carried out in a stainless steel autoclave. The reaction conditions and the results are listed in Table 1.

Table 1. THE REACTION CONDITIONS AND THE RESULTS OF DIELS-ALDER REACTION OF 2-SUBSTITUTED TROPONES WITH ETHYLENE

Tropone	Conditions (°C, day)	Product (ratio)[a)]	Total yield[a)]
2	135, 3.5	**2a** (40.5), **2b** (59.5)	100
3	140, 3	**3a** (12.3), **3b** (87.7)	100
4	135, 3	**4a** (100)	87.5
5	140, 3	**5a** (58), **5b**(42)	91.5
6	135, 3	**6a** (60), **6b**(40)[b)]	78[b)]

a) By VPC analysis using 1 m×3 mm columns containing 5% PDEGS on Diasolid H or 10% SE-30 on Diasolid H. b) After isolation.



X=H	**1**	A-type	B-type
X=Cl	**2**	**2a**	**2b**
X=OCH$_3$	**3**	**3a**	**3b**
X=Ph	**4**	**4a**	(**4b**)
X=CH$_3$	**5**	**5a**	**5b**
X=OCOPh	**6**	**6a**	**6b**

A reaction of 2-chlorotropone (**2**) with ethylene gave the two types of adducts (**2a** and **2b**) in a ratio of 40.5 to 59.5, which were separated by chromatography on silica gel. Struture elucidation of the products was performed easily by means of their NMR spectra. A reaction of 2-methoxytropone (**3**) with ethylene proceeded regioselectively giving **3a** (12.3%) and **3b** (87.7%). 2-Phenyltropone (**4**) afforded only the A-type adduct (**4a**), while 2-methyltropone (**5**) gave both types of adducts (**5a** and **5b**: 58 and 42% respectively). The adducts (**6a** and **6b**) were obtained from benzoate of tropolone (**6**) in 60 and 40%, respectively. Thus, regioselectivities of the Diels-Alder reactions are quite random. The cycloadditions should be kinetically controlled: compound **2b** was completely recovered under the cycloaddition conditions, and when it was heated in C_6D_6 (in a sealed tube) at 135 °C for 3 d.

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† Deceased February 4, 1976.

Table 2. Caluculated interaction energies (β) based on Eq. 2a)

Adduct	E_{int}	E_{repul}	E_{stab}
2a	0.0125	−0.4393	0.4518
2b	0.0128	−0.4382	0.4510
3a	0.0116	−0.4395	0.4511
3b	0.0123	−0.4372	0.4495
4a	0.0101	−0.4401	0.4502
(**4b**)	0.0024	−0.4400	0.4424
5a	0.0093	−0.4400	0.4493
5b	0.0087	−0.4367	0.4454

a) The overlap integral is 0.2. The ratio of the interaction integral to the overlap integral is 2.85 β.

The frontior orbital approach2) to the regioselectivity of the reaction of the tropones (**2**—**5**) did not reproduce the experimental results, when we used the Hückel MO calculations based on Streitwieser's parameters.5) Our calculations6) based on Eq. 1 indicated preferred formation of the A-type adduct in every case. In reality, **2a** and **3a** are not predominant adducts. Thus the stabilization energy concept through the interconjugation is not sufficient to explain the regioselectivities.

It has been mentioned by Salem that the repulsion energy term must be included in a quantitative evaluation of interaction energies.4) The interaction energies calculated from Eq. 2 for the transition states of the present Diels-Alder reactions are shown in Table 2. The differences in E_{int} between the A- and B-type adduct formations are uniformly small, and yet they are qualitatively in line with the observed preponderance of one adduct isomer over the other.

The overlap energies (E_{stab}), from the second and third terms of Eq. 2, also show that the predominant adducts are A-type ones in all cases. Thus, the closed-shell repulsion is not negligible in PMO approach to the regioselectivities.

Experimental

General. Melting points were determined on a Thomas Hoover MP apparatus, and are not corrected. Infrared spectra were recorded on Hitachi EPI-3 and Model 215 spectrophotometers. Ultraviolet spectra were recorded on a Hitachi EPS-2T spectrometer. NMR spectra were obtained on Varian A-60 and HA-100 spectrometers equipped with spin decouplars, using tetramethylsilane as the internal standard. The mass spectral studies were conducted using a Hitachi RMU-6D spectrometer. VPC analyses were carried out on a Hitachi gas chromatograph K-53 equipped with a FID. Preparative GLC were done on a Varian Aerograph Model 700 gas chromatograph equipped with a TCD.

*Diels-Alder Reaction of Tropones (**2**—**6**) with Ethylene.* A solution of a tropone (1—2.5 g) in toluene (10—15 ml) was placed in a stainless steel autoclave (100 ml), and heated with excess of ethylene (*ca.* 13 MPa, at 130 °C). After removal of the solvent *in vacuo*, the adducts were isolated by respective way.

*3- and 1-Chlorobicyclo[3.2.2]nona-3,6-dien-2-ones (**2a** and **2b**, respectively).* A mixture of **2a** and **2b**, obtained from 1.65 g of 2-chlorotropone, was chromatographed on silica gel (Wako C-200, 50 g). Elution with hexane gave 245 mg of **2a** and that with benzene gave 450 mg of **2b**. **2a**: Colorless oil; UV$_{\mathrm{max}}$ (CH_3OH) 238 (log ε 3.69), 265 (3.44)$^{\mathrm{sh}}$ and 330 nm (1.94); IR (CCl_4) 1689, 1630 and 1600 cm^{-1}; NMR (CCl_4) δ=7.23 (d, J=9.4 Hz, H_4), 6.54 (ddd, J=8.0, 7.2 and 1.2 Hz, H_6), 6.06 (ddd, J=8.2, 7.6, and 1.2 Hz, H_7), 3.65 (m, H_1), 3.40 (m, H_5), and 2.1—1.5 (4H, m). 2,4-DNP of **2a**: 203—205 °C (dec). Found: C, 51.70; H, 3.92; N, 15.69%. Calcd for $C_{15}H_{13}ClN_4O_4$: C, 51.51; H, 3.75; N, 15.62%. **2b**: Colorless needles; mp 55—56 °C; UV$_{\mathrm{max}}$ (CH_3OH) 226.5 (log ε 3.82) and 330 nm (1.97); IR (KBr) 1680 and 1615 cm^{-1}; NMR ($CDCl_3$) δ=7.12 (dd, J=11.2 and 8.9 Hz, H_4), 6.55 (dd, J=9.0 and 7.2 Hz, H_6), 6.01 (dd, J=9.0 and 0.8 Hz, H_7), 5.89 (dd, J=11.2 and 0.8 Hz, H_3), 3.43 (m, H_5), 2.4 (2H, m), and 1.9 (2H, m). Found: C, 64.08; H, 5.35%. Calcd for C_9H_9ClO: C, 64.10; H, 5.38%.

*3- and 1-Methoxybicyclo[3.2.2]nona-3,6-dien-2-ones (**3a** and **3b**, respectively).* Isolation of the adducts was performed by preparative GLC using a 10 ft × 3/8 in aluminium column containing 5% PDEGE on Diasolid H at 180 °C. **3a**: Colorless prisms (from hexane-ether); mp 48—49 °C; UV$_{\mathrm{max}}$ (CH_3OH) 234.5 (log ε 3.64), 276.5 (3.68) and 335 nm (2.43)$^{\mathrm{sh}}$; IR (CCl_4) 1686, 1635 and 1620 cm^{-1}; NMR ($CDCl_3$) δ=6.60 (ddd, J=8.3, 7.5 and 1.0 Hz, H_6), 6.06 (bd, J=9.5 Hz, H_4), 5.95 (ddd, J=8.3, 6.5 and 1.0 Hz, H_7), 3.65 (m, H_1), 3.52 (3H, s), 3.40 (m, H_5), and 2.0—1.6 (4H, m). Found: M$^+$, 164. Calcd for $C_{10}H_{12}O_2$: M, 164. 2,4-DNP of **3a**: mp 207 °C (dec). **3b**: Colorless oil; UV$_{\mathrm{max}}$ (CH_3OH) 228 (log ε 3.77) and 340 nm (2.22); IR (CCl_4) 1685 and 1635 cm^{-1}; NMR ($CDCl_3$) δ=7.02 (dd, J=11.1 and 8.5 Hz, H_4), 6.54 (dd, J=9.0 and 7.1 Hz, H_6), 6.03 (dd, J=9.0 and 0.9 Hz, H_7), 5.83 (dd, J=11.4 and 0.8 Hz, H_3), 3.49 (3H, s), 3.38 (m, H_5), and 2.2—1.7 (4H, m). 2,4-DNP of **3b**: mp 217 °C (dec). Found: C, 55.71; H, 4.79; N, 16.64%. Calcd for $C_{16}H_{16}N_4O_5$: C, 55.81; H, 4.68; N, 16.77%.

*3-Phenylbicyclo[3.2.2]nona-3,6-dien-2-one (**4a**).* Recrystallization of the crude product, from 1 g of 2-phenyltropone (**4**), was performed from hexane–ether yielding 750 mg of **4a**. The mother liquor gave 270 mg of **4a** and trace of **4**, after chromatography on silica gel. **4a**: Colorless needles (from ethanol); mp 93—95 °C; UV$_{\mathrm{max}}$ 223.5 (log ε 4.07), 275 (3.56) and 335 nm (2.05)$^{\mathrm{sh}}$; IR (KBr) 1670 and 1628 cm^{-1}; NMR ($CDCl_3$) δ=7.24 (5H, m), 7.07 (d, J=9.0 Hz, H_4), 6.58 (ddd, J=8.1, 7.2 and 1.0 Hz, H_6), 6.13 (ddd, J=8.1, 8.1 and 1.1 Hz, H_7), 3.68 (m, H_1), 3.46 (m, H_5), and 2.15—1.6 (4H, m). Found: C, 85.97; H, 6.86%. Calcd for $C_{15}H_{14}O$: C, 85.69; H, 6.71%.

*3- and 1-Methylbicyclo[3.2.2]nona-3,6-dien-2-ones (**5a** and **5b**, respectively).* A mixture of **5a** and **5b**, and unreacted 2-methyltropone (**5**, 8.5%) were separated by preparative GLC (5% PDEGS). The adducts **5a** and **5b** were separated by preparative GLC using a 20 ft × 3/8 in column containing 20% SE-30, at 180 °C. **5a**: Colorless oil; UV$_{\mathrm{max}}$ (CH_3OH) 231.5 (log ε 3.82), 255 (3.68)$^{\mathrm{sh}}$ and 330 nm (2.10); IR (CCl_4) 1668 and 1638 cm^{-1}; NMR ($CDCl_3$) δ=6.91 (dq, J=9.0 and 1.5 Hz, H_4), 6.53 (ddd, J=8.3, 6.3 and 1.2 Hz, H_6), 6.06 (ddd, J=8.3, 7.3 and 1.0 Hz, H_7), 3.55 (m, H_1), 3.30 (m, H_5), 2.0—1.6 (4H, m), and 1.72 (3H, d, J=1.5 Hz); MS (25 eV), *m/e* (rel intensity), 148 (69, M$^+$), 133 (96), 131 (73), 106 (62), 105 (99), 93 (48), 92 (100), and 91 (89). 2,4-DNP of **5a**: mp 193—194.5 °C. Found: C, 58.22; H, 4.81; N, 16.94%. Calcd for $C_{16}H_{16}N_4O_4$: C, 58.53; H, 4.91; N, 17.07%. **5b**: Colorless oil; UV$_{\mathrm{max}}$ (CH_3OH) 227.5 (log ε 3.90) and 326 nm (2.17); IR (CCl_4) 1665 and 1633 cm^{-1}; NMR ($CDCl_3$) $\delta=7.01$ (dd, $J=11.2$ and 8.6 Hz, H_4), 6.53 (dd, $J=8.8$ and 6.2 Hz, H_6), 5.77 (dd, $J=8.8$ and 1.0 Hz, H_7), 5.65 (dd, $J=11.2$ and 0.5 Hz, H_3), 3.30 (m, H_5), 2.0—1.6 (4H, m), and 1.29 (3H, s); MS (25 eV), *m/e* (rel intensity), 148 (69, M^+), 133 (96), 131 (73), 106 (62), 105 (99), 93 (48), 92 (100), 91 (89), 79 (64), and 55 (60).

*2-Oxobicyclo[3.2.2]nona-3,6-dien-3-yl and 7-yl Benzoates (**6a** and **6b**, Respectively).* Chromatography of a mixture of **6a** and **6b**, obtained from 1 g of benzoate of tropolone (**6**), on 50 g of silica gel (elution with benzene–ether, 10:1) gave 320 mg of **6a** and a mixture of **6a** and **6b**. The latter was chromatographed on Florisil (eluted with benzene) yielding 165 mg of **6a**, 363 mg of **6b** and 95 mg of 1 : 1 mixture of them. **6a**: Colorless needles; mp 104—105 °C (from ethanol); UV_{max} (CH_3OH) 232 (log ε 4.37) and 330 nm (2.04); IR (KBr) 1740, 1675, 1643, and 1625 cm^{-1}; NMR ($CDCl_3$) $\delta=8.2$—7.95 (2H, m), 7.65—7.4 (3H, m), 6.87 (d, $J=9.8$ Hz, H_4), 6.67 (ddd, $J=8.7$, 7.2 and 1.0 Hz, H_6), 6.15 (ddd, $J=8.7$, 7.6 and 1.0 Hz, H_7), 3.72 (m, H_1), 3.45 (m, H_5), and 2.2—1.7 (4H, m). Found: C, 75.57; H, 5.57%. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55%. **6b**: Colorless needles (from ethanol); mp 74—75 °C; UV_{max} (CH_3OH) 230.5 (log ε 4.33) and 333 nm (1.83); IR (KBr) 1722, 1672 and 1635 cm^{-1}; NMR ($CDCl_3$) $\delta=8.2$—8.0 (2H, m), 7.6—7.35 (3H, m), 7.00 (dd, $J=11.2$ and 8.5 Hz, H_4), 6.52 (dd, $J=9.0$ and 7.0 Hz, H_6), 6.28 (bd, $J=9$ Hz, H_7), 5.92 (d, $J=11.2$ Hz, H_3), 3.42 (m, H_5), and 2.8—1.75 (4H, m). Found: C, 75.52; H, 5.48%. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55%.

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6) PMO calculations in this paper were performed using NEAC-2200-700 at Tohoku University Computer Center.