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A Remote Substituent Can Determine Magnitude of Facial Selectivity in Benzobicyclo[2.2.2]octatrienes

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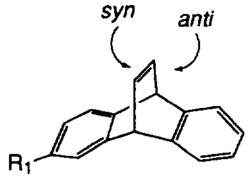
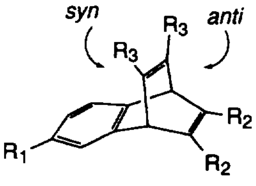
Abstract Benzobicyclo[2.2.2]octatrienes bearing electron-withdrawing groups such as ester and cyano groups on one of the olefin moieties showed *anti*-facial preference toward oxidative electrophiles in epoxidation and dihydroxylation. The magnitude of the selectivity changed significantly upon aromatic nitration.

Remote substituents potentially unsymmetrize the π faces of olefins and ketones.[1,2,3] Facial selectivity in dibenzobicyclo[2.2.2]octatrienes **1** is an example in which the distal substituent (R_1) on the aromatic ring modifies facial selectivity: a nitro group favors *syn* addition of oxidative electrophiles, while a methoxy group shows a negligible preference.[4] This system (**1**) essentially involves orbital interaction of three composite π orbitals, i.e., the olefinic π orbital as the reaction center, and two aromatic π orbitals. We are interested in a simplified interaction network, i.e., *two π component systems free from steric bias*. Herein we describe the facial selectivities of benzobicyclo[2.2.2]octatrienes (**2-5**) bearing two electron-withdrawing groups at one of the olefin groups.[5] Remote substituents do not change facial preference, but do change the magnitude of the selectivity.



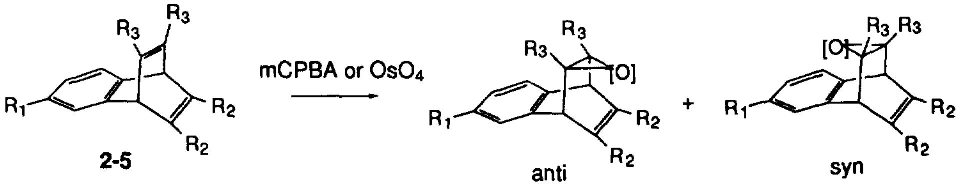
1 (R_1=H, NO_2, OCH_3)



2 - 5a,b

R_1=H, NO_2
R_2=CO_2CH_3,CO_2tBu,CN
R_3=H,CH_3

Unsubstituted benzobicyclo[2.2.2]octatriene **2a** bearing two methoxycarbonyl groups at the C_2 and C_3 positions exhibited strong *anti* preference (with respect to the benzene moiety) with two oxidative electrophilic reagents, m-chloroperbenzoic acid (mCPBA) and osmium tetroxide (Table 1).[6] The diastereomeric excess (d.e.) of **2a** reached 72% (epoxidation) and 98% (dihydroxylation). Nitro



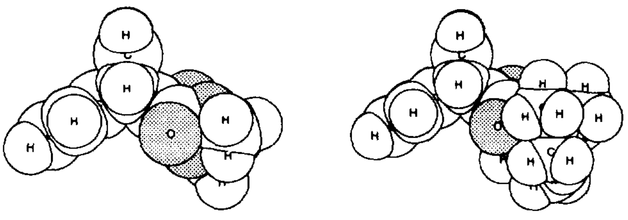
substitution on the aromatic ring (as in **2b**) significantly reduced the selectivity (increased the *syn* proportion), although *anti* preference was still conserved in epoxidation (20% d.e.) and in dihydroxylation (68% d.e.).

Table 1 Selectivities of Benzobicyclo[2.2.2]octatrienes [a,b]

			R_1=H			R_1=NO_2		
R_2	R_3	Reagent		ratio(*anti*:*syn*)	d.e. %		ratio(*anti*:*syn*)	d.e. %
CO_2CH_3	H	mCPBA [c]	**2a**	86:14	72	**2b**	60:40	20
CO_2tBu	H	mCPBA [c]	**3a**	63:37	26	**3b**	54:46	8
CN	H	mCPBA [c]	**4a**	94:6	88	**4b**	79:21	58
CO_2CH_3	CH_3	mCPBA [d]	**5a**	79:21	58	**5b**	61:39	22
CO_2CH_3	H	OsO_4 [e]	**2a**	>99:<1	>98	**2b**	84:16	68
CO_2tBu	H	OsO_4 [e]	**3a**	95:5	90	**3b**	73:27	46

a) *Anti/syn* ratios are determined from signal integration values in the ^1H NMR spectrum. b) Isolated yields of epoxides and diols were 71~91 %. c) The reaction temperature was 23 °C. d) The reaction temperature was 3 °C. e) The reaction temperature was -22 °C.

The *anti* face, i.e., the *syn* side with respect to the diester groups, seems to suffer from steric congestion owing to the out-of-plane conformations of the proximate diester functional groups (Figure 1). This is supported by the results with the bis(*tert*-butoxycarbonyl) compound **3a**: the sterically demanding *tert*-butyl groups did reduce the selectivity in both epoxidation (26% d.e.) and dihydroxylation (90% d.e.). However, *anti* preference survived, indicating that the intrinsic nature of the benzobicyclo[2.2.2]octatriene motif is as proposed. An aromatic nitro group (**3b**) also reduced (in dihydroxylation) or almost abrogated (in epoxidation) the selectivity. *Therefore the selectivity is determined by non-sterical bias.*



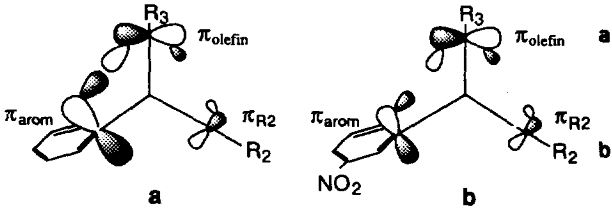
2a **3a**

Figure 1 Schematic Maximum Steric Demand of Out-of-plane Diester Groups

In the case of dicyanodibenzobicyclo[2.2.2]octatriene **4a** and its nitro substrate **4b**, a similar effect on the magnitude of selectivity is observed in the epoxidation reaction. These results exclude a contribution of electrostatic attraction of the reagent to the *anti* side, owing to the electronegative oxygen atoms of the ester groups of **2** and **3**.[7]

Dimethyl substitution (R_2) on the olefin moderately activates reactivity, as in the case of **5a**. Epoxidation occurred readily even at 3 °C. In this case the observed *anti* preference of **5a** was also reduced upon substitution of a nitro group on the aromatic ring (as in **5b**).

These substituent effects on the selectivity might be accounted for in terms of the Cieplak postulate [8]: the nitro substituent reduced the electron-donating effect of the vicinal C-C sigma bond, which is relevant to stabilization of the electron-deficient incipient bond in the *anti* addition transition state. However, comparison of the ^{13}C NMR chemical shifts of the olefinic and bridge-head carbon atoms of the unsubstituted and nitro-substituted substrates, **2a** (139.1 ppm; 50.3 ppm) and **2b** (139.1 ppm and 138.4 ppm; 50.1 ppm), and **4a** (138.0 ppm; 51.7 ppm) and **4b** (138.6 ppm and 138.0 ppm; 51.9 ppm), indicated some shielding shifts upon nitration, tending to rule out significant transmission of the inductive effect of the nitro group to the bridge-head and to the olefin moieties. Within the framework of the perturbation theory,[9,10] the HOMO of dibenzobicyclic **1** can be represented as a combination of the three π orbitals, i.e., $\Psi_{HOMO} = a\pi_{olefin} + b\pi_{aromatic} + c\pi_{aromatic}$. However, owing to the low energy of the π orbital (π_{R2}) of the ethylene substituted with electron-withdrawing groups, the HOMO of **2-5** can be approximated as a two π interacting system (Figure 2): the orbital components of **2-5** are assumed to involve the π orbital (π_{olefin}) of the ethylene (as the reaction center) and that (π_{arom}) of the aromatic ring.[10] In this system, the remote nitro substituent significantly modifies the magnitude of selectivity by causing the *anti*-orbital side of the HOMO π olefin to be less distorted (less unsymmetrized).



a: Unsymmetrization of the π_{olefin} on the side of π_{R2} is much smaller than that on the side of π_{arom} because the π_{R2} orbital is lower-lying in energy due to electron-with-drawing groups.

b: Unsymmetrization of the π_{olefin} on the side of π_{arom} is smaller than that of **2a**, but there is still bias.

Figure 2 Unsymmetrization of the Olefinic π Orbital

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