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# A Cyclopropyl Group Shows Reverse Facial Selectivity Depending on the Bicyclic Ring System

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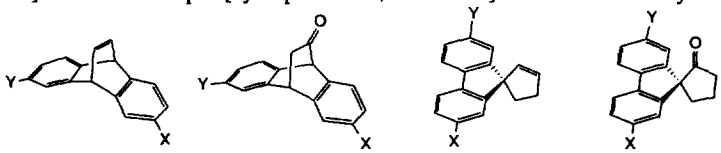
**Abstract** *We describe a reverse perturbation effect of a cyclopropyl group on facial selectivities in two bicyclic systems, bicyclo[2.2.2]octane and norbornane (bicyclo[2.2.1]heptane). In terms of facial selective behavior, the cyclopropyl group embedded in the bicyclo[2.2.2]octene seems to be equivalent to a substitution of an electron-withdrawing group, although this is in sharp contrast to the conventional understanding of this group as strongly electron-donating.* © 1997 Elsevier Science Ltd.

A remote substituent can potentially unsymmetrize the π faces of olefin and ketone compounds. We have detected facial selectivities of non-sterically biased olefins (**1** and **3**) and ketones (**2** and **4**), embedded in dibenzobicyclo[2.2.2]octadiene and spiro[cyclopentane-1,9'-fluorene] motifs.[1, 2] These systems essentially



**1** **2** **3** **4**

involve the interactions of three composite π functional groups, i.e., the olefinic or ketonic π group as the reaction center, and the two aromatic π orbitals. In both systems, the π faces of the olefins and ketones are

**A** **B** **5** **6**

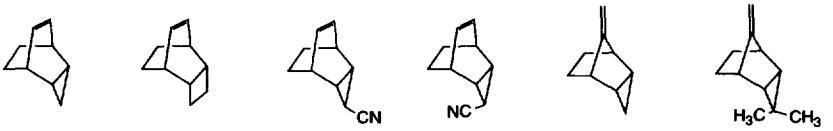
**Figure 1 Different Arrangements of Composite Molecules**

subject to unsymmetrization due to the difference of the aromatic groups (arising from a remote substituent) with respect to the π plane. In terms of the interactions, dibenzobicyclo[2.2.2]octadiene and spiro[cyclopentane-1,9'-fluorene] contain similar composite fragments, but the connectivity of these fragments, i.e., the topology of the π systems,[3] is different (**A** and **B**, Figure 1). This divergent three-dimensional connectivity might modify chemical behaviors such as facial selectivity. While an electron-withdrawing group such as a nitro group (X=$NO_2$,Y=H) on an aromatic ring of the olefins (**1** and **3**) and the ketones (**2** and **4**) favors the *syn* attack of reagents, the perturbation arising from a methoxy group (X=$OCH_3$,Y=H) shows appreciably divergent effects on the facial selectivity depending on the bicyclic system: in the cases of the olefin (**3**) and ketones (**4**) in the spiro system, the aromatic methoxy group favors the *syn* addition of the reagents, while in the dibenzobicyclo[2.2.2]octane system, the methoxy group shows no influence on the facial selectivities of the olefin **1** and the ketone **2**.

**Table 1** Electrophilic Oxidations of Isomeric Bicyclic Olefins.

| | R1 | R2 | Reagent | Time (hr) | Yield | Ratio (*syn*: *anti*) | |
|---|---|---|---|---|---|---|---|
| **5a** | -$(CH_2)$- | | $OsO_4$ [a] | 3 | 91 % | 95 : 5 | *this work* |
| **5a** | -$(CH_2)$- | | mCPBA [b] | 1 | 89 % | 92 : 8 | *this work* |
| **5a** | -$(CH_2)$- | | $B_2H_6$ | - | - | 74 : 26 | *reference 8* |
| **5b** | -$(CH_2)_2$- | | $OsO_4$ [a] | 3 | 100 % | 40 : 60 | *this work* |
| **5b** | -$(CH_2)_2$- | | mCPBA [b] | 1 | 97 % | 42 : 58 | *this work* |
| **5c** | -(CH)-*exo*-CN | | $OsO_4$ [a] | 2 | 71 % | 98 : 2 | *this work* |
| **5c** | -(CH)-*exo*-CN | | mCPBA [b] | 165 | 89 % | 82 : 18 | *this work* |
| **5d** | -(CH)-*endo*-CN | | $OsO_4$ [a] | 2 | 66 % | >99 : <1 | *this work* |
| **5d** | -(CH)-*endo*-CN | | mCPBA [b] | 71 | 95 % | 94 : 6 | *this work* |
| **5e** | CN | H | $OsO_4$ [a] | - | - | 86 : 14 | *reference 17* |
| **5e** | CN | H | mCPBA [b] | - | - | 85 : 15 | *reference 17* |
| **5f** | $CO_2CH_3$ | H | $OsO_4$ [a] | - | - | 84 : 16 | *reference 17* |
| **5f** | $CO_2CH_3$ | H | mCPBA [b] | - | - | 68 : 32 | *reference 17* |
| **6a** | -$(CH_2)$- | | $OsO_4$ [a] | 3 | 67 % | 12 : 88 | *this work* |
| **6a** | -$(CH_2)$- | | $CCl_2$ | - | - | 44: 56 | *reference 9* |
| **6a** | -$(CH_2)$- | | 9-BBN | - | - | 11: 89 | *reference 9* |
| **6b** | -$C(CH_3)_2$- | | $CCl_2$ | - | - | 34 : 66 | *reference 9* |
| **6b** | -$C(CH_3)_2$- | | 9-BBN | - | - | 5 : 95 | *reference 9* |
| **6c** | Et | Et | mCPBA | - | - | 30 : 70 | *reference 11* |
| **6c** | Et | Et | $B_2H_6$ | - | - | 38 : 62 | *reference 11* |

a) Pyridine, -23 °C. b) $CHCl_3$, 3 °C.




**5a** **5b** **5c** **5d** **6a** **6b**

Herein, we describe a reverse perturbation effect of a cyclopropyl group on facial selectivities in two bicyclic systems, bicyclo[2.2.2]octane **5** and norbornane (bicyclo[2.2.1]heptane) **6**. Bicyclo[2.2.2]octene **5a**, annulated with an *exo*-cyclopropyl group, i e., *exo*-tricyclo[3.2.2.$0^{2,4}$]non-6-ene,[4] and 7-methylene-norbornane **6a**, annulated with an *endo*-cyclopropyl group, i.e., 8-methylene-*endo*-tricyclo[3.2.1.$0^{2,4}$]octane,[5] are isomers wherein the olefin group is faced with the same structural units while the orientations of the olefin are different (**5** as in **A**, and **6** as in **B**, Figure 1). The annulated cyclopropyl group introduces no direct steric bias in either of these bicyclic systems.[6,10] Thus, the reactivities of the olefin, in particular the facial selectivities are expected to be similar. However, experimentally this is not the case. Dihydroxylation of **5a** with osmium tetroxide in pyridine and epoxidation of **5a** with *m*-chloroperbenzoic acid (mCPBA) both showed high *syn* preference of the addition ($OsO_4$: *syn*: *anti*=95:5; mCPBA: *syn*; *anti*=92: 8 ) (Table 1).[7] This preference is in sharp contrast to the *anti* preference of **6a** (*syn*: *anti* = 12: 88), observed under similar dihydroxylation conditions with osmium tetroxide in pyridine (Table 1).[7] While the facial selectivity of **6a** has been examined previously,[9,13] that of **5a** has been little studied,[8] and the topology-dependent behavior described here has not previously been documented nor characterized.

The *anti* facial preference of the norbornane **6a** was previously found in the additions of dichlorocarbene (*syn*; *anti* = 44: 56)[9] and of 9-BBN (*syn*; *anti* = 11: 89).[9] The *anti*-preference was also observed in the reactions of methylidenebicyclo[2.2.1]heptane (**6b**) bearing an *endo*-dimethylcyclopropyl group ($R_1$,$R_2$=$C(CH_3)_2$)[9] with dichlorocarbene (*syn*; *anti* = 34: 66) and 9-BBN (*syn*; *anti* = 5: 95). Therefore, we can conclude that the *anti*-

preference, induced by a cyclopropyl group, is intrinsic to the methylidene-norbornane **6a**. The *anti* preference was also observed in alkyl-substituted **6c** ($R_1$=$R_2$=Et), supporting the idea that a cyclopropyl group behaves as an electron-donating substituent.[11]

On the other hand, the observed *syn* preference of **5a** is consistent with the previous study of hydroboration of **5a** with diborane by Schueler and Rhodes,[8] who obtained a mixture of the monoalcohols (*syn*:*anti*=74: 26) upon oxidative work-up. A similar magnitude of the *syn*-preference was found (*syn*:*anti*=73: 27) in the hydroboration with a bulkier borane, 2,3-dimethyl-2-butylborane (thexyl borane).[8] This lack of effect of the bulk of the reagent in the hydroboration of **5a** is consistent with the idea that the π face of **5a** is free from steric bias,[8] and that the *syn* preference of **5a** found in dihydroxylation and epoxidation is non-sterically determined.[6]

The *syn*-preference of **5a** is concluded to be attributed to the fused cyclopropyl ring, based on the observation that the bicyclo[2.2.2]octene (**5b**) fused with a cyclobutane ring ($R_1$,$R_2$=$(CH_2)_2$)[12] changes the preference to the *anti* direction, in both the dihydroxylation (*syn*; *anti* = 40: 60) and epoxidation (*syn*; *anti* = 42: 58).[7] The *anti*-preference of the 7-methylene-norbornane **6a** is also diminished when the cyclopropyl ring is replaced with a cyclobutane ring; in the attack of diphenylketene, the *syn*; *anti* ratio is 45: 55.[13]

A cyclopropyl group is known to act as a strong π donor due to a high-lying occupied Walsh orbital, which is frequently regarded as an equivalent of a double bond.[14,15,16] Photoelectron spectra of the olefins **5a** and **6a** were previously measured and the signals were assigned.[16] Vertical ionization potentials of the olefin π orbitals of **5a** and **6a** were found to be higher than those of the unsubstituted parent bicyclo[2.2.2]octene **5** ($R_1$=$R_2$=H) and 7-methylene-norbornane **6** ($R_1$=$R_2$=H), respectively, indicating a sizable interaction of the π orbital of the double bond with the occupied Walsh orbital of the fused cyclopropane ring. The previous account of the observed *anti* facial preference of **6a** was based on this interaction, in particular, out-of-phase interaction of the relevant orbitals (Figure 2 (b)).[9,13] Out-of-phase orbital motif in the neighborhood of the reaction center

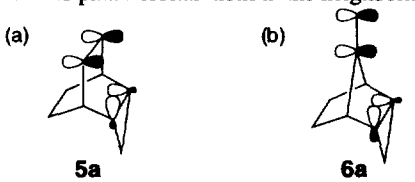



**Figure 2**

has been proposed to be generally crucial for the facial selectivities of olefins.[1,2,17] However, the corresponding out-of-phase interaction of the olefinic π orbital with the Walsh orbital of the cyclopropyl group (Figure 2 (a)) seems not to be relevant to **5a**, because of the observed reverse *syn* preference.

This view is consistent with the following observation. Because substitution of a cyano group on the cyclopropane ring lowers the energy of the Walsh orbital of the cyclopropyl group,[18] the resultant attenuation of the interaction of the olefin orbital with the Walsh orbital, if this interaction is indispensable, would reduce the facial selectivity. However, substitution of a cyano group on the cyclopropyl group as in *exo*-cyano **5c** and *endo*-cyano **5d** essentially does *not* modify the *syn*-preference in dihydroxylation and epoxidation, but even increases the *syn* preference (**5c** (98: 2) and **5d** (>99:<1)) in the case of dihydroxylation.[7]

Phenomenologically, the effect of the cyclopropyl group observed in the bicyclo[2.2.2]octene (**5a**) is equivalent to that of an electron-withdrawing substituents, such as a cyano (**5e**) or a methoxycarbonyl (**5f**) group, which shows *syn* preference in dihydroxylation and epoxidation (Table 1).[17] Thus, in summary, a cyclopropyl group can produce a reverse facial selectivity, strongly depending on the orientation of the olefin

group. In terms of facial selective behavior, the cyclopropyl group embedded in the bicyclo[2.2.2]octene (**5a**) seems to be equivalent to a substitution of an electron-withdrawing group, although this is in sharp contrast to the conventional understanding of this group as strongly electron-donating.[16,19] We are attempting to rationalize these observed divergent behaviors.

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