

## ORBITAL DISTORTION IN DIBENZOBICYCLO[2.2.2]OCTATRIENES. BIASED EPOXIDATION AND DIHYDROXYLATION OF THE OLEFIN MOIETY

Naoki HAGA, Tomohiko OHWADA, \* Iwao OKAMOTO, and Koichi SHUDO

Faculty of Pharmaceutical Sciences, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan

Epoxidation and dihydroxylation of the olefin moiety of 2-substituted dibenzobicyclo[2.2.2]octatrienes were investigated. These reactions exhibited substituent effect: 2-nitrodibenzobicyclo[2.2.2]octatriene gave predominantly the *syn*-epoxide and the *syn*-diol, with a diastereomeric excess of 54 % to 76 %, respectively. On the other hand, the 2-methoxy substrate showed only a small preference in the reactions, giving a slight excess of the *anti*-products. This effect can be interpreted in terms of the perturbation of the occupied  $\pi$  orbital of the ethylene moiety arising from the mixing of the  $\pi$  orbitals (in particular, the HOMO) of convex-substituted dihydroxyanthracene, wherein the  $\sigma$  type overlaps are involved in a manner similar to the longicyclic conjugation.

**KEYWORDS** orbital distortion; olefin; dibenzobicyclo[2.2.2]octatriene; diastereomeric excess

An unsymmetrical  $\pi$  face of a carbonyl or an olefin group is a reasonable consequence of the presence of an intrinsically nonequivalent substituent.<sup>1, 2)</sup> Reagents which can probe such asymmetry of the reaction center will yield a biased distribution of products. Several different ideas have been proposed and discussed so far to explain these biased reactions.<sup>3, 4, 5)</sup> We have been interested in the possible modification of these  $\pi$  orbitals arising from an interaction of  $\pi$  fragments in a molecule.<sup>6)</sup> In this paper we will describe detection of the unsymmetrical  $\pi$  face of the olefin group in 2-substituted dibenzobicyclo[2.2.2]octatrienes.<sup>7)</sup> This asymmetry can modulate the epoxidation and dihydroxylation of the olefin moiety. 2-Nitrodibenzobicyclo[2.2.2]octatriene **1b** undergoes preferential *syn*-addition (with respect to the nitro group) of peroxidic reagents, i. e., *m*-chloroperbenzoic acid, osmium tetroxide and potassium permanganate. The results are summarized in Table I, together with those for the parent **1a**. In the epoxidation of **1b** with *m*CPBA, the *syn* epoxide **2b-syn** is favored over the *anti* epoxide **2b-anti**.<sup>8)</sup> In the dihydroxylation with osmium tetroxide<sup>9)</sup> or potassium permanganate,<sup>10)</sup> the *syn* diol **3b-syn** is also favored over the *anti* diol **3b-anti**.<sup>11)</sup> The epoxidation with *m*CPBA at high reaction temperature (20 °C) did not significantly alter the ratio of *syn* to *anti* isomers (see Table I). Diastereomeric excess recorded in these reactions amounted to 54 % to 76 %. Direct participation of the oxygen atoms of the nitro group at the reaction center, as a coordinative interaction, cannot account for these results, judging from the distance (at least 6 Å) from the ethylenic carbon atom.

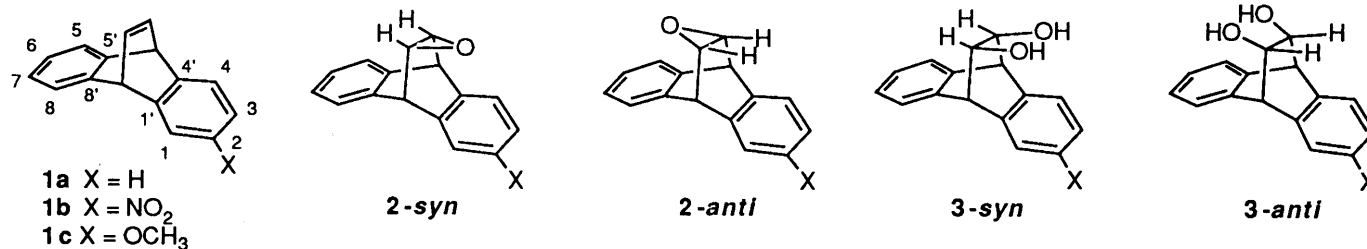
Symmetry in these reactions allows the interaction of a vacant MO of the peracid, the permanganate ion, and osmium tetroxide with the occupied MO of the ethylenic  $\pi$  bond (in particular, the HOMO).<sup>12)</sup> In order to reveal the perturbation of the  $\pi$  orbital of the ethylene moiety arising from the

**Table I. Isomer Distributions in the Attack of Electrophilic Oxidative Reagents on 2-Substituted Dibenzobicyclo[2.2.2]octatrienes**

Substituent X	Reagent	Conditions	Yield	<i>syn: anti</i>
H	<i>m</i> CPBA	0 °C, 41 h	88 % <sup>a)</sup>	50 : 50
H	OsO <sub>4</sub>	-27 °C, 3 h	90 %	50 : 50
H	KMnO <sub>4</sub>	-14 °C, 0.5 h	58 %	50 : 50
NO <sub>2</sub>	<i>m</i> CPBA	0 °C, 48 h	46 % <sup>b, c)</sup>	77 : 23
NO <sub>2</sub>	OsO <sub>4</sub>	-27 °C, 3 h	67 %	85 : 15
NO <sub>2</sub>	KMnO <sub>4</sub>	-14 °C, 0.5 h	48 %	88 : 12
OCH <sub>3</sub>	<i>m</i> CPBA	0 °C, 42 h	63 %	48 : 52
OCH <sub>3</sub>	OsO <sub>4</sub>	-27 °C, 1.5 h	96 %	48 : 52

a) 20 °C, 2 hrs: 83 % yield. b) 43 % recovery. c) 20 °C, 48 hrs: 89 % (*syn: anti* = 76: 24).

nonequivalent substituent in the substituted dibenzobicyclo[2.2.2]octatrienes, the molecules are assumed to be constructed from the orbitals of the convex-substituted dihydroanthracene and the ethylene. The  $\pi$  orbitals of the dihydroanthracene can be further analyzed as a combination of  $\pi$  orbitals of the two aromatic moieties. The HOMO's of the substituted dihydroanthracene in convex geometry are essentially derived from the out-of-phase combination of the HOMO's of the two aromatic nuclei.<sup>13, 14, 15)</sup> Thus, the



HOMO of substituted dihydroanthracene is energetically high-lying as compared with the HOMO (MNDO: -10.17 eV) of the ethylene. The lower-lying HOMO of the ethylene can mix with the HOMO of the substituted dihydroanthracene in an out-of-phase fashion to give the high-lying hybridized HOMO of the whole molecules, which will determine the direction of attack of the vacant orbital of the oxidative reagent. The HOMO of 2-nitrodihydroanthracene is essentially localized on the unsubstituted benzene moiety, stemming predominantly from the HOMO (MNDO: -9.39 eV; degenerate) of benzene, which is higher in energy than the HOMO (MNDO: -10.31 eV and -10.48 eV; almost degenerate) of the nitrobenzene.<sup>16)</sup> The orbital phase agreement favors the interaction of the ethylene (HOMO) with the HOMO (MNDO: - 9.60 eV) of the 2-nitrodihydroanthracene. The out-of-phase overlap of these  $\pi$  orbitals raises the energy of the olefin moiety, involving the depletion of the electron density in the interacting region, i.e., the antibonding orbital diffusion (Chart 1).<sup>6b, 17)</sup> Therefore the electrophilic oxidative reagents attack the olefinic  $\pi$  lobe opposite the antibonding region, that is, from the same side as the substituent.

In the case of an electron-donating hydroxy group, the HOMO of 2-hydroxydihydroanthracene can also be derived from the out-of-phase combination of the HOMO's of benzene and phenol (MNDO: - 8.89 eV): the latter is higher in energy than the former, having a smaller energy separation as compared with the case of the combination of benzene and nitrobenzene.<sup>16)</sup> Therefore the HOMO (MNDO: - 8.80 eV) of 2-hydroxydihydroanthracene has biased orbital magnitudes favoring the phenol moiety, though the

diversity of the two rings is smaller than in the HOMO of 2-nitrodihydroxy-anthracene. These biased magnitudes perturb the  $\pi$  orbital of the ethylene in the out-of-phase mixing, favoring the *anti*-attack of an electrophile. However, the large energy gap of these two interactive fragments would decrease the effect. The reactions of 2-methoxydibenzobicyclo[2.2.2]octatriene **1c** with *m*CPBA and osmium tetroxide were also investigated, indicating a slightly biased  $\pi$  face of the olefin moiety (Table I). The small but consistent preference for *anti*-attack of the reagents, i.e., formation of **2c-anti** and **3c-anti**, in these two reactions is compatible with the orbital mixing model.<sup>8,11)</sup>

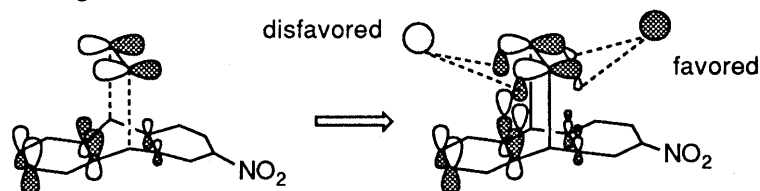


Chart 1

## REFERENCES AND NOTES

- 1) M. Cherest, H. Felkin and N. Prudent, *Tetrahedron Lett.*, 2201, 2205 (1968). N. T. Anh and O. Eisenstein, *Nouv. J. Chim.*, **1**, 62 (1977).
- 2) C. K. Chung, L. T. Tseng, M. -H. Lin, S. Srivastava and W. J. le Noble, *J. Am. Chem. Soc.*, **108**, 1598 (1986); W. -S. Chung, N. J. Turro, S. Srivastava, H. Li and W. J. le Noble, *ibid.*, **110**, 7882 (1988); S. Srivastava and W. J. le Noble, *ibid.*, **109**, 5874 (1987).
- 3) A. S. Cieplak, *J. Am. Chem. Soc.*, **103**, 4540 (1981); C. R. Johnson, B. D. Tait and A. S. Cieplak, *ibid.*, **109**, 5875 (1987).
- 4) G. Frenking, K. F. Köhler and M. T. Reetz, *Angew. Chem. Int. Ed. Engl.*, **30**, 1146 (1991).
- 5) Y-D. Wu, J. A. Tucker and K. N. Houk, *J. Am. Chem. Soc.*, **113**, 5018 (1991).
- 6) a) T. Ohwada and K. Shudo, *Chem. Pharm. Bull.*, **39**, 2176 (1991); b) T. Ohwada, *J. Am. Chem. Soc.*, **114**, 8818 (1992).
- 7) H. P. Figeys and A. Dralants, *Tetrahedron* **28**, 3031 (1972). 2-Nitrodibenzobicyclo[2.2.2]octatriene **1b** was prepared by usual nitration of the parent **1a**. 2-Methoxydibenzobicyclo[2.2.2]octatriene **1c** was prepared from the 2-nitro derivative **1b** through reduction, diazotization, hydrolysis and methylation.
- 8) The configuration of the major isomer of the epoxide of **1b** (**2b-syn**) was elucidated by X-ray crystallographic analysis. We thank Dr. Kentaro Yamaguchi, Showa College of Pharmacy, for conducting this analysis. The configurations of the epoxides **2c** were also elucidated on the basis of the <sup>1</sup>H NMR spectra. The solid epoxides (**2b**) are satisfied with the combustion analysis.
- 9) A slight excess (1.1 eq.) of osmium tetroxide was used in pyridine.
- 10) An excess (1.5 eq.) of potassium permagnate was used in a mixture of pyridine and water.
- 11) The diols **1b** and **3b-syn** can be converted to dimethyl acetals, confirming the *cis* relationship. NOE enhancement between the acetal methyl protons (of the more deshielded methyl group) and the aromatic protons (H<sub>1</sub>-H<sub>4</sub>) also supports the configurations. All the isolated compounds are satisfied with the combustion analysis. The inseparable diols **3c** were converted to the dimethyl acetals which can be separated, and are satisfied with the combustion analysis.
- 12) K. Fukui, *Bull. Chem. Soc. Jpn.*, **39**, 498 (1966).
- 13) The convexity brings the two aromatic  $\pi$  orbitals close together, favoring through-space coupling. In the case of the planar dihydroanthracene, the through-bond coupling of the two aromatic  $\pi$  orbitals through the pseudo  $\pi$  orbital ( $\pi_{CH_2}$ ) of the insulating methylene group modulates the level ordering: the in-phase combination of the HOMO's of the two aromatic rings is higher in energy than the out-of-phase combination. R. Hoffmann, *Acc. Chem. Res.*, **4**, 1 (1971); T. A. Albright, J. K. Burdett and M-H. Whangbo, "Orbital Interactions in Chemistry," John Wiley & Sons, Inc., New York (1985); P. H. Mazzocchi, B. Stahly, J. Dodd, N. G. Rondan, L. N. Domelsmith, M. D. Roseboom, P. Caramella and K. N. Houk, *J. Am. Chem. Soc.*, **102**, 6482 (1980).
- 14) Calculations on the minimal STO-3G basis sets showed that the orbital level ordering (in particular, of  $\pi$  orbitals) of the 1,4-cyclohexadiene (CHD) depends on the geometry. The HOMO (-0.2841 au) of the planar CHD is in in-phase combination of the olefinic  $\pi$  orbitals while that (-0.2942 au) of the convex CHD is essentially in out-of-phase combination.
- 15) K. Fukui, *Science*, **218**, 747 (1982), and references cited therein.
- 16) A. Pross and L. Radom, *Prog. Phys. Org. Chem.*, R. Taft, Ed., vol **13**, 1 (1981).
- 17) The removal of bonding electron from the internuclear region is regarded as diffusion of the electron of each fragment into each antibonding region along the internuclear axis. For details see ref 6b.

(Received October 5, 1992)