of the two acetates was noted.

Method B. In a dry flask under nitrogen atmosphere were added 10 mg of 14, 3 mL of acetic anhydride, and one drop of concentrated HCl. After the mixture was stirred at room temperature for 1 h, the excess acetic anhydride was removed by rotary evaporation and the residue was taken up in dichloromethane. The workup was the same as in method A, to give a quantitative yield of the two acetates (1:1): ^{1}H NMR (on mixture) δ 6.18 and 6.13 (1 H, s, vinyl proton), 2.29 and 2.28 (3 H, s, acetate methyl), 2.15–1.20 (11 H, m), 1.04 and 1.01 (3 H, d, *J* = 2.4 Hz, isomeric methyl groups); HRMS for $C_{14}H_{18}O_2$, calcd 234.1232, found for 19, 234.1244, found for 20, 234.1244.

Preparation of 4-Methoxy-8-methyltricyclo[3.3.3.0]undec-3-en-2-one (21). A solution containing 20 mL of absolute MeOH and two drops of concentrated HCl was stirred under a nitrogen atmosphere while 570 mg of 18 was added in a minimum amount of methanol. This reaction mixture was stirred at reflux for 36 h, after which time the solvent was removed to leave about 600 mg of crude product. The crude product was subjected to flash chromatography (8:2, hexane–ethyl acetate) to give two fractions. The first fraction contained the desired 21 (379 mg) and the second fraction contained starting material (223 mg). On the basis of recovered starting material, this constituted a quantitative conversion. ^{1}H NMR δ 5.14 (1 H, s), 3.81 (3 H, s), 2.02 (1 H, m), 1.81 (4 H, m), 1.70–1.20 (10 H, m), 1.02 (3 H, d, *J* = 6.7 Hz); ^{13}C NMR δ 207.1 (s), 191.8 (s), 104.1 (d), 69.9 (s), 64.4 (s), 58.3 (q), 42.6 (d), 35.0 (t), 34.9 (t), 34.7 (t), 33.0 (t), 26.9 (t), 14.9 (q), *no* evidence in for any isomer; HRMS for $C_{13}H_{18}O_2$, calcd 206.1307, found 206.1320.

Preparation of 4,6-Dimethyltricyclo[3.3.3.0]undec-3-en-2-one (5). In a nitrogen-flushed flask were injected 20 mL of dry toluene and 370 mg of 21. This was followed by 5 equiv of MeLi. After refluxing for 24 h the reaction was quenched with MeOH, rinsed with 5% HCl, and then dried. Removal of solvent left 306 mg of a yellow oil. Flash chromatography (7:3 hexane–ethyl acetate) afforded two fractions. The second fraction was shown to be 79% 5: ^{1}H NMR δ 5.81 (1 H, d, *J* = 2.6 Hz), 2.08 (3 H, d,

J = 2.6 Hz), 2.00–1.20 (11 H, m), 0.97 (3 H, d, *J* = 6.9 Hz); HRMS for $C_{13}H_{18}O$, calcd 190.1355, found 190.1356.

Synthesis of Modhephene. A flame-dried flask was placed under an argon atmosphere and charged with 20 mL of freshly distilled dichloromethane. After the mixture was cooled to 0 °C, 1 equiv of TiCl$_4$ was added, followed by 2 equiv of dimethylzinc.[11] The presence of the Me$_2$Ti could be ascertained from the proton NMR spectrum, where the methyl resonance appears at –1.90 ppm (Me$_2$Zn has a methyl resonance at –1.90 ppm). After the mixture was cooled at 0 °C for 15 min, 239 mg of 5 was injected into the reaction vessel. The reaction mixture was protected from light and was allowed to stir overnight. *In the hood*, the reaction mixture was quenched by pouring the contents into a beaker and cautiously adding methanol and dry ice. When the evolution of gases had ceased, the reaction mixture was diluted with saturated ammonium carbonate and extracted with dichloromethane. Following drying and removal of solvents, there remained a liquid that was shown to consist of 200 mg of unreacted starting material and 20 mg of modhephene. We made no attempts to maximize yields or to recycle the starting material. The mass spectral fragmentation patterns of our synthetic material matched those for synthetic modhephene: HRMS for $C_{15}H_{24}$, calcd 204.1767, found 204.1822.

The Oxyiodination of 5,8-Dimethoxy-1,4-dihydro-1,4-ethanonaphthalene

William B. Smith

Department of Chemistry, Texas Christian University, Fort Worth, Texas 76129

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The Wagner–Meerwein rearrangements produced when iodine is added to 5,8-dimethoxy-1,4-dihydro-1,4-ethanonaphthalene (5,8-dimethoxybenzobicyclo[2.2.2]octadiene) in water, methanol, a water–methanol mixture, and acetic acid, respectively, have been studied. The amount of addition anti to the aryl ring increased directly with the electrophilic strength of the reagent. This result is consistent with the increasing importance of a homoconjugative stabilization of the transition state with weaker electrophiles. The results stand in contrast to earlier predictions based on MINDO/3 calculations.

Recently, Paquette et al.[1] have published an extensive experimental and theoretical study of electrophilic additions to a series of rigid olefins containing aryl groups located in such a fashion that π-electron interactions between the two systems might occur. The contrasting stereoselection offered by weak and strong electrophiles has been detailed. Of particular interest here are those additions in the benzobicyclo[2.2.2]octadiene systems I.[1b] Among the reactions studied were photooxidation, ep-
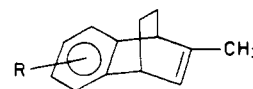

Ia, R = H
b, R = 5,8-(OCH$_3$)$_2$
c, R = 5,6,7,8-(F)$_4$

oxidation, cyclopropanation, oxymercuration, and hydroboration. For each substrate and in each reaction it was found that electrophilic attack came preponderantly from the sterically more favored side of the double bond syn to the aromatic ring. In discussing these results, they produced a list of five potential contributing factors that might influence the course of these additions. Most obvious of these was the steric interference offered by the ethano

(1) (a) Paquette, L. A.; Hertel, L. W.; Gleiter, R.; Bohm, M. C.; Beno, M. A.; Christoph, G. C. *J. Am. Chem. Soc.* **1981**, *103*, 7106–7121. (b) Paquette, L. A.; Bellamy, F.; Wells, G. J.; Bohm, M. C.; Gleiter, R. *Ibid.* **1981**, *103*, 7122–7133. (c) Paquette, L. A.; Klinger, F.; Hertel, L. W. *J. Org. Chem.* **1981**, *46*, 4403–4413.

bridge protons to the anti mode of addition. A significant through-space interaction of the aryl π-electron system with the developing positively charged center was ruled out both as a consequence of the experimental observations and as a result of MINDO/3 calculations carried out on these systems. (Actually the calculations were done on I minus the olefin methyl group.) These calculations were reported as indicating an interaction of the σ-bonded electrons of the molecular frame with the π-electrons of the double bond. The consequence was a concentration of charge density on the syn face of the double bond. It is the purpose of this article to summarize existing data and to present new experimental evidence supporting the thesis that, in fact, a weak π-electron interaction does exist in these systems and that it may become an important factor in determining the stereochemistry of addition for weak electrophiles.

Shortly after the publication of the above, a study of the epoxidation of a related series of benzobicyclo[2.2.2]octadienes (II) in a variety of solvents appeared.[2] As in the
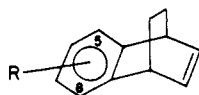
IIa, R = 5,8-(OAc)₂
  b, R = 5,8-(OCH₃)₂
  c, R = 6-NO₂-5,8-(OCH₃)₂

report above, m-chloroperoxybenzoic acid in methylene chloride, benzene, or acetonitrile was found to react rapidly, primarily with syn attack. However, in oxygen-containing solvents (diethyl ether, dimethoxyethane, ethyl acetate) the rate of the reaction was considerably decreased. Furthermore as the reactivity was muted by the solvent change, the stereoselectivity of the reagent altered in favor of the formation of the sterically less favored anti epoxides. These results were interpreted as indicating that as hydrogen bonding to the solvent increased, the internal hydrogen-bonded structure of the peracid was disrupted with a consequent weakening of its electrophilic character. The enhanced selectivity of the peracid suggested that homoconjugation in the transition state for epoxidation became increasingly important in determining product stereochemistry. Subsequent to this report, the epoxidation of Ib in ether was carried out.[3] The ratio of syn to anti epoxides (oxygen in relation to aryl ring) was found to be 0.85 in ether as opposed to the reported value of 1.7 in chloroform.[1b] This result is detailed in the Experimental Section.

The Paquette group[1b] deliberately avoided the use of electrophiles which might lead to rearrangements of the molecular skeleton on the grounds that phenonium ion formation in the Wagner–Meerwein rearrangement might obscure the interplay between steric factors and electronic interactions in the transitions states leading to product formation. The results of the Barkhash group in Russia were cited regarding the addition of bromine to tetra-fluorobenzobicyclo[2.2.2]octadiene (Ic less the methyl) which was reported to yield only the product of trans addition to the double bond.[4] In contrast, addition of acetyl hypochlorite gave only the rearranged product III. Chlorination gave a mixture of trans addition and rearrangement forming the dichloro analogue of III. Strangely, both of the reported rearranged products in these tetra-
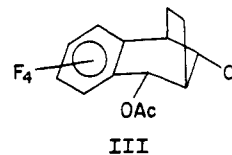

III

fluorobenzobicyclo[2.2.2] octadiene additions involve the attack of the electrophile on the sterically more favored side of the olefin and subsequent migration of the ethano bridge. No involvement of phenonium ions is indicated in these reactions.

The major tool used for the structural assignments in the Barkhash study was 100-MHz proton NMR spectroscopy, which produced spectra of limited dispersion and resolution permitting only partial analysis.[5] Reservations regarding these structures have been expressed before.[6] In summary, these proton spectra are described by eleven vicinal and two geminal proton–proton coupling constants as well as eight chemical shifts. Furthermore, there are uncertainties in the application of the Karplus equation both in strained systems and in systems containing electronegative substituents. Even complete proton NMR analysis leaves exact structural assessment in doubt.

The bromination of IIa has been shown to yield only one product.[6] The complete panoply of high-field 1-D and 2-D proton and carbon NMR spectra were brought to bear in establishing the structure of product as IV. Clearly attack
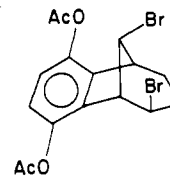
IV

has occurred from the sterically less favored side of the double bond with subsequent aryl migration. While the aryl π-electron densities must be different in the IIa and the tetrafluoro compound above, this result stands in rather striking contrast to the Russian results.

In the earlier work,[2] the addition of hypoiodous acid to IIb was reported to give Va below. This result corresponds to the expectations from the results of both the Paquette and Barkhash groups, i.e., syn electrophile attack with subsequent ethano bridge migration. Since the steric consequences of epoxidation can be altered by changing the strength of the electrophile, it seemed a real possibility that a similar effect was in operation in reactions involving Wagner–Meerwein rearrangement. What was required was a series of closely related reagents with rational differences in electrophilic character. The oxyiodination reaction appeared to offer an ideal set of reagents for this purpose, and the results of this study are reported below.

Experimental Section

The preparation of 5,8-dimethoxy-1,4-dihydro-1,4-ethano-naphthalene has been described previously.[2] All other reagents were used as supplied by the Aldrich Chemical Co. NMR spectra were determined in deuterochloroform with Me₄Si as an internal standard on a Varian XL-300 operating at 300 MHz for protons and 75 MHz for carbon. In addition to the standard spectra, the relative lanthanide shifts were determined, and conformational studies utilizing NOE-difference spectra were carried out. The 2-D INADEQUATE spectra were determined for Va and Vb.[7]

(2) Smith, W. B.; Stock, L.; Cornforth, Sir J. *Tetrahedron* **1983**, *39*, 1379–1385.

(3) Appreciation is extended to undergraduate research student Vincent Michaud who carried out the synthesis and epoxidation of Ib.

(4) Provoloskaya, N. N.; Limosova, T. I.; Berus, E. I.; Exner, O.; Barkhash, V. A. *J. Org. Chem. USSR (Engl. Transl.)* **1970**, *6*, 1615–1622.

(5) Access to copies of these spectra was kindly provided by Professor Harry Heaney of The University of Loughborough.

(6) Smith, W. B.; Saint, C.; Johnson, L. *J. Org. Chem.* **1984**, *49*, 3771–3774.

Homonuclear and heteronuclear correlation spectra were determined for all compounds. Because of the extensive and specialized nature of these spectral studies, these data will appear elsewhere.[8] However, for convenience the ^{13}C chemical shifts are included by assigned carbon. Melting points were determined on a Kofler Heizbank. Gas chromatographic analyses were carried out on a Perkin-Elmer Sigma-3 instrument using a 6 ft × $^1/_8$ in. glass column packed with 3% OV-17 on Chromosorb W. The following temperature regimen was used throughout: 1 minute at 175 °C, programmed temperature advance at 15°/min to 250 °C and 5 min at 250 °C. Peak areas were determined by cutting out and weighing. Elemental analyses were performed by high-resolution mass spectrometry by Dr. David Russell of Texas A&M University.

Reactions in Water. (a) The dimethoxyolefin IIb was reacted with iodine–iodic acid in water–sulfolane as described previously.[2] The olefin (0.40 g) in 5 mL of sulfolane and 1 mL of water was allowed to react at room temperature with stirring with 0.19 g of iodine and 0.065 g of iodic acid for 18 h. The mixture was poured into 50 mL of dilute sodium thiosulfate solution and extracted with two 50-mL portions of 1:1 petroleum ether (low boiling)–benzene. The solvent was removed by evaporation under reduced pressure, yielding 0.72 g of crude product. This workup procedure will be referred to hereafter as the standard procedure. Gas chromatographic analysis indicated no starting material, ca. 80% of the previously reported iodohydrin Va (mp 172–174 °C from methanol, reported[2] mp 175 °C, and 20% of a new material, VIa. As noted above, Va was subjected to complete NMR analysis: ^{13}C NMR δ 71.28 (C1), 43.40 (C2), 23.07 (C3), 40.93 (C4), 131.50 (C4a), 149.96 (C5), 110.72 (C6), 108.44 (C7), 152.49 (C8), 123.84 (C8a), 29.69 (C9), 25.92 (C10), 55.55 and 56.40 (CH$_3$'s). TLC of the reaction product showed a slight separation of Va and VIa with 5% ethyl acetate in toluene. The separation could not be realized at the preparative TLC level though a variety of solvent compositions were tried. Consequently, VIa was characterized by ^{13}C NMR from the residue following removal of the majority product by crystallization. The chemical shifts were very similar to those for VIb below given allowances for the conversion of a hydroxyl group to a methoxyl: ^{13}C NMR δ 46.45 (C1), 67.06 (C2)8 26.97 (C3), 20.81 (C4), 42.85 (C5), 130.87 (C5a), 147.82 (C6), 110.11 (C8), 131.84 (C9), 30.89 (C10), 56.48 and 57.37 (2C, CH$_3$'s). Carbons 7 and 9a were hidden under other peaks.

(b) The above procedure was repeated with the exception that dioxane replaced the sulfolane. The product (0.64 g) was obtained as above, and the GC analysis was identical.

Reactions in Methanol. (a) A solution of 2.0 g (9.3 mmol) of dimethoxyolefin IIb in 30 mL of methanol was reacted for 3 days at room temperature with 2.54 g of iodine and 2.3 g of copper acetate monohydrate.[9] The standard workup was applied yielding 3.0 g of material, which analyzed by GC as 18% starting material, 47% Vb and 35% VIb. Since the products were better prepared by the procedure below, their description is deferred.

(b) A solution of 0.43 g (2 mmol) of dimethoxyolefin IIb in 25 mL of methanol was treated with 0.510 g of iodine and 0.20 g of iodic acid at room temperature for 20 h. Workup produced 0.74 g of material analyzing by GC as 15% starting material with the balance a mixture of two compounds, Vb and VIb, in the ratio 3:2. Separation was effected by flash column chromatography using 5% ethyl acetate in toluene as the eluant. Starting material was eluted first followed by the less polar product VIb (0.20 g) which proved to be a viscous oil (found 374.03697, calcd for C$_{15}$H$_{19}$O$_3$I 374.03790): ^{13}C NMR δ 41.66 (C1), 74.97 (C2), 24.92 (C3), 20.97 (C5), 131.80 (C5a), 147.90 (C6), 109.89 (C7), 110.56 (C8), 132.15 (C9), 27.10 (C10), 55.73, 55.84, and 55.95 (CH$_3$'s). The more polar Vb (0.32 g) was crystallized readily from acetone, mp 158–159 °C (found 374.03695, calcd for C$_{15}$H$_{19}$O$_3$I 374.03790). The NMR spectral properties of Vb were very similar to those of Va: ^{13}C NMR δ 79.54 (C1), 38.63 (C2), 21.67 (C3), 41.06 (C4), 131.46 (C4a), 149.54 (C5), 111.07 (C6), 108.54 (C7), 153.28 (C8), 122.31 (C8a), 30.40 (C9), 24.67 (C10), 56.46 and 57.37 (2 C, CH$_3$'s). In like fashion, the NMR spectra of VIb resembled VIa. A complete study was carried out on both.[8]

Scheme I

Scheme I

Va, R = H
b, R = CH₃
c, R = C(O)CH₃

VI

[VI / V]
0.25
0.67
0.0
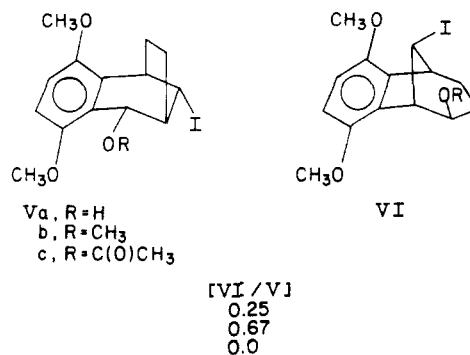
(c) A mixture of 0.43 g (2 mmol) of dimethoxyolefin IIb, 0.508 g (2 mmol) of iodine, and 0.352 g of iodic acid was reacted for 18 h in a mixed solvent of 25 mL of methanol and 10 mL of water. The crude yield was 0.67 g. GC analysis in order of elution gave 37% *Va*, 9% *VIa*, 20% *VIb*, and 34% *Vb*. This order of elution was carefully confirmed by running standard mixtures of these compounds prepared above.

Reaction in Acetic Acid. The dimethoxyolefin IIb (0.43 g, 2 mmol) in 30 mL of glacial acetic acid was reacted at room temperature with 0.51 g of iodine and 0.35 g of iodic acid for 17 h. Examination of the crude product (0.62 g) by ^{13}C NMR showed only the one product Vc. With appropriate allowances for the presence of an acetoxyl group, the NMR spectral properties were entirely in accord with structures Va and Vb above: ^{13}C NMR δ 70.19 (C1), 42.32 (C2), 21.74 (C3), 40.88 (C4), 132.27 (C4a), 42.85 (C5), 111.78 (C6), 108.61 (C7), 152.67 (C8), 119.54 (C8), 30.19 (C9), 24.80 (C10), 21.26, 56.53, and 55.59 (CH$_3$'s). Crystallization was from acetone, mp 195–196 °C. Anal. Found: 402.03344. Calcd for C$_{16}$H$_{19}$O$_4$I: 402.03296.

Epoxidation of Ib. A solution of 0.92 g (4 mmol) of Ib[1b] in 40 mL of diethyl ether was reacted at room temperature with 1.4 g (8 mmol) of m-chloroperbenzoic acid for 6 days. The mixture was washed with dilute sodium bisulfite, dilute sodium hydroxide, and water. After drying over sodium sulfate, the ether was removed by rotary evaporation, yielding 0.93 g of crude residue. Proton NMR examination indicated 34% of starting olefin and 62% of an epoxide mixture. The composition of the epoxide mixture was calculated from the methyl absorptions at 1.25 and 1.5 ppm[1b] as 54% oxygen anti to the aryl ring and 46% syn. TLC and ^{1}H and ^{13}C NMR confirmed that only starting material and the two epoxides were present.

Results and Discussion

Initially the addition of iodine in methanol to IIb was carried out in the presence of copper acetate as a trap for hydrogen iodide.[9] However, it was found that better yields and a cleaner product could be obtained by the use of iodic acid for this purpose. The reaction proceeded in less than 1 day at room temperature to give an 85% conversion to a mixture of two readily separated iodohydrin methyl ethers. NMR examination led to the assignments of structure as Vb and VIb (Scheme I).[8] This result was sufficiently different from our previous experience in water that a more detailed examination of that reaction was undertaken.

When IIb in water–sulfolane was treated with iodine–iodic acid as previously described,[2] the iodohydrin Va was readily isolated. Examination of the crude product showed Va to have been formed to the extent of 80%. A ^{13}C NMR examination of the residue showed the presence of a second compound. While detectable by GC and analytical TLC, no conditions were found that allowed a separation of VIa completely free from Va. The ^{13}C NMR of the new compound (with the exception of two overlapping lines) was readily ascertained from the enriched mixture and was so closely related to that of VIb as to leave no question of the structure as VIa.

(7) Bax, A.; Freeman, R.; Frenkiel, T. A. *J. Am. Chem. Soc.* **1981**, *103*, 2102–2104.

(8) Smith, W. B. *Magn. Reson. Chem.*, in press.

(9) Georgoulis, C.; Vallery, J. M. *Synthesis* **1978**, 402–403.

When the iodination was carried out in a mixture of 0.47 mole fraction water in methanol, the iodohydrin products made up 46% of the total. The ratio of VIa/Va was 0.20; while that for VIb/Vb was 0.59. These ratios resemble closely the ratios found for each series in water or methanol alone (Scheme I).

Finally, when the iodination was carried out in acetic acid only Vc was found in the product.

Reasonably, the product ratios in the above reactions are determined by the relative amounts of the initial attack by the electrophile above or below the plane of the olefin double bond. The direction of this attack establishes whether phenyl group or ethano bridge migration occurs. If the attacking electrophile were an iodonium ion, it would be expected that the same product ratios would occur in each reaction. This statement assumes no preferential solvation of one carbocation over the other in covalents of differing solvating power. This assumption seems justified as there is no change in product composition when the reaction with hypoiodous acid is carried out in water–sulfolane or in water–dioxane. Similarly, the distribution of the appropriate rearrangement products in a water–methanol mixture closely parallel the distribution found in water or methanol alone. Reasonably the electrophiles in these rearrangements are hypoiodous acid, methyl hypoiodidte, and acetyl hypoiodite formed in water, methanol, and acetic acid, respectively. A summary of the chemistry of these reagents has been provided by Roedig in the Houben–Weyl series.[10]

Conceptually, one might project a large number of products from the addition of electrophiles to IIb. In fact the number of products realized is small requiring a limited number of mechanistic pathways. There is support for the concept that attack by the electrophile to the syn face of the double bond leads directly to the formation of the ion VII. Tanido, Tori, and Kitahonoki[11] showed a number
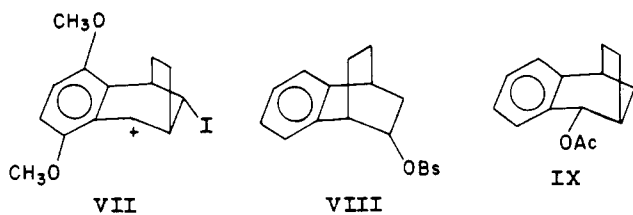
of years ago that the solvolysis of VIII gave a 98% conversion to IX. Similar results had been obtained on the analogous bicyclo[2.2.2]octenyl brosylate by Goering and Towns.[12] In both studies, stereochemical evidence and kinetic data were used to argue that migration of the ethano bridge occurs simultaneously with carbocation formation.

The pathway involving attack of the electrophile to the anti face of the double bond is less well-defined. Intui-

tively, one would expect the iodine to become less electrophilic in the series acetyl hypoiodite, hypoiodous acid, and methyl hypoiodite. This pattern parallels the decrease in syn attack on the double bond in IIb and follows the earlier observations on peracid epoxidation. The implication is that attack on the anti face of the double bond becomes more favored as the electrophile becomes weaker. This, in turn, requires that the aryl π-electrons become involved in transition-state stabilization as otherwise it would be hard to understand why the reagent would prefer to attack the sterically less favored side of the double bond. This transition state may be pictured as X. Intermediate formation from this transition state could be either to a homobenzyllic-like phenonium ion XI or to a classical carbocation XII stabilized by homoconjugation. Tanida,
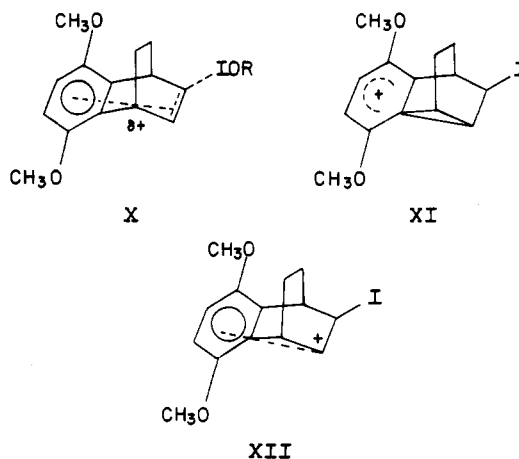
Tori, and Kitahonoki[12] in their consideration of the solvolysis of the anti isomer of VIII found insufficient rate enhancement to warrant the postulation of a nonclassical ion formed by delocalization of the C-1 to aryl group sigma electrons with no aryl π-electron involvement, i.e. XIII.
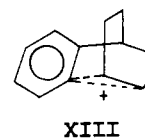
They considered formulations analogous to XI and XII in their system to be indistinguishable. The present study provides no evidence for a bridged intermediate since attack of the nucleophile at C-2 would lead to a sterically disfavored cis 1,2-addition product.

In conclusion, for 5,8-dimethoxybenzobicyclo[2.2.2]octadiene it would appear that for a series of increasingly weak electrophiles the homoconjugative interaction between the developing cationic center and the aryl π-electron center becomes of increasing importance with a resultant enhanced amount of attack from the sterically least favored side of the double bond. No doubt this same reasoning explains the sole formation of IV in the bromination of the diacetate analogue.

(10) Roedig, A. "Methoden Der Organischen Chimie (Houben–Weyl)"; Georg Thieme Verlag: Stuttgart, 1960; Vol. V/4, pp 517 ff.

(11) Tanida, H.; Tori, K.; Kitahonoki, K. *J. Am. Chem. Soc.* **1967**, *89*, 3212–3224.

(12) Goering, H. L.; Towns, D. L. *J. Am. Chem. Soc.* **1963**, *85*, 2295–2298.