found for $M^+ - (H_2O + HNCO)$ m/z 704.2711, $C_{35}H_{45}ClN_2O_{11}$ requires m/z 704.2711.

Treflorine (11). Band F, from preparative TLC of fraction B, gave substantially pure 11: 46 mg (1.7×10^{-4}% yield based on seed material); mp 205–208 °C dec (after recrystallization from CH_2Cl_2–hexane); IR ($CHCl_3$) 3600, 3440, 1760, 1715, 1675, 1640, 1610, 1590 cm^{-1}; UV_{max} (EtOH) 233 nm (ϵ 24000), 243 (sh, 18500), 253 (19850), 282 (5060), 288 (5060); $[\alpha]^{23}_D$ −138° (c 0.045, $CHCl_3$); mass spectrum (70 eV), m/z (relative intensity) 688 (M^+ – a, 2.7), 188 (5.7), 149 (4.2), 69 (14.7), 58 (32.1), 55 (13.4), 44 (100); found for $M^+ - (H_2O + HNCO)$ m/z 688.2751, $C_{35}H_{45}ClN_2O_{10}$ requires m/z 688.2762.

Acknowledgment. Comparison samples of maytansine were obtained from Dr. Matthew Suffness, National Cancer Institute, and from Dr. A. T. Sneden, Virginia Commonwealth University. We thank Dr. John Kozlowski of Purdue University Medicinal Chemistry Department and the Purdue Biological Magnetic Research Laboratory for providing several 360-MHz NMR spectra; this NMR investigation was supported in part by the National Institutes of Health, Division of Research Resources (Grant No. RR 01077). We also thank Dr. A. I. Meyers, Colorado State University, for ^1H and ^{13}C NMR spectra of maytansine, maysine, and maytansinol. R. D. Plattner and Dr. W. K. Rohwedder provided mass spectra.

Registry No. 1, 78987-26-5; 2, 78987-27-6; 3, 78987-28-7; 4, 35846-53-8; 7, 78987-29-8; 10, 79101-56-7; 11, 79101-55-6.

Electronic Control of Stereoselectivity. 10. Aryl Substituent Effects on Electrophilic Stereoselection in 11-Isopropylidenedibenzonorbornadienes. Direct Competition of Dissimilarly Functionalized Benzo Groups[1]

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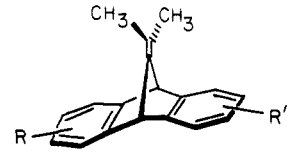
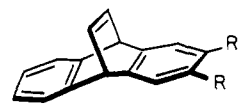
Three 11-isopropylidenedibenzonorbornadienes (**8**, **15a**, and **15b**) carrying dissimilarly substituted benzene rings have been prepared. To bypass a later need for product stereochemical assignment by X-ray analysis, we designed the synthetic schemes to be mediated by pure epoxide intermediates of spectroscopically definable syn configuration (**7**, **14a**, and **14b**). Perepoxidation, the prototypical weakly electrophilic reaction examined, gave rise in each instance to a pair of epoxide isomers whose identities could be readily established by spectral correlation with the precursor compounds. Ring opening of the six individual epoxide isomers with diethylaluminum 2,2,6,6-tetramethylpiperidide produced the corresponding isomerically pure allylic alcohols (**17**, **18**) whose ozonolysis furnished the structurally related α-hydroxy ketones (**19**, **20**). The chemical shifts of the methyl groups in these several types of compounds, although not widely divergent, proved to be sufficiently diagnostic of stereochemistry to permit reliable structural assignments to be made to the products of Friedel–Crafts acylation (**21**, **22**) and Prins hydroxymethylation (**23**, **24**). The syn/anti ratios observed for epoxidation are shown to correlate well with the relative abilities of the internally competing aromatic rings to enter into homoaromatic charge delocalization. When strong electrophiles are involved, the experimental data correlate most reasonably with the intervention of π complexes. Consequently, the latter reactions represent interesting examples of "guided" electrophile capture.

Previously, we reported our observations dealing with the addition of a variety of electrophiles to 9-isopropylidenebenzonorbornenes whose aryl substituents were varied in electronic character.[3] With weak electrophiles, a marked preference for contrathermodynamic anti attack was noted. In contrast, strong electrophiles were captured by the exocyclic double bond exclusively from the syn direction. These widely differing stereoselectivities were attributed to operation of long-range homoaromatic delocalization from the aromatic ring in the first instance (variably effective in proportion to available electron density) and to controlling steric accessibility in the latter situation. Second-order electronic influences were relegated to a significantly lesser role except for the possible involvement of coulombic interaction forces or charge-transfer complexation.

In a comparable study of benzobicyclo[2.2.2]octatriene derivatives where through-space coupling is nonoperational,[1] more subtle electronic effects surface, although a built-in steric bias persists. Understandably, our interpretative analysis of the nicely divergent directive influences showed by these two classes of compounds would be further substantiated if these stereoselectivity differences were to persist in the absence of steric imbalances. These requirements appeared to be met in the dibenzo systems **1** and **2** where the dissimilarly substituted aromatic rings are placed in direct competition. As matters turn out, 11-isopropylidenedibenzonorbornadienes (**1**) have been



1



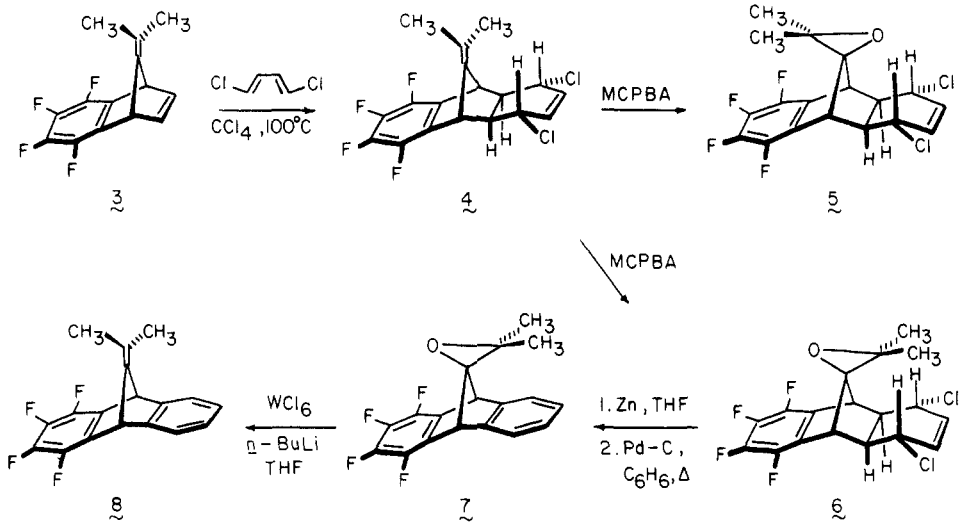
2

little studied. Tanida and his co-workers have succeeded in preparing the parent hydrocarbon[4] and in demonstrating that its nitration with copper(II) nitrate and acetic anhydride in dichloromethane at room temperature gives rise to the 2-nitro derivative.[5] For our purposes, substrate

(1) Part 9: Paquette, L. A.; Bellamy, F.; Wells, G. J.; Böhm, M. C.; Gleiter, R. *J. Am. Chem. Soc.* **1981**, *103*, in press.
(2) NATO Postoctoral Fellow.
(3) (a) Paquette, L. A.; Hertel, L. W.; Gleiter, R.; Böhm, M. *J. Am. Chem. Soc.* **1978**, *100*, 6510. (b) Hertel, L. W.; Paquette, L. A. *Ibid.* **1979**, *101*, 7620. (c) Paquette, L. A.; Hertel, L. W.; Gleiter, R.; Böhm, M. C.; Beno, M. A.; Christoph, G. G. *Ibid.* **1981**, *103*, in press.
(4) Tanida, H.; Tsushima, T.; Irie, T. *Tetrahedron Lett.* **1970**, 4331.
(5) Irie, T.; Tanida, H. *J. Org. Chem.* **1979**, *44*, 1002.

0022-3263/81/1946-4403$01.25/0

Scheme I



symmetry remained a highly desirable feature and successful approaches to three such molecules were therefore devised.

On the other hand, a number of electrophilic additions to **2** (R = CH_3 and Cl) have been studied by Cristol and Kochansky.[6] With weak electrophiles such as diborane, mercuric acetate, or benzenesulfenyl chloride, no preference was found for oriented attack on the double bond. Preferential bonding from the direction anti to the more electron-rich ring was exhibited by more powerful reagents, but these observations could be kinetically biased by phenonium ion intervention and skeletal rearrangement and need not be relevant to the questions at issue. The Cristol–Kochansky findings are in agreement with the belief that neither through-space coupling nor homoconjugative interaction comes into play during the reactions of **2** with weak electrophiles. It is entirely possible that the substitution plans which they selected do not perturb the two surfaces of the double bond sufficiently to have a measurable impact. The same logic could allow for roughly comparable coulombic interaction forces to come into play, the end result being approximately 50:50 product distributions.

In actuality, the electronic and structural characteristics of **1** are more well suited to resolving the questions being posed. Since 11-isopropylidenebenzonorbornadienes were not expected to be prone to cationic rearrangement, the full range of electrophilic capacity is made available. Should **1** respond much in the manner of its lower benzologue[3] then the opportunity for independent scrutiny of the impact of homoconjugative (weak electrophiles) and complexation (strong electrophiles) phenomena would present itself.

Results

Synthesis. Since the question of product stereochemistry ultimately had to be dealt with, attention was given to the development of a synthetic plan where the orientation of substituents at C-11 relative to the aromatic rings would be known by chemical intercorrelation and NMR shift data. As a consequence, the need for X-ray crystal structure studies would be obviated. The strategy which proved successful for gaining access to **8** appears in Scheme I. Following efficient Diels–Alder reaction of **3** with (*E*,*E*)-1,4-dichlorobutadiene,[7] adduct **4** was regioselectively epoxidized at its exocyclic double bond with *m*-chloroperbenzoic acid. There was produced a readily separable mixture of **5** and **6** (ratio 12:88) whose stereochemistries were easily deduced on the basis of their ^1H NMR spectra. For example, shielding by the aromatic ring causes the methyl singlets in **5** to appear significantly upfield of those in **6** (δ 1.30 vs. 1.48). Additionally, the two protons geminal to the chlorine atoms in **5** (δ 4.68) are dramatically downfield shifted as compared to those in **6** ($\sim$4.2) due to the deshielding effect of the epoxide oxygen. This observation also substantiates the exo stereochemical assignment to **5**.

Isomerically pure **6** underwent smooth dechlorination with zinc in refluxing tetrahydrofuran and subsequent aromatization with palladium on carbon to deliver **7** whose stereochemistry is unequivocally defined. Deoxygenation of **7** to give **8** could be accomplished with a lower valent tungsten chloride reagent.[8]

Since the 5,8-dimethoxy analogue of **3** is not readily available,[3c] the expedient synthesis of **15a** required a scheme which would allow for the introduction of the alkoxy groups in a less direct manner at a later stage. To this end, **9**[4] was selectively epoxidized to provide a mixture of **10** and **11** (ratio 1:2), and the major component was dechlorinated with zinc as before (Scheme II). Attention is called to the thermal stability of **12** which differs strikingly from that of known 11-isopropylidene congeners. Compounds of the latter type happen to be labile intermediates which are subject either to facile [3.3] sigmatropic (Cope) rearrangement[9] or to [10 + 4] retrograde fragmentation leading to benzene and 8,8-dimethylbenzo[6]fulvene.[10] When exposed to singlet oxygen, **12a** was converted to a mixture of endo peroxides which was directly isomerized to **13a** with triethylamine. Since manganese dioxide oxidation of **13a** gave rise to both enedione and hydroquinone products, the unpurified reaction mixture was directly O-methylated. Like **7**, the resulting syn[11]

(6) Cristol, S. J.; Kochansky, M. C. *J. Org. Chem.* **1975**, *40*, 2171.

(7) Pettit, R.; Henery, *J. Org. Synth.* **1970**, *50*, 36.

(8) Sharpless, K. B.; Umbreit, M. A.; Niel, M. T.; Flood, T. C. *J. Am. Chem. Soc.* **1972**, *94*, 6538.

(9) Warrener, R.; Russell, R. A. *Tetrahedron Lett.* **1978**, 4447.

(10) Tanida, H.; Irie, T.; Tori, K. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1999.

(11) The term syn is applied herein to define the stereochemistry of those molecules where the (noncarbon) functional group at C-11 is proximal to the aromatic ring in such molecules as **6** and **11**–**13** and positioned consequently as shown in dibenzobornadienes of the type **7**, **14**, and related molecules. In the case of **15**, the syn face is similarly ascribed to that above the fluorine-substituted ring to conform to its method of preparation (from **6**).

Scheme II

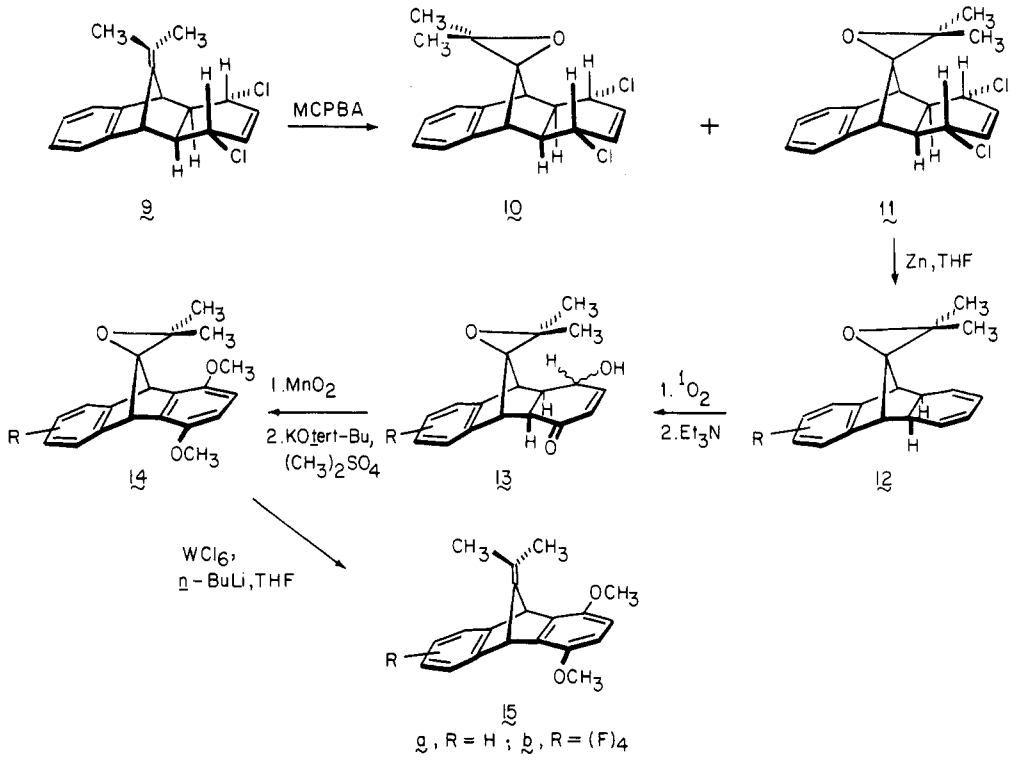


Table I. Summary of Syn/Anti Ratios for Various Electrophilic Additions to 8, 15a, and 15b[a]

compd	MCPBA	CH_3COCl, $AlCl_3$	$(CH_3CO)_2O$, $ZnCl_2$	CH_3O (H_2SO_4)
8	77/23	46/54		41/59
15a	45/55	35/65	30/70	38/62
15b	77/23	28/72		41/59

[a] All values are reliable to ±5%.

epoxide (**14a**) was also smoothly deoxygenated by Sharpless' reagent.

Although the reactivity of tetrafluoro diene **12b** toward singlet oxygen was not closely comparable to that of **12a**, we were nevertheless able to obtain **13b** by treatment of this cyclohexadiene with triphenylphosphite ozonide[12,13] in dichloromethane solution at −35 to −10 °C for 6 h followed by exposure of the endo peroxide to triethylamine. Oxidation and O-methylation as before led to **14b**, the progenitor of the highly functionalized dibenzonorbornadiene **15b**.

Epoxidation Results and Structural Interconversions. Epoxidation was selected as the prototypical weakly electrophilic reaction because of its recognized high efficiency, the possibility of direct stereochemical correlation with **7**, **14a**, and **14b**, and the further structural interconversions achievable with the individual epoxide isomers (see below). The peroxidation reactions were generally conducted in triplicate, and the data in Table I represent the average of these experiments. In the case of **8**, there was produced a mixture of chromatographically separable **7** and **16a** in a ratio of 77:23. The product distribution was diagnosed by integration of the methyl singlets of the two isomers whose chemical shifts are seen at δ 1.27 and 1.32, respectively (in $CDCl_3$). Since the spectral properties of **7** had previously been ascertained, this configurational assignment could be made with confidence. Similar treatment of **15a** indicated that epoxides **14a** and **16b** were produced in a 45:55 ratio. The relevant methyl signals were observed at δ 1.26 and 1.30. Dreiding models of these epoxides indicate the methyl protons to be skewed outward at an angle of ca. 30° from the underlying aromatic ring which is 3.1 Å removed at the closest point. Our data indicate that the tetrafluoro and dimethoxy substitution patterns exert *lower* levels of long-range diamagnetic shielding relative to the unsubstituted benzo ring and to a very similar degree ($\Delta\delta$ = −0.04 to −0.05 ppm). Our interest in this phenomenon was heightened when the peracid oxidation of **15b** was examined. The ^1H NMR spectra of the resulting epoxide isomers (**14b** and **16c**) were indistinguishable, the methyl signal appearing at δ 1.32. A distinction could, however, be made on the basis of ^{13}C NMR spectroscopy, since the methyl carbon of **14b** (20.876 ppm) appeared slightly downfield of that which characterizes **16c** (20.572 ppm). On the assumption that integration of this pair of ^{13}C signals closely approximates the product distribution, the formation of **14b** was seen to be favored (77%). This value was further substantiated by integration of the bridgehead carbon signals at 45.393 and 45.029 ppm, respectively.

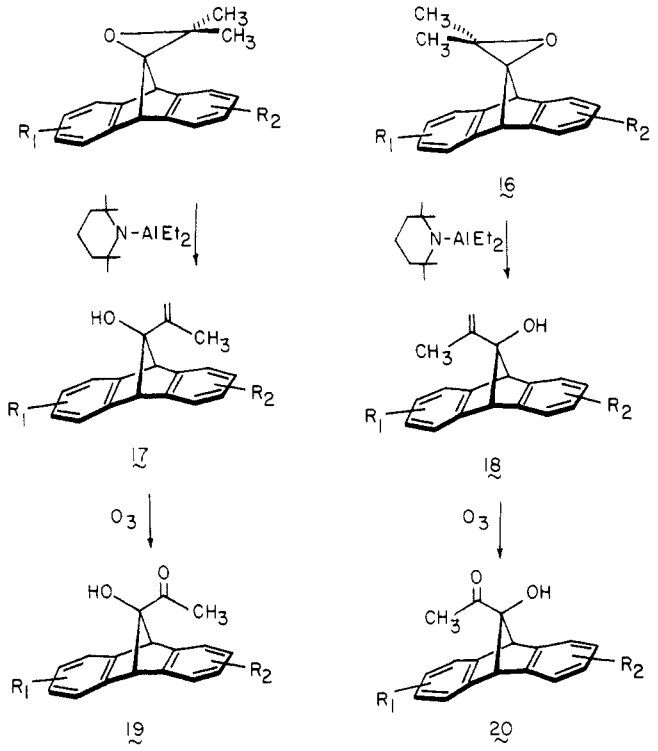
In order to enable assignments to be made with reasonable confidence in the work which follows, all six epoxides were subjected to the action of diethylaluminum 2,2,6,6-tetramethylpiperidide[14] and thereby converted to the corresponding allylic alcohols **17** and **18** (Scheme III). Although the methyl group of the isopropenyl substituent finds it possible to penetrate additionally into the aromatic shielding cone, chemical shifts remain closely comparable: **17a** (δ 1.72)/**18a** (δ 1.78), $\Delta\delta$ = −0.06; **17b** (δ 1.75)/**18b** (δ 1.73), $\Delta\delta$ = −0.02; **17c** (δ 1.74)/**18c** (δ 1.79), $\Delta\delta$ = −0.05. Evident here is the somewhat lesser capability of a benzene ring bonded to four fluorines to exert an upfield shift

(12) (a) Bartlett, P. D.; Mendenhall, G. D. *J. Am. Chem. Soc.* **1970**, *92*, 210. (b) Schaap, A. P.; Bartlett, P. D.; *Ibid.* **1970**, *92*, 6055.

(13) (a) Bartlett, P. D.; Chu, H.-K. *J. Org. Chem.* **1980**, *45*, 3000. (b) Bartlett, P. D.; Mendenhall, G. D.; Durham, D. L. *Ibid.* **1980**, *45*, 4269.

(14) Yasuda, A.; Tanaka, S.; Oshima, K.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 6513.

Scheme III



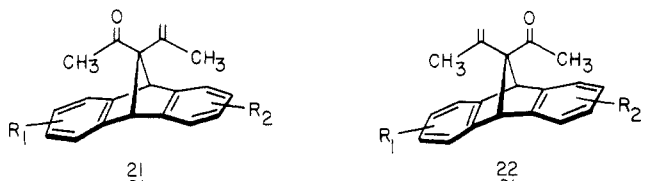
16 17 18 19 20

a, R_1 = (F)$_4$, R_2 = H
b, R_1 = H, R_2 = 1,4-$(OCH_3)_2$
c, R_1 = (F)$_4$, R_2 = 1,4-$(OCH_3)_2$

relative to that containing two methoxyl groups. The extensive aryl substitution pattern found in **17c** and **18c** makes possible a spectral observation of a different sort. When the isopropenyl double bond is positioned above the two aryl protons as it is in **17c**, the latter experience a rather sizeable shielding (δ 6.53) not encountered in its isomer (δ 6.67).

Ozonolysis of five of these allylic alcohols (unresolved experimental complications were encountered with **18c**) afforded the acetyl compounds **19** and **20**. Their ^{1}H NMR features are detailed in the Experimental Section.

Friedel–Crafts Acetylation. The Friedel–Crafts and Prins reactions were selected as exemplary strongly electrophilic processes. When **8** was treated with the acetyl chloride–$AlCl_3$ complex in dichloromethane solution at −15 °C to room temperature, a mixture of **21a** and **22a** was

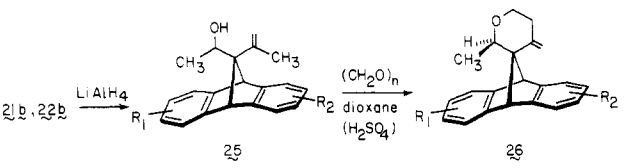


21 22

a, R_1 = (F)$_4$, R_2 = H
b, R_1 = H, R_2 = 1,4-$(OCH_3)_2$
c, R_1 = (F)$_4$, R_2 = 1,4-$(OCH_3)_2$

produced quantitatively. Integration of the pair of methyl singlets indicated the ratio to be closely balanced (46:54; average of four runs). The structural assignments are founded upon ^{1}H NMR data, with considerable reliance placed on the chemical shift values garnered from **17–20**. Thus, the acetyl singlet in **21a** (δ 2.06) appears downfield of that in **22a** (δ 1.98), while the reverse effect is encountered with the isopropenyl methyl signals (**21a**, δ 1.57; **22a**, δ 1.63). These patterns conform nicely to the diminished

Scheme IV



25 26

a, R_1 = H, R_2 = 1,4-$(OCH_3)_2$
b, R_1 = 1,4-$(OCH_3)_2$, R_2 = H

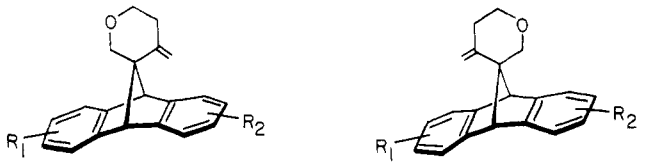
shielding contributions seen earlier for tetrafluoro substitution.

The situation was equally clear when the more reactive **15a** was subjected to comparable acetylation (−15 °C, 45 min). Under these conditions, there was produced a 35:65 mixture of **21b** (CH_3CO, δ 1.98; $CH_3C{=}CH_2$, δ 1.60) and **22b** (CH_3CO, δ 2.01; $CH_3C{=}CH_2$, δ 1.59). Although a third product believed to result from direct acetylation of one of the aromatic rings invariably accompanied the two products of interest, medium-pressure liquid chromatography achieved separation of all three components.

This byproduct did not materialize when **15a** was treated with anhydrous zinc chloride in acetic anhydride solution at room temperature.[3,15] These milder conditions gave rise to a similar distribution of **21b** and **22b** (30:70).

On exposure of **15b** to the acetyl chloride–$AlCl_3$ reagent, there materialized clean conversion to a mixture of **21c** and **22c** (28:72). In this instance, the isolated yields of the products were somewhat lessened because of their sensitivity to silica gel. The spectral characteristics of **21c** (CH_3CO, δ 2.05; $CH_3C{=}CH_2$, δ 1.58) and **22c** (CH_3CO, δ 2.00; $CH_3C{=}CH_2$, δ 1.61) again conform to the general trend established earlier.

Prins Reaction. When **8** was heated with excess paraformaldehyde in dioxane containing concentrated sulfuric acid (ca. 10 equiv), the cyclic ethers **23a** and **24a** were



23 24

a, R_1 = (F)$_4$, R_2 = H
b, R_1 = H, R_2 = 1,4-$(OCH_3)_2$
c, R_1 = (F)$_4$, R_2 = 1,4-$(OCH_3)_2$

formed in a 41:59 ratio. In both compounds, the insulated methylene group α to oxygen appears as an easily integrated sharp singlet well separated from other signals. As before, its chemical shift depends upon the underlying aromatic environment. Following the established pattern, we have assumed that the major isomer with its more deshielded peak (δ 3.43 vs. 3.30) has its CH_2O moiety positioned above the less electron-rich benzene ring.

When samples of **15a** were comparably treated, the two resulting products (**23b** and **24b**, 38:62) were seen to be characterized by CH_2O chemical shifts identical with those of the **a** series (δ 3.30 and 3.43, respectively). The grounds for structural assignment were the same as in the preceding examples. Additional substantiation was sought (and obtained) in the form of independent two-step conversions of the pure isomeric acetyl compounds **21b** and **22b** to **26a** and **26b** as outlined in Scheme IV. Although the ^{1}H NMR

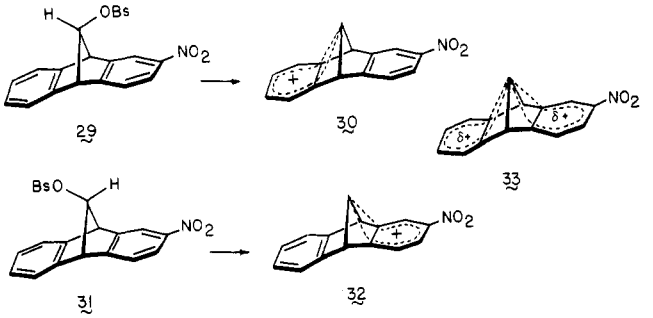
(15) Beak, P.; Berger, K. R. *J. Am. Chem. Soc.* **1980**, *102*, 3848 and relevant references cited therein.

spectra of these unsymmetrical ethers were complex, measurements made at high field strength (300 MHz) clearly showed the relevant α protons in these isomers to fall in the appropriate order (δ 3.62 and 3.78, respectively).

Finally, the Prins reaction of **15b** afforded a 41:59 mixture of **23c** and **24c**. In this instance, use was again made of the fact that the pairs of aryl protons in the individual isomers appear as well-separated singlets. In **23c**, these protons are weakly, though unmistakably shielded (δ 6.51) relative to those in **24c** (δ 6.60) by the proximal double bond of the heterocyclic subunit.

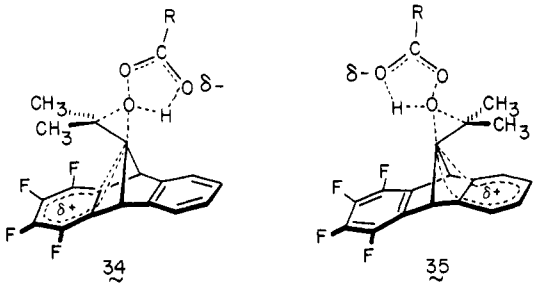
Discussion

The discovery by Tanida and co-workers that brosylates **29** and **31** undergo acetolysis to form only the acetate of



retained configuration[4] demonstrated that the ionization of these epimers proceeds along discretely different pathways between which there is no leakage. Intervention of the homoaromatic cations **30** and **32** was deemed significant because their intervention was also consistent with the higher reactivity of **29**. These findings point to the existence of an energy barrier between **30** and **32** which is too high to permit facile conversion from the less stable (**32**) to the more stable species (**30**) prior to solvent capture. Clearly disproven is the involvement of the more symmetrical cation **33**.

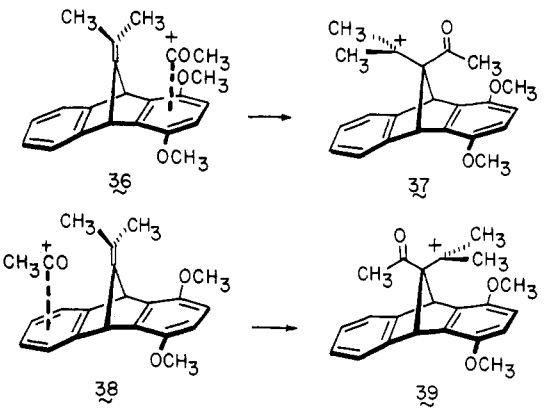
Long-range homoaromatic stabilization has been shown earlier to be important in the transition states involving 9-isopropylidenebenzonorbornenes and *weak electrophiles*.[3] We now find that this concept can be extended without modification to compounds of general type **1**. In the case of **8**, for example, the need for π-electron donation to the approaching electrophile generates low-level carbocation character at C-11. To the extent that unsymmetrical transition states **34** and **35**, as favored by Plesnicar, Tasevski, and Azman on the basis of ab initio calculations,[16] do intervene, the one involving charge dispersal to the unsubstituted benzene ring will necessarily be more energetically favorable. This should be reflected in turn in the stereoselectivity of epoxide formation (faster rate of formation of **7**), and it is (**7**/**16a** ratio of 77:23). The powerfully electronegative influence of the four fluorine atoms is also seen in **15b** where an identical 77:23 epoxide product distribution was encountered.



It is important at this junction that a clear distinction be made between the levels of homoaromatic interaction present in **30** on the one hand (stabilization of unit positive charge) and **34** and **35** on the other (delocalization of weakly positive charge within a zwitterionic structure). Not unexpectedly, stereoselectivity is observed during the epoxidation of **8** and **15b**. What is more satisfying is the relative magnitude of the energy which separates transition states **34** and **35**. When an unsubstituted benzene ring and a 1,4-dimethoxy-substituted system are allowed to vie with each other as they are in **15a**, little discrimination, if any, materializes between syn and anti attack by the peracid (Table I). This behavior conforms to the low level of charge development which is involved.

The attractiveness and consistency of the preceding mechanistic proposal cause us once again[3] to relegate π-orbital distortion[17] to an inconsequential role within such systems. Simply stated, 11-isopropylidenedibenzonorbornadienes can gain access to a homoaromatic polarization component which is too overwhelming for other factors to become influential during reaction with weak electrophiles. In systems which lack the potential for comparable long-range stabilization, e.g., **2**, a causal connection between more subtle electronic influences and stereoselectivity can be established.

Since strong electrophiles are not nearly as dependent upon prior polarization of the π bond for chemical reaction, extended transition-state stabilization of the predescribed type is no longer of consequence. In other words, the crossover from a bridged ion pathway to an open ion mechanism (see **37** and **39**) places entirely new electronic



demands on the substrate. In our earlier work,[1,3] it was recognized that steric accessibility to the π bond was an important stereochemical determinant in such reactions. Chiefly, for this reason, the possibility of transient complex formation between the acceptor orbital of the attacking electrophile and the proximal underlying aromatic segment could not be addressed. The three dibenzonorbornadienes prepared in this work were designed to minimize steric imbalances as much as possible while maintaining reasonably divergent electronic character in the two aromatic rings. Since the exocyclic isopropylidene double bond is positioned directly above the central region of these molecules, the peripheral fluoro and methoxyl substituents were expected to exert minimal stereoselectivity contri-

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butions because of their location and size.

The product distributions realized for acetylation and hydroxymethylation (Prins reaction) indicate that a preference exists for electrophilic capture syn to the more electron-rich aromatic ring and correlate most reasonably with the intervention of π complexes such as **36** and **38**. Although correlation is admittedly not causality, a direct relationship between syn/anti stereoselection and π-donor ability seems likely. Historically, the pathway for aromatic substitution by a strong electrophile was thought to involve as rate-determining step the formation of a π complex, with positional selectivity being decided in a subsequent, more rapid process.[18] More recent work has given rise to the interpretation that a single transition state is involved, the character of which is decidedly π-complex-like for reactive electrophiles.[19]

Although widely scattered, literature data can be found on the relative abilities of substituted benzenoid systems to function as electron-donor molecules. In their pioneering study of charge-transfer interactions involving tetracyanoethylene (TCNE), Merrifield and Phillips showed benzene to be a weaker donor than anisole.[20] Voigt's more extensive study of the same phenomenon established that the electronic interplay of para substituents with benzene π networks affected donor interaction toward TCNE in the following quantitative manner (benzene = 1): *p*-dimethoxybenzene, 5.3; *p*-difluorobenzene, 2.2; *p*-xylene, 1.7.[21] With hexafluoro substitution, the donor interaction toward TCNE is weak,[22] although somewhat stronger (3.1) than some may have initially assumed.[21]

Vertical ionization potentials (IP's) which generally correlate with electron removal from highest occupied MO's provide a useful and accurate indication of the abilities of various aryl substituents to perturb π energy levels (and indirectly π-donor abilities).[23] The detailed study of 1,4-disubstituted benzenes by Baker, May, and Turner demonstrated that the IP for benzene (9.40 eV) compares rather closely to that of the *p*-difluoro derivative (9.50 eV).[24] Frazier and co-workers have determined that the IP for 1,2,4,5-tetrafluorobenzene (9.59 eV) does not differ substantially from that of the para-disubstituted example.[25]

In these terms, the syn/anti reactivity of **8** toward such reactive intermediates as CH_3CO^+[26] and H_2COH^+ (46:54 and 41:59) correlates well with the small added level of π complexation that can be garnered by the electrophile when positioned above the unsubstituted ring. Because of the superior capability of the *p*-dimethoxy-substituted arene moieties in **15a** and **15b** for π complexation (as in **36**), electrophilic capture syn to this ring dominates to the extent of 60–70%.

Such interesting "guided" electrophilic bonding, which can be expected to gain importance in future synthetic and physical-organic studies, is not entirely new. While this work was well underway, Wilt and Narutis described the effect of π complexation between a *syn*-7-aryl substituent and BH_3 on the stereochemical outcome of norbornene hydroboration and norbornanone reduction.[27] Examples are also known of stereochemically directed reactions mediated by Lewis acid complexes between alkoxy groups and reactive electrophiles.[28]

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer Model 467 spectrophotometer. The ^1H NMR spectra were determined with Varian T-60 and EM-390 spectrometers, and apparent splittings are given in all cases. Mass spectra were measured with an AEI-MS9 spectrometer at an ionizing energy of 70 eV. Microanalytical determinations were made at the Scandinavian Microanalytical Laboratory.

11-Isopropylidene-1,2,3,4-tetrafluoro-5,8-dichloro-4a,5,8,8a,9,10-hexahydro-9,10-methanoanthracene (4). A thick-walled Carius tube was charged with a solution of **3**[29] (3.22 g, 12.7 mmol) and (*E,E*)-1,4-dichlorobutadiene[7] (4.7 g, 38.2 mmol) in carbon tetrachloride (20 mL). The tube was sealed under vacuum at −78 °C and heated at 100 °C in a copper tube furnace for 30 h. The solvent was removed under reduced pressure. Chromatography of the residue on silica gel (petroleum ether elution) gave 3.7 g (77%) of **4**: mp 128–132 °C; ^1H NMR ($CDCl_3$) δ 5.83 (s, 2 H), 4.25–3.9 (m, 4 H), 2.3–2.05 (m, 2 H), 1.78 (s, 6 H); mass spectrum, calcd *m/e* 376.0408, obsd 376.0414.

Epoxidation of 4. A solution of **4** (0.50 g, 1.33 mmol) in methylene chloride was treated with *m*-chloroperbenzoic acid (0.23 g, 1.33 mmol) for 16 h at room temperature. Water was added, the organic layer was separated, and the aqueous layer was extracted twice with methylene chloride. The combined organic layers were washed with saturated sodium bicarbonate solution and brine prior to drying. After removal of solvent, the residue was purified, and the isomers were separated by preparative layer chromatography on silica gel (benzene elution).

Syn epoxide **6**: 308 mg (59.1%); mp 186–188 °C (from 2-propanol); ^1H NMR ($CDCl_3$) δ 6.02 (s, 2 H), 4.11 (m, 2 H), 3.59 (distorted t, J_{app} = 2 Hz, 2 H), 2.33–2.13 (m, 2 H), 1.42 (s, 6 H).

Anal. Calcd for $C_{18}H_{14}Cl_2F_4O$: C, 54.98; H, 3.59. Found: C, 54.70; H, 3.60.

Anti epoxide **5**: 62 mg (11.9%); ^1H NMR ($CDCl_3$) δ 5.90 (s, 2 H), 4.76 (m, 2 H), 3.45 (distorted t, J_{app} = 2 Hz, 2 H), 2.4–2.19 (m, 2 H), 1.28 (s, 6 H); mass spectrum, calcd *m/e* 392, obsd 392.

Syn Epoxide of 11-Isopropylidene-1,2,3,4-tetrafluoro-4a,8a,9,10-tetrahydro-9,10-methanoanthracene. A solution of **6** (100 mg, 0.254 mmol) in tetrahydrofuran was added dropwise to a refluxing suspension of zinc metal (83 mg, 1.27 mmol) in tetrahydrofuran. Two additional portions of zinc metal (83 mg each, 1.27 mmol) were added at 45-min intervals, and the reaction mixture was heated at the reflux temperature for a further 60 min after the final addition. The cooled reaction mixture was diluted with saturated sodium chloride solution and extracted three times with ether. The combined organic layers were washed with 5% hydrochloric acid solution, saturated sodium bicarbonate solution, and brine prior to drying. Removal of the solvent gave 79.4 mg (97%) of diene **12b** (mp 180–195 °C) which was carried on to the next step without further purification: ^1H NMR ($CDCl_3$) δ 6.0–5.37 (m, 4 H), 3.25 (m, 2 H), 2.65 (m, 2 H), 1.35 (s, 6 H); mass

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(26) The Friedel–Crafts acylation of benzene with acetyl chloride and $AlCl_3$ has been shown to involve a complex between the acylating agent and Lewis acid (Corriu, R.; Dore, M.; Thomassin, R. *Tetrahedron* **1971**, *27*, 5819. Hashimoto, I.; Kawasaki, A.; Ogata, Y. *Ibid.* **1972**, *28*, 217). The donor–acceptor nature of this complex in methylene chloride solution has recently been demonstrated by ^{27}Al NMR (Wilinski, J.; Kurland, R. J. *J. Am. Chem. Soc.* **1978**, *100*, 2233). In this present instance, the similar syn/anti ratios observed for acetylation and hydroxymethation (where no Lewis acid is present) suggests that the nearby Lewis acid (omitted in **36** and **38** for reasons of clarity) has little effect on the overall stereochemical outcome in these examples.

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spectrum, calcd m/e 322.0980, obsd 322.0991.

Syn Epoxide of 11-Isopropylidene-1,2,3,4-tetrafluoro-9,10-dihydro-9,10-methanoanthracene (7). To a solution of the above diene (3.28 g, 10.2 mmol) in benzene was added 10 g of 10% palladium on carbon and this mixture was heated at the reflux temperature for 12 h, cooled, and filtered through a pad of Celite. The solvent was removed from the filtrate, and the residue was recrystallized from 2-propanol to yield 1.24 g (38%) of **7** as a white crystalline solid: mp 231–232 °C; ^{1}H NMR ($CDCl_3$) δ 7.5–7.03 (m, 4 H), 4.45 (distorted t, J = 1 Hz, 2 H), 1.27 (s, 6 H).

Anal. Calcd for $C_{18}H_{12}F_4O$: C, 67.50; H, 3.78. Found: C, 67.25; H, 3.96.

11-Isopropylidene-1,2,3,4-tetrafluoro-9,10-dihydro-9,10-methanoanthracene (8). Tungsten hexachloride (1.6 g, 4.0 mmol) was added to 10 mL of tetrahydrofuran (freshly distilled from sodium–benzophenone and maintained under nitrogen) while cooled to –62 °C in a dry ice–acetone bath. While this suspension was stirred at –62 °C, 6.25 mL (10 mmol) of 1.6 M n-butyllithium in hexane was added slowly over a 5-min period. The mixture was allowed to warm slowly to room temperature where it soon became homogeneous. After returning the temperature of the solution to 0 °C, a solution of **7** (340 mg, 1.06 mmol) in tetrahydrofuran was added dropwise. After 45 min at 0 °C, the reduction mixture was poured into 20 mL of an aqueous solution which was 1.5 M in sodium tartrate and 2 M in sodium hydroxide and extracted three times with hexane. The combined organic layers were washed with brine prior to drying. After removal of solvent, the residue was purified by preparative layer chromatography on silica gel (petroleum ether elution) to yield 262 mg (81%) of **8** as a white crystalline solid: mp 218–219 °C (from 2-propanol); ^{1}H NMR ($CDCl_3$) δ 7.38–6.85 (m, 4 H), 5.05 (distorted t, J = 1 Hz, 2 H), 1.65 (s, 6 H); mass spectrum, calcd m/e 304.0875, obsd 304.0880.

Anal. Calcd for $C_{18}H_{12}F_4$: C, 71.05; H, 3.97. Found: C, 71.16; H, 4.00.

11-Isopropylidene-5,8-dichloro-4a,5,8,8a,9,10-hexahydro-9,10-methanoanthracene (9). A thick-walled Carius tube was charged with a solution of 9-isopropylidene-1,4-dihydro-1,4-methanonaphthalene (2.5 g, 13.6 mmol) and (*E,E*)-1,4-dichlorobutadiene (1.9 g, 15.6 mmol) in carbon tetrachloride (12 mL). The tube was sealed under vacuum at –78 °C and heated at 100 °C in a copper tube furnace for 28 h. Removal of the solvent gave 4.2 g (100%) of **9** which was carried on to the next step without further purification: mp 108–122 °C (lit.[4] mp 123–129 °C); ^{1}H NMR ($CDCl_3$) δ 7.17–6.94 (m, 4 H), 5.81 (s, 2 H), 4.12–3.92 (m, 2 H), 3.82 (s, 2 H), 2.25–2.02 (m, 2 H), 1.68 (s, 6 H).

Epoxidation of 9. A solution of **9** (250 mg, 0.814 mmol) in methylene chloride was reacted with m-chloroperbenzoic acid (141 mg, 0.814 mmol) for 17 h at room temperature. Water was added, the organic layer was separated, and the aqueous layer was extracted twice with methylene chloride. The combined organic layers were washed with saturated sodium sulfate and sodium bicarbonate solutions and brine prior to drying. After removing of the solvent, the residue was purified by preparative layer chromatography on silica gel (benzene elution).

Syn epoxide **11**: 117 mg (44.4%); mp 168–169 °C (from 2-propanol); ^{1}H NMR ($CDCl_3$) δ 7.2–7.03 (m, 4 H), 5.95 (s, 2 H), 4.16 (m, 2 H), 3.18 (s, 2 H), 2.28–2.07 (m, 2 H), 1.46 (s, 6 H); mass spectrum, calcd m/e 292.1463, obsd 292.1471.

Anti epoxide **10**: 48 mg (18%); mp 111–112 °C (from 2-propanol); ^{1}H NMR ($CDCl_3$) δ 7.22–7.1 (m, 4 H), 5.90 (s, 2 H), 4.70 (m, 2 H), 3.14 (s, 2 H), 2.36–2.16 (m, 2 H), 1.33 (s, 6 H); mass spectrum, calcd m/e 292.1463, obsd 292.1471.

Syn Epoxide of 11-Isopropylidene-4a,8a,9,10-tetrahydro-9,10-methanoanthracene (12a). A solution of **11** (1.7 g, 5.23 mmol) in tetrahydrofuran was added dropwise to a refluxing suspension of zinc metal (508 mg, 7.76 mmol) in tetrahydrofuran. Another portion of zinc (508 mg, 7.76 mmol) was added after 45 min, and the reaction mixture was refluxed for a further 60 min after the final addition. The cooled reaction mixture was diluted with saturated sodium chloride solution and extracted three times with ether. The combined organic layers were washed with 5% hydrochloric acid, saturated sodium bicarbonate solution, and brine prior to drying. Removal of the solvent gave 1.32 g (100%) of **12a** which was carried into the next step without further purification: ^{1}H NMR ($CDCl_3$) δ 7.1–6.9 (m, 4 H), 5.75–5.49 (m, 4 H), 2.95 (s, 2 H), 2.56 (m, 2 H), 1.32 (s, 6 H).

Anti Epoxide of 11-Isopropylidene-1,4-dimethoxy-9,10-dihydro-9,10-methanoanthracene (14a). An ice–methanol cooled solution of **12a** (8.58 g, 34.3 mmol) and methylene blue (1 mg/mL) in methylene chloride (600 mL) was irradiated with a 500-W tungsten filament projector bulb while oxygen was bubbled through the solution. The irradiation was carried out for 0.5 h. Most of the solvent was removed under reduced pressure at a temperature below 15 °C. The residue was dissolved in chloroform, and triethylamine (4.35 g, 43 mmol) was added. This solution was stirred at room temperature for 12 h, poured onto a column containing 120 g of neutral alumina (activity III), and filtered through with 500 mL of ethyl acetate. After solvent removal, the dark oil was dissolved in methylene chloride and stirred for 91 h at room temperature with Attenburrow manganese dioxide (45 g, 0.514 mol). After filtration and removal of solvent from the filtrate, the residue was purified by column or layer chromatography on silica gel (elution with hexane–ethyl acetate, 30:70) to yield 3.02 g (31%) of ene dione [^{1}H NMR ($CDCl_3$) δ 7.34–7.12 (m, 4 H), 6.82 (s, 2 H), 3.55 (s, 2 H), 2.8 (s, 2 H), 1.14 (s, 6 H)] and 0.61 g (6.3%) of hydroquinone [^{1}H NMR (Me_2SO-d_6) δ 8.22 (br s, 2 H), 7.34–6.77 (m, 4 H), 6.26 (s, 2 H), 4.35 (s, 2 H), 1.28 (s, 6 H)].

A sample of the predescribed mixture (20 mg, 0.07 mmol) and dimethyl sulfate (27 mg, 0.213 mmol) in dry tetrahydrofuran (3 mL) at 0 °C under nitrogen was treated with three portions of potassium *tert*-butoxide (3 × 8 mg, 0.213 mmol) at 1-h intervals. The mixture was stirred overnight and filtered through a pad of Celite. The filtrate was dried and concentrated to leave a brown solid residue which was purified by rapid preparative layer chromatography on silica gel (chloroform elution) to give 16.7 mg (76%) of **14a**: mp 214–215 °C (from 2-propanol); ^{1}H NMR ($CDCl_3$) δ 7.36–6.84 (m, 4 H), 6.48 (s, 2 H), 4.33 (s, 2 H), 3.75 (s, 6 H), 1.30 (s, 6 H); mass spectrum calcd m/e 308.1412, obsd 308.1418.

Anal. Calcd for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54. Found: C, 77.77; H, 6.53.

11-Isopropylidene-1,4-dimethoxy-9,10-dihydro-9,10-methanoanthracene (15a). Tungsten hexachloride (1.58 g, 3.98 mmol) was added to 5 mL of tetrahydrofuran (freshly distilled from sodium–benzophenone) and maintained under nitrogen while cooled to –62 °C in a dry ice–acetone bath. While this suspension was stirred at –62 °C, 8.32 mL (9.96 mmol) of 1.2 M n-butyllithium in hexane was added slowly over a 5-min period. The mixture was allowed to warm slowly to room temperature. Shortly after reaching room temperature, the solution was homogeneous, at which time it was cooled to 0 °C by using an ice–water bath. A solution of **14a** (122 mg, 0.39 mmol) in tetrahydrofuran was added dropwise to the cold solution. After 30 min at 0 °C, the mixture was allowed to warm to room temperature. After 2.5 h at room temperature, the reduction mixture was poured into 25 mL of an aqueous solution, which was 1.5 M in sodium tartrate and 2 M in sodium hydroxide, and extracted three times with hexane. The combined organic layers were washed with brine prior to drying. After removal of the solvent, the residue was purified by preparative layer chromatography on silica gel (chloroform elution) to yield 91 mg (79%) of **15a** as a white crystalline solid: mp 223–224 °C; ^{1}H NMR ($CDCl_3$) δ 7.34–7.14 (m, 2 H), 6.95–6.75 (m, 2 H), 6.4 (s, 2 H), 4.96 (s, 2 H), 3.75 (s, 6 H), 1.58 (s, 6 H); calcd m/e 292.1463, obsd 292.1471.

Anal. Calcd for $C_{20}H_{20}O_2$: C, 82.16; H, 6.89. Found: C, 82.05; H, 6.99.

Syn Epoxide of 11-Isopropylidene-1,2,3,4-tetrafluoro-5,8-dimethoxy-9,10-dihydro-9,10-methanoanthracene (14b). A solution of **6** (5.04 g, 15.7 mmol) in dry tetrahydrofuran (100 mL) was added dropwise to a refluxing suspension of zinc powder (5.0 g, 76.4 mmol) in tetrahydrofuran (100 mL). Another portion of zinc (2.0 g, 30.6 mmol) was added after 45 min, and the reaction mixture was heated at reflux for a further 60 min after the final addition. Following the predescribed workup, there was isolated 4.04 g (98%) of **12b** which was utilized directly without purification.

A solution of freshly distilled triphenyl phosphite (35.52 g, 0.114 mol) in 200 mL of dichloromethane was cooled to –78 °C and oxygen containing ozone was bubbled through the solution until

the blue color of excess ozone appeared. The mixture was flushed with nitrogen until moist starch–iodine paper gave a negative reaction to the effluent gas. A solution of **12b** (12.20 g, 37.88 mmol) in dichloromethane (110 mL) was added dropwise during 30 min with stirring. The reaction mixture was allowed to warm to −35 °C and then slowly from −35 to −10 °C during 6 h. The solution was returned to −78 °C where it was treated with triethylamine (7.25 g, 71.8 mmol). Upon completion of the addition, the mixture was allowed to warm slowly to room temperature where it was stirred overnight.

The solvent was evaporated, and the residual oil was chromatographed on silica gel. Elution with chloroform removed triphenyl phosphate; elution with ethyl acetate afforded a white solid which was dissolved in dichloromethane (700 mL) and stirred with activated manganese dioxide (45 g, 0.717 mol) at room temperature for 72 h. Filtration through a pad of Celite and filtrate evaporation left a viscous oil. Chromatography of this material on silica gel (elution with petroleum ether–ethyl acetate, 3:7) afforded 4.15 g (24% from **6**) of the hydroquinone [^{1}H NMR ($CDCl_3$) δ 6.63 (s, 2 H), 4.53 (s, 2 H), 1.26 (s, 6 H)] and 2.63 g (15%) of enedione [^{1}H NMR ($CDCl_3$) δ 6.86 (s, 2 H), 3.90 (m, 2 H), 2.83 (s, 2 H), 1.13 (s, 6 H)].

To a cold (0 °C) solution of the enedione (200 mg, 0.568 mmol) in tetrahydrofuran (20 mL) was added a solution of sodium hydroxide (2 g, 50 mmol) in water (20 mL). With continued cooling, the vigorously stirred reaction mixture was treated dropwise with dimethyl sulfate (1.33 g, 10 mmol) during 30 min. After 4 h at 0 °C, an additional 1.33 g of dimethyl sulfate was added. After 5 hr at 0 °C and 17 h at room temperature, the reaction mixture was saturated with sodium chloride and extracted with ether (3 × 20 mL). The combined organic layers were washed with brine to neutrality, dried, and evaporated. The residual brown solid (256 mg) was recrystallized from ethanol to give 120 mg (56%) of **14b** as colorless crystals: mp 255–258 °C dec; ^{1}H NMR ($CDCl_3$) δ 6.60 (s, 2 H), 4.65 (m, 2 H), 3.76 (s, 6 H), 1.32 (s, 6 H); ^{13}C NMR ($CDCl_3$, only 8 signals seen) 148.68, 132.66, 111.24, 98.37, 64.99, 56.56, 45.51, 20.88 ppm; mass spectrum, calcd m/e 380.1035, obsd 380.1031.

Anal. Calcd for $C_{20}H_{16}F_4O_3$: C, 63.16; H, 4.24. Found: C, 63.08; H, 4.35.

11-Isopropylidene-1,4-dimethoxy-5,6,7,8-tetrafluoro-9,10-dihydro-9,10-methanoanthracene (15b). Tungsten hexachloride (0.998 g, 2.52 mmol) was added to 50 mL of tetrahydrofuran (freshly distilled from sodium) and cooled to −78 °C. The suspension was treated with 4.40 mL of a 1.15 M solution of *n*-butyllithium in hexane (5.05 mmol), allowed to warm to room temperature, and recooled to 0 °C. A solution of **14b** (203 mg, 0.534 mmol) in tetrahydrofuran (25 mL) was introduced dropwise, and stirring was continued for 2 h at 0 °C and 3 h at room temperature. The reaction mixture was poured into 200 mL of an aqueous solution which was 1.5 M in sodium tartrate and 2 M in sodium hydroxide and extracted with hexane (3 × 75 mL). The combined organic layers were washed with brine, dried, and evaporated. Preparative TLC purification of the residue (silica gel, elution with chloroform–petroleum ether, 1:3) gave 117 mg (60%) of **15b** as a white solid: mp 204–205 °C (from ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 6.50 (s, 2 H), 5.30 (br s, 2 H), 3.78 (s, 6 H), 1.61 (s, 6 H); mass spectrum, calcd m/e 364.1086, obsd 364.1092.

Epoxidation of 8. A solution of **8** (40 mg, 0.13 mmol) in dichloromethane (2 mL) was allowed to react with *m*-chloroperbenzoic acid (25 mg, 0.14 mmol) at room temperature for 18 h. Water was added, the organic layer was separated, and the aqueous layer was extracted twice with methylene chloride. The combined organic layers were washed with saturated sodium sulfite solution, saturated sodium bicarbonate solution, and brine prior to drying. After removal of solvent, the residue was purified, and the isomers were separated by preparative layer chromatography on silica gel (benzene elution). There was obtained 28.8 mg (68.4%) of syn epoxide **7** [mp 231–232 °C (from 2-propanol)] whose spectra were superimposable upon those of the sample prepared above.

Also obtained was 9.9 mg (23.5%) of anti epoxide **16a**: mp 166–168 °C; ^{1}H NMR ($CDCl_3$) δ 7.5–7.03 (m, 4 H), 4.45 (distorted t, J = 1 Hz, 2 H), 1.32 (s, 6 H); mass spectrum, calcd m/e 320.0824, obsd 320.0830.

Epoxidation of 15a. An ice-cold solution of **15a** (152 mg, 0.52 mmol) in dichloromethane (10 mL) was treated with *m*-chloroperbenzoic acid (133 mg of 80% purity, 0.616 mmol) dissolved in 10 mL of the same solvent. The reaction mixture was stirred at 0 °C for 30 min and at room temperature for 3 h. The predescribed workup led to isolation of a white solid (169 mg). The two epoxide isomers could not be chromatographically separated, but the ratio of **14a** and **16b** (45:55) was easily determined by integration of the pair of methyl singlets at δ 1.26 and 1.30 (in $CDCl_3$), respectively.

2,2,6,6-Tetramethylpiperidine (445 mg, 3.15 mmol) in dry benzene (6 mL) was cooled in an ice bath while *n*-butyllithium in hexane (2.62 mL of 1.2 M solution, 3.15 mmol) was added. After this solution had been stirred at 0 °C for 15 min, diethylaluminum chloride (380 mg, 3.15 mmol) was introduced as a 25% solution in toluene, and stirring was continued for an additional 30 min. The unpurified epoxide mixture dissolved in 10 mL of benzene was added during 30 min, and the resulting mixture was stirred at 0 °C for 3 h. After treatment with 20 mL of 1 N hydrochloric acid, the organic phase was separated, and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic solutions were washed with saturated sodium bicarbonate solution and brine prior to drying and solvent evaporation. Preparative TLC on silica gel (elution with petroleum ether–ethyl acetate, 7:3) gave 58 mg (36% from **15a**) of syn allylic alcohol **17b** as a white solid: mp 180–181 °C (from 2-propanol); IR (KBr) 3590, 3495, 1650, 1610, 1585 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.36 (m, 2 H), 6.96 (m, 2 H), 6.40 (s, 2 H), 4.93 (br s, 1 H), 4.76 (m, 1 H), 4.56 (s, 2 H), 3.70 (s, 6 H), 2.56 (br s, 1 H), 1.75 (br s, 3 H); mass spectrum, calcd m/e 308.1412, obsd 308.1418.

Anal. Calcd for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54. Found: C, 77.87; H, 6.51.

Also obtained was 34 mg (21%) of anti alcohol **18b** as a white solid: mp 156–157 °C (from 2-propanol); ^{1}H NMR ($CDCl_3$) δ 7.20 (m, 2 H), 6.90 (m, 2 H), 6.53 (s, 2 H), 4.90 (s, 1 H), 4.83 (m, 1 H), 4.60 (s, 2 H), 3.73 (s, 6 H), 2.76 (s, 1 H), 1.73 (br s, 3 H); mass spectrum, calcd m/e 308.1412, obsd 308.1421.

The individual isomers were identified by the independent preparation of authentic **17b** as described below.

Independent Ring Opening of 14a. A 250-mg sample of **14a** was subjected to preparative thin-layer chromatography on highly active silica gel plates (chloroform elution). Proper extraction of the large band of product, filtration, and solvent evaporation led to the isolation of 220 mg (88%) of allylic alcohol **17b**, a colorless solid of melting point 180–180.5 °C (from 2-propanol). The IR and ^{1}H NMR spectra of this substance were superimposable upon those of the syn isomer described above.

Epoxidation of 15b. A solution of **15b** (40 mg, 0.11 mmol) in dichloromethane (2 mL) was treated at room temperature with *m*-chloroperbenzoic acid (30 mg of 80% purity, 0.139 mmol) dissolved in the same solvent (3 mL). After 20 h, the identical workup afforded 44 mg of a white solid whose ^{1}H NMR spectrum was identical with that of pure **14b**. However, the presence of both epoxide isomers was demonstrated by analytic TLC analysis and ^{13}C NMR spectroscopy ($CDCl_3$, only 11 signals seen): 148.62, 132.54, 111.18, 98.31, 64.93, 56.50, 56.19, 45.39, 45.03, 20.82, 20.57 ppm. Preparative TLC was unsuccessful in separating the isomers. Integrals of the ^{13}C peaks were utilized to determine isomer composition (see Table I).

The epoxide mixtures from two identical experiments were combined, dissolved in dry benzene (10 mL), and added over 10 min to a cold (0 °C) solution of reagent prepared as above from 2,2,6,6-tetramethylpiperidine (149 mg, 1.05 mmol) in dry benzene (4 mL), *n*-butyllithium in hexane (0.89 mL of a 1.18 M solution, 1.05 mmol), and a 25% solution of diethylaluminum chloride in toluene (equivalent to 127 mg, 1.05 mmol). After 3 h at 0 °C, the reaction mixture was treated at 0 °C with 20 mL of 1 N hydrochloric acid. The organic layer was separated, and the aqueous layer was extracted with ether (3 × 15 mL). The combined organic layers were washed with saturated sodium bicarbonate solution and brine prior to drying and solvent evaporation. Preparative TLC on silica gel (petroleum ether–ethyl acetate, 7:3) resulted in separation of the two allylic alcohols.

The most rapidly eluted substance was identified as **17c**: 53 mg (63% from **15b**); mp 206–209 °C (from dichloromethane–hexane); ^{1}H NMR ($CDCl_3$) δ 6.53 (s, 2 H), 4.97 (br s, 1 H), 4.90

(br s, 2 H), 4.80 (br s, 1 H), 3.76 (s, 6 H), 2.17 (br s, 1 H), 1.74 (s, 3 H).

Anal. Calcd for $C_{20}H_{16}F_4O_3$: C, 63.16; H, 4.24. Found: C, 62.99; H, 4.37.

Anti isomer **18c** (28 mg, 33%) was later eluted: mp 151–152 °C (from hexane); ^{1}H NMR ($CDCl_3$) δ 6.67 (s, 2 H), 4.95 (m, 4 H), 3.83 (s, 6 H), 2.73 (s, 1 H), 1.79 (br s, 3 H); mass spectrum, calcd *m/e* 380.1035, obsd 380.1044.

Independent Ring Opening of 14b. A sample of **14b** (121 mg, 0.316 mmol) in 10 mL of dry benzene was added to a cold (0 °C) solution of reagent prepared from 200 mg (1.41 mmol) of 2,2,6,6-tetramethylpiperidine in 4 mL of dry benzene, 1.18 mL of 1.2 M *n*-butyllithium in hexane (1.41 mmol), and 685 mg of a 25% solution of diethylaluminum chloride in toluene (1.41 mmol). After 3 h at 0 °C and utilization of the standard workup procedure, there was obtained a residue which was purified by TLC on silica gel. The resulting white solid (115 mg, 95%) was pure **17c**, the ^{1}H and ^{13}C NMR spectra of which were identical with those of the more rapidly eluted isomer of the preceding experiment.

Ring Opening of 7. Lithium 2,2,6,6-tetramethylpiperidine was prepared as before from 119 mg (0.844 mmol) of the piperidine and 0.545 mL of 1.55 M *n*-butyllithium in hexane (0.844 mmol). Following the addition of diethylaluminum chloride (407 mg of a 25% solution in toluene) and a solution of **7** (60 mg, 0.188 mmol) in benzene (3 mL), the reaction mixture was stirred at 0 °C for 3 h and at room temperature for 2 h. Following the customary workup, the residue was purified by TLC on silica gel (benzene elution). There was isolated 51 mg (85%) of **17a** as a white solid: mp 105–105.5 °C (from petroleum ether); ^{1}H NMR ($CDCl_3$) δ 7.06 (m, 4 H), 4.90 (m, 2 H), 4.66 (br s, 2 H), 2.20 (s, 1 H), 1.72 (br s, 3 H).

Anal. Calcd for $C_{18}H_{12}F_4O$: C, 67.50; H, 3.78. Found: C, 67.37; H, 4.07.

Ring Opening of 16a. 2,2,6,6-Tetramethylpiperidine (93.6 mg, 0.656 mmol) was treated with *n*-butyllithium (0.44 mL of 1.5 M solution, 0.656 mmol) and later with diethylaluminum chloride (316.5 mg of 25% toluene solution, 0.656 mmol). Epoxide **16a** (42 mg, 0.131 mmol) was added in benzene (2 mL). After the workup, 62 mg of a pale yellow oil was obtained. Chromatographic purification on a silica gel plate (benzene elution) gave 28 mg (66%) of **18a** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.55–7.0 (m, 4 H), 5.02 (br s, 2 H), 4.75 (m, 2 H), 2.56 (br s, 1 H), 1.78 (br s, 3 H); mass spectrum, calcd *m/e* for $C_{18}H_{12}F_4O$ 320.0824, obsd 320.0833.

Ozonolysis of 17a. A solution of **17a** (100 mg, 0.312 mmol) in anhydrous methanol (25 mL) cooled to −78 °C was ozonolyzed for 20 min. After removal of the excess ozone by entrainment (10 min), dimethyl sulfide (846 mg, 13.6 mmol) was added, and the mixture was stirred at −78 °C for 2 h, allowed to warm to room temperature, and stirred overnight. Following evaporation of the solvent under reduced pressure, the residue was dissolved in ether (30 mL) and washed with water (3 × 10 mL) and brine (10 mL) prior to drying. Preparative TLC purification of the residue on silica gel (chloroform elution) furnished 96 mg (95%) of **19a** as a colorless solid: mp 178–180 °C dec (from ethyl acetate–hexane); ^{1}H NMR ($CDCl_3$) δ 7.20 (m, 4 H), 4.73 (br s, 2 H), 3.43 (br s, 1 H), 2.03 (s, 3 H); mass spectrum, calcd *m/e* 322.0616, obsd 322.0624.

Anal. Calcd for $C_{17}H_{10}F_4O_2$: C, 63.36; H, 3.13. Found: C, 63.00; H, 3.15.

Ozonolysis of 18a. α-Hydroxy ketone **20a** was obtained by epoxidation of **8** (83 mg, 0.27 mmol), ring opening of the resulting epoxide mixture to the allylic alcohols **17a** and **18a**, and direct ozonolysis of this mixture as before. The residual oil was separated into its two components by medium-pressure liquid chromatography on silica gel (elution with dichloromethane). There was isolated 9 mg of **20a** (10% from **8**) and 39 mg (44%) of **19a** already described. For **20a**: ^{1}H NMR ($CDCl_3$) δ 7.43 (m, 2 H), 7.18 (m, 2 H), 4.71 (br s, 2 H), 2.76 (br s, 1 H), 2.12 (s, 3 H); mass spectrum, calcd *m/e* 322.0616, obsd 322.0621.

Ozonolysis of 17b. A solution of **17b** (90 mg) in methanol (35 mL) was ozonolyzed for 6 min at −78 °C. After treatment with dimethyl sulfide and workup as predescribed, the residual oil was subjected to preparative TLC on silica gel (elution with petroleum ether–ethyl acetate, 7:3). There was obtained 55 mg (61%) of **19b** as a colorless solid: mp 175–179 °C dec (from ethyl acetate–hexane); ^{1}H NMR ($CDCl_3$) δ 7.41 (m, 2 H), 7.06 (m, 2 H), 6.50 (s, 2 H), 4.63 (s, 2 H), 3.77 (s, 6 H), 2.93 (br s, 1 H), 2.08 (s, 3 H).

Anal. Calcd for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found: C, 73.33; H, 5.88.

***syn*-11-Acetyl-*anti*-11-hydroxy-1,4-dimethoxy-9,10-dihydro-9,10-methanoanthracene (20b).** Treatment of a solution of **18b** (58 mg) in methanol (10 mL) with ozone in the predescribed manner (4.5 min) afforded an oil which was subjected to preparative TLC on silica gel plates (elution with petroleum ether–ethyl acetate, 7:3). There was isolated 11 mg (19%) of **20b** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.27 (m, 2 H), 7.00 (m, 2 H), 6.58 (s, 2 H), 4.70 (br s, 2 H), 3.76 (s, 6 H), 3.03 (s, 1 H), 2.10 (s, 3 H); mass spectrum, calcd *m/e* 310.1205, obsd 310.1212.

***anti*-11-Acetyl-*syn*-11-hydroxy-1,4-dimethoxy-5,6,7,8-tetrafluoro-9,10-dihydro-9,10-methanoanthracene (19c).** Ozonolysis of **17c** (90 mg) in the predescribed manner (3 min) and preparative TLC of the residue on silica gel provided 28 mg of unreacted **17c** and 34 mg (53%) of **19c**: a colorless solid; mp 178–180 °C (from cyclohexane); ^{1}H NMR ($CDCl_3$) δ 6.57 (s, 2 H), 4.95 (br s, 2 H), 3.80 (s, 6 H), 3.32 (s, 1 H), 2.05 (s, 3 H); mass spectrum, calcd *m/e* 382.0828, obsd 382.0820.

Friedel–Crafts Acetylation of 8. A suspension of anhydrous aluminum chloride (120 mg, 0.902 mmol) in dry dichloromethane (4 mL) was treated with acetyl chloride (82.5 mg, 1.05 mmol) at −15 °C. A solution of **8** (158 mg, 0.519 mmol) in dry dichloromethane was introduced dropwise during 15 min at this temperature. The reaction mixture was stirred for 15 min at −15 °C and at room temperature for 1 h, poured onto ice containing a little hydrochloric acid, and extracted with dichloromethane (2 × 10 mL). The combined organic layers were washed with saturated bicarbonate solution and brine, dried, and evaporated. There remained 220 mg of yellowish oil, the ^{1}H NMR spectrum of which indicated the syn/anti ratio to be 46:54. The two isomers were separated by medium-pressure liquid chromatography on silica gel (elution with petroleum ether–ethyl acetate, 95:5).

For syn isomer **21a**: 81 mg (45%); colorless solid; mp 122–123 °C (from hexane); ^{1}H NMR ($CDCl_3$) δ 7.3 (m, 2 H), 7.03 (m, 2 H), 5.01 (m, 4 H), 2.06 (s, 3 H), 1.57 (br s, 3 H); *m/e* calcd 346.0981, obsd 346.0989.

Anal. Calcd for $C_{20}H_{14}F_4O$: C, 69.36; H, 4.07. Found: C, 69.25; H, 4.16.

For anti isomer **22a**: 95 mg (53%); mp 68–71 °C; ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 2 H), 7.02 (m, 2 H), 5.08 (br s, 2 H), 5.01 (m, 2 H), 1.98 (s, 3 H), 1.63 (br s, 3 H); mass spectrum, calcd *m/e* 346.0980, obsd 346.0987.

Friedel–Crafts Acetylation of 15a. (A) With Acetyl Chloride. A suspension of anhydrous aluminum chloride (259 mg, 1.95 mmol) in dry dichloromethane (4 mL) cooled to −15 °C was added 183 mg (2.34 mmol) of acetyl chloride. To this mixture was slowly added a solution of **15a** (329 mg, 1.13 mmol) in dichloromethane (12 mL) over a 20-min period. The reaction mixture was stirred for 45 min at −15 °C, poured onto ice containing a little concentrated hydrochloric acid, and extracted with dichloromethane (3 × 25 mL). Further processing as described above (isomer ratio 35:65) and isomer separation by medium-pressure liquid chromatography on silica gel (elution with petroleum ether–ethyl acetate, 9:1) gave 54 mg (14%) of syn isomer **21b** as a colorless solid: mp 168–169 °C (from ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 7.20 (m, 2 H), 6.86 (m, 2 H), 6.40 (m, 2 H), 5.03 (s, 1 H), 4.90 (m, 3 H), 3.73 (s, 6 H), 1.98 (s, 3 H), 1.60 (s, 3 H); *m/e* calcd 334.1568, obsd 334.1562.

For anti isomer **22b**: 118 mg (31%); colorless solid; mp 189–190 °C (from ethanol); ^{1}H NMR ($CDCl_3$) δ 7.20 (m, 2 H), 6.87 (m, 2 H), 6.40 (s, 2 H), 5.00 (s, 1 H), 4.90 (m, 3 H), 3.70 (s, 6 H), 2.01 (s, 3 H), 1.59 (s, 3 H); mass spectrum, calcd *m/e* 334.1568, obsd 334.1562.

Anal. Calcd for $C_{22}H_{22}O_3$: C, 79.01; H, 6.63. Found: C, 78.87; H, 6.65.

A third product (82 mg) believed to be a ring-acetylated compound was also isolated: ^{1}H NMR ($CDCl_3$) δ 7.30 (m, 4 H), 6.53 (s, 2 H), 5.50 (s, 1 H), 5.06 (s, 1 H), 3.73 (s, 3 H), 3.67 (s, 3 H), 2.00 (s, 3 H), 1.50 (s, 3 H), 1.37 (s, 3 H).

(B) With Acetic Anhydride. To a solution of **15a** (51 mg, 0.175 mmol) in acetic anhydride (5 mL) was added 41 mg (0.30 mmol) of anhydrous zinc chloride. The mixture was stirred at room temperature for 20 h, poured into a 10% aqueous solution of sodium carbonate, and extracted with ether (3 × 20 mL). The combined organic layers were washed with brine, dried, and evaporated. The ^{1}H NMR spectrum of the **21b/22b** mixture indicated their ratio to be 30:70.

Friedel–Crafts Acetylation of 15b. Treatment of **15b** (54 mg, 0.148 mmol) with aluminum trichloride (40 mg, 0.30 mmol) and acetyl chloride (27.6 mg, 0.35 mmol) in dry dichloromethane (30 min at −15 °C, 1.5 h at room temperature) afforded a yellow oil (66 mg) whose ^{1}H NMR spectrum showed the ratio of **21c** to **22c** to be 28:72. Preparative TLC separation on silica gel (elution with petroleum ether–ethyl acetate, 9:1) gave 11 mg (18%) of syn isomer **21c** as a white solid: mp 163–164 °C (from ethanol); ^{1}H NMR ($CDCl_3$) δ 6.55 (s, 2 H), 5.23 (br s, 2 H), 5.05 (s, 1 H), 4.98 (s, 1 H), 3.78 (s, 6 H), 2.05 (s, 3 H), 1.58 (br s, 3 H); mass spectrum, calcd m/e 406.1192, obsd 406.1183.

There was also isolated 24 mg (40%) of anti isomer **22c** as a colorless solid: mp 139–140 °C (from ethanol); ^{1}H NMR ($CDCl_3$) δ 6.54 (s, 2 H), 5.23 (br s, 2 H), 5.03 (m, 2 H), 3.78 (s, 6 H), 2.00 (s, 3 H), 1.61 (br s, 3 H); mass spectrum, calcd m/e 406.1192, obsd 406.1183.

Anal. Calcd for $C_{22}H_{18}F_4O_3$: C, 65.02; H, 4.46. Found: C, 64.76; H, 4.57.

Prins Reaction of 8. To a mixture of **8** (100 mg, 0.329 mmol) and paraformaldehyde (110 mg, 3.66 mmol of CH_2O) was added anhydrous dioxane (6 mL) containing 3.3 mmol of 96% sulfuric acid. The mixture was heated to reflux for 1 h, additional paraformaldehyde (90 mg) was added, and heating was resumed for an additional 2 h. Following cooling, dilution with water (20 mL), and extraction with ether (3 × 15 mL), the combined organic layers were washed with 10% ammonium chloride, saturated sodium bicarbonate, and brine solutions prior to drying. Solvent evaporation left 158 mg of a light brown oil, the ^{1}H NMR spectrum of which indicated the syn/anti ratio to be 41:59. These products were separated by preparative TLC on silica gel (two elutions with petroleum ether–ether, 95:5).

For syn isomer **23a**: 41 mg (36%); colorless solid; mp 157–157.5 °C (from ethanol); ^{1}H NMR ($CDCl_3$) δ 7.43–6.87 (m, 4 H), 4.76 (br s, 1 H), 4.66 (m, 2 H), 4.50 (br s, 1 H), 3.73 (t, J = 5.5 Hz, 2 H), 3.43 (s, 2 H), 2.20 (t, J = 5.5 Hz, 2 H); mass spectrum, calcd m/e 346.0981, obsd 346.0987.

Anal. Calcd for $C_{20}H_{14}F_4O$: C, 69.36; H, 4.07. Found: C, 69.32; H, 4.21.

For anti isomer **24a**: 35 mg (31%); ^{1}HNMR ($CDCl_3$) δ 7.46–6.93 (m, 4 H), 4.83 (br s, 1 H), 4.66 (m, 2 H), 4.53 (br s, 1 H), 3.70 (t, J = 5.5 Hz, 2 H), 3.30 (s, 2 H), 2.23 (t, J = 5.5 Hz, 2 H); mass spectrum, calcd m/e 346.0981, obsd 346.0984.

Prins Reaction of 15a. A mixture of **15a** (104 mg, 0.355 mmol), paraformaldehyde (135 mg, 4.49 mmol of CH_2O), concentrated sulfuric acid (340 mg, 3.46 mmol), and dioxane (10 mL) was heated at reflux for 3 h, cooled, poured into water (50 mL), and extracted with ether. The above workup yielded a yellowish oil (194 mg), the ^{1}H NMR spectrum of which indicated the syn/anti ratio to be 38:62. The mixture was separated by preparative TLC on silica gel (two elutions with petroleum ether–ethyl acetate, 9:1).

For syn isomer **23b**: 51 mg (42%); colorless solid; mp 162–163 °C (from ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 2 H), 6.90 (m, 2 H), 6.40 (s, 2 H), 4.70 (s, 1 H), 4.53 (s, 3 H), 3.70 (m, 8 H), 3.30 (s, 2 H), 2.23 (t, J = 5.5 Hz, 2 H) mass spectrum, calcd m/e 334.1568, obsd 334.1561.

Anal. Calcd for $C_{22}H_{22}O_3$: C, 79.02; H, 6.63. Found: C, 79.01; H, 6.63.

For anti isomer **24b**: 63 mg (53%); colorless solid; mp 181–182 °C (from ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 7.20 (m, 2 H), 6.83 (m, 2 H), 6.43 (s, 2 H), 4.70 (s, 1 H), 4.56 (s, 2 H), 4.50 (s, 1 H), 3.73 (m, 8 H), 3.43 (s, 2 H), 2.20 m, 2 H); mass spectrum, calcd m/e 334.1568, obsd 334.1561.

Prins Reaction of 15b. A suspension of **15b** (25 mg, 0.06 mmol) and paraformaldehyde (72 mg, 2.33 mmol) in dry dioxane (2.5 mL) was heated with concentrated sulfuric acid (230 mg, 2.34 mmol) at the reflux temperature for 1 h, cooled, poured into water (60 mL), and extracted with ether (4 × 10 mL). The combined organic layers were processed in the usual manner to give 39 mg of an oil whose ^{1}H NMR spectrum showed the syn/anti ratio to be 46:54. In two additional runs involving 25 and 35 mg of **15b**, the product distributions were 43:57 and 33.67 (average 41:59). The products of the three runs were combined and subjected to medium-pressure liquid chromatography on silica gel (elution with petroleum ether–ethyl acetate, 9:1).

For syn product **23c**: 17 mg (21%); colorless solid; mp 165–166 °C (from ethanol); ^{1}H NMR ($CDCl_3$) δ 6.51 (s, 2 H), 4.88 (br s, 2 H), 4.73 (s, 1 H), 4.48 (s, 1 H), 3.77 (s, 6 H), 3.70 (t, J = 5 Hz, 2 H), 3.35 (s, 2 H), 2.22 (t, J = 5 Hz, 2 H); mass spectrum, calcd m/e 406.1192, obsd 406.1199.

For anti product **24c**: 26 mg (33%); colorless solid; mp 147.5–148.5 °C (from ethanol); ^{1}H NMR ($CDCl_3$) δ 6.60 (s, 2 H), 4.90 (br s, 2 H), 4.82 (br s, 1 H), 4.52 (br s, 1 H), 3.78 (s, 6 H), 3.70 (t, J = 5 Hz, 2 H), 3.38 (s, 2 H), 2.25 (t, J = 5 Hz, 2 H); mass spectrum, calcd m/e 406.1192, obsd 406.1180.

Anal. Calcd for $C_{22}H_{18}F_4O_3$: C, 65.02; H, 4.46. Found: C, 64.80; H, 4.58.

Preparation of 26a. To a cold (0 °C), stirred suspension of lithium aluminum hydride (20 mg, 2.37 mmol) in anhydrous tetrahydrofuran (3 mL) was added dropwise a solution of **21b** (87 mg, 0.26 mmol) in the same solvent (7 mL) during 10 min. The reaction mixture was stirred at room temperature for 4 h, treated at 0 °C with 2 mL of saturated aqueous sodium sulfate solution (30 min), and poured over a mixture of ice and 10% sulfuric acid solution. This solution was saturated with sodium chloride and extracted with ether (3 × 25 mL). The combined organic layers were washed with saturated sodium bicarbonate and sodium chloride solutions, dried, and evaporated. Purification of the residue by preparative TLC on silica gel (elution with petroleum ether–ethyl acetate, 7:3) gave 78 mg (89%) of alcohol **25a**: mp 155–156 °C (from ether–hexane); ^{1}H NMR ($CDCl_3$) δ 7.27 (m, 2 H), 6.93 (m, 2 H), 6.43 (s, 2 H), 4.97 (m, 1 H), 4.83 (br s, 1 H), 4.68 (br s, 1 H), 4.36 (br s, 1 H), 3.75 (s, 6 H), 3.50 (m, 1 H), 1.73 (br s, 3 H), 1.47 (m, 1 H), 1.05 (d, J = 6.75 Hz, 3 H); mass spectrum, calcd m/e 336.1725, obsd 336.1733.

Alcohol **25a** (75 mg, 0.23 mmol) and paraformaldehyde (150 mg, 5 mmol) were dissolved in 5 mL of dioxane, treated with 3 drops of concentrated sulfuric acid, and stirred overnight at room temperature. The reaction mixture was poured into water (100 mL) and extracted with ether (4 × 15 mL). The combined organic layers were washed with saturated solutions of sodium bicarbonate and brine prior to drying and solvent evaporation. Preparative TLC purification of the residue on silica gel (elution with hexane–ethyl acetate, 7:3) afforded 41 mg (53%) of **26a**: colorless solid; mp 168–170 °C (from ethyl acetate–hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (m, 2 H), 6.96 (m, 2 H), 6.47 (d, J = 8.8 Hz, 1 H), 6.43 (d, J = 8.8 Hz, 1 H), 4.90 (d, J = 1.5 Hz, 1 H), 4.88 (d, J = 1.5 Hz, 1 H), 4.55 (s, 1 H), 4.25 (d, J = 1.5 Hz, 1 H), 3.77 (s, 3 H), 3.74 (s, 3 H), 3.73 (m, 1 H), 3.62 (m, 2 H), 2.45 (m, 1 H), 1.94 (dd, J = 12.5, 2.5 Hz, 1 H), 1.03 (d, J = 7 Hz, 2 H); mass spectrum, calcd m/e 348.1725, obsd 348.1734.

Synthesis of 26b. A 102-mg (0.305 mmol) sample of **22b** was reduced as above with 90 mg (2.37 mmol) of lithium aluminum hydride. There was obtained 82 mg (80%) of alcohol **25b**: colorless solid; mp 168–168.5 °C (from ethyl acetate); ,^{1}H NMR ($CDCl_3$) δ 7.20 (m, 2 H), 6.88 (m, 2 H), 6.50 (s, 2 H), 5.02 (m, 1 H), 4.78 (m, 1 H), 4.70 (br s, 1 H), 4.40 (br s, 1 H), 3.78 (m, 7 H), 1.70 (br s, 3 H), 1.47 (m, 1 H), 1.08 (d, J = 6.8 Hz, 3 H); mass spectrum, calcd m/e 336.1725, obsd 336.1730.

Treatment of 52 mg (0.155 mmol) of **25b** with 175 mg (5.83 mmol) of paraformaldehyde in the predescribed manner furnished 42 mg (78%) of **26b**: colorless solid; mp 144–144.5 °C (from hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (m, 2 H), 6.91 (m, 2 H), 6.51 (s, 2 H), 4.92 (d, J = 1.5 Hz, 1 H), 4.86 (d, J = 1.5 Hz, 1 H), 4.53 (s, 1 H), 4.31 (d, J = 1.5 Hz, 1 H), 3.78 (m, 2 H), 3.77 (s, 3 H), 3.76 (s, 3 H), 3.62 (m, 1 H), 2.31 (m, 1 H), 1.91 (dd, J = 12.5, 2.5 Hz, 1 H), 1.06 (d, J = 7 Hz, 3 H); mass spectrum, *calcd* m/e 348.1725, obsd 348.1733.

Anal. Calcd for $C_{23}H_{24}O_3$: C, 79.28; H, 6.94. Found: C, 79.21; H, 7.06.

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Registry No. 3, 32704-36-2; 4, 78965-02-3; 5, 78965-03-4; 6, 79027-04-6; 7, 78965-04-5; 8, 78965-05-6; 9, 79027-05-7; 10, 78965-06-7; 11, 79027-06-8; 12a, 78965-07-8; 12b, 78965-08-9; 13a enedione, 78965-09-0; 13b enedione, 78965-10-3; 14a, 78965-11-4; 14b, 78965-12-5; 15a, 78965-13-6; 15b, 78965-14-7; 16a, 79027-07-9; 16b, 79081-88-2; 17a, 78965-15-8; 17b, 78965-16-9; 17c, 78965-17-0; 18a, 79027-08-0; 18b, 79027-09-1; 18c, 79027-10-4; 19a, 78965-18-1; 19b, 78965-19-2; 19c, 78965-20-5; 20a, 79027-11-5; 20b, 79027-12-6; 21a, 78965-21-6; 21b, 78965-22-7; 21c, 78965-23-8; 22a, 79027-13-7; 22b, 79027-14-8; 22c, 79027-15-9; 23a, 78965-24-9; 23b, 78965-25-0; 23c, 78965-26-1; 24a, 79027-16-0; 24b, 79027-17-1; 24c, 79027-18-2; 25a, 78965-27-2; 26a, 78965-28-3; 26b, 79027-19-3; (*E,E*)-1,4-dichlorobutadiene, 3588-12-3; 9-isopropylidene-1,4-dihydro-1,4-methanonaphthalene, 7350-72-3.

Reaction of Diazonium Salts with Transition Metals. 6. Preparation of Mixed Acid Anhydrides from Arenediazonium Salts and Sodium Carboxylates under Palladium(0) Catalysis[1]

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The palladium(0)-catalyzed reaction of arenediazonium tetrafluoroborates with carbon monoxide and sodium carboxylates in acetonitrile at 25 °C gave mixed acid anhydrides, ArCOOCOR (Ar = 3-Me-Ph, 4-Me-Ph, 2-MeO-Ph, 4-Br-Ph, 4-I-Ph, 3-NO_2-Ph, 4-NO_2-Ph, and Ph; R = H, Me, Et, *t*-Bu, and Ph), in good yields. Homoaromatic acid anhydrides, $(ArCO)_2O$, were obtained by heating of ArCOOCOMe at 100–120 °C under vacuum. ArCOO-CO-*t*-Bu can be utilized to obtain the corresponding arenecarboxamides by the reaction with some amines.

Recently we reported a convenient carboxylation of arenediazonium tetrafluoroborates, ArN_2BF_4 (**1**), with carbon monoxide and sodium acetate in the presence of $Pd(OAc)_2$.[2] The initial product in the carboxylation was proposed to be a mixed acid anhydride (**3**) in which one of the acyl groups came from **1** and another from the sodium carboxylate (**2**) (eq 1).[2,3]

$$\underset{\mathbf{1}}{ArN_2BF_4} + CO + \underset{\mathbf{2}}{RCOONa} + Pd(OAc)_2 \rightarrow \underset{\mathbf{3}}{ArCOOCOR} \quad (1)$$

This paper presents a convenient preparation of the mixed acid anhydrides (**3**), especially those carrying various aliphatic acyl groups as one of the acyl components. Facile transformation of ArCOOCOMe to arenecarboxylic anhydrides, $(ArCO)_2O$ (**4**), and utilization of ArCOOCO-t-Bu to obtain arenecarboxamide, $ArCONR^1R^2$ (**5**) are also described.

Results and Discussion

Preparation of Mixed and Homo Acid Anhydrides. The reaction was carried out with **1** (10 mmol), **2** (15 mmol), $Pd(OAc)_2$ (0.1–0.2 mmol), and carbon monoxide (9 kg/cm^2) in acetonitrile (60 mL) at room temperature (25 °C) for 0.5 h. Since **1** reacts with **2** spontaneously in acetonitrile to form tarry materials in the absence of carbon monoxide, a precaution should be taken against contact of **1** with **2** until the reaction atmosphere has been replaced by carbon monoxide. After removal of precipitates, consisting of palladium black and sodium tetrafluoroborate, and concentration of the filtrate, the residue was extracted with hexane at 30–35 °C. The crystalline products precipitated on cooling and were collected, while the liquid products were obtained by removal of the solvent under vacuum. Although the liquid products could be distilled by rapid short-pass distillation except for benzoic formic anhydride, only benzoic acetic and *p*-toluic acetic anhydrides [40 °C (0.5 mmHg)] were obtained in almost pure form (~99%). HPLC analysis of the products showed the presence of only a trace of benzoic (or *p*-toluic) anhydride and acetanilide (or aceto-*p*-toluide). The anilide content was less than 0.1% as judged by elemental analysis in which nitrogen could not be detected. The formation of a trace amount of *N*-arylacetamides by the reaction of diazonium salts with acetonitrile will be described in a separate paper. Benzoic (or *p*-toluic) formic anhydride decomposed to benzoic acid during distillation (vide infra). Results are summarized in Table I. In most of the products, peak areas of each acyl (or aroyl) group in the ^1H NMR spectra were consistent with their 1:1 composition (last column of Table I). The presence of homo acid anhydrides was evaluated by a deviation of the area ratio from the expected value in the ^1H NMR spectra. The IR spectra of the products showed two carbonyl absorptions characteristic of acid anhydrides. Homo aliphatic acid anhydrides, which can be easily detected by carbonyl absorption near 1825 cm^{-1} in the IR spectra, could not be found in all products listed in Table I. The contamination with acids could be estimated by the presence of a carbonyl absorption near 1690 cm^{-1} in the IR and by the ^1H NMR resonance near 10–12 ppm (from Me_4Si in CCl_4; (see footnote in Table I). HPLC analysis of some liquid products also showed a few percent of benzoic anhydride and/or benzoic acid in the liquid products. The contamination of the crystalline products with acids or homo acid anhydrides was proved to be negligible by IR and NMR measurements. Some of the liquid products contained small amount of acids and/or homo acid anhydrides, but further purification of the mixed acid anhydrides was difficult because of their facile disproportionation by heat.[4] The disproportionation of both liquid and crystalline products proceeded easily on standing even at room temperature; i.e., considerably scrambled mixture of acid anhydrides were obtained within 1 day for liquid compounds

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