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Stabilized and Destabilized Carbocations in the 1,6-Methano[10]annulene Series

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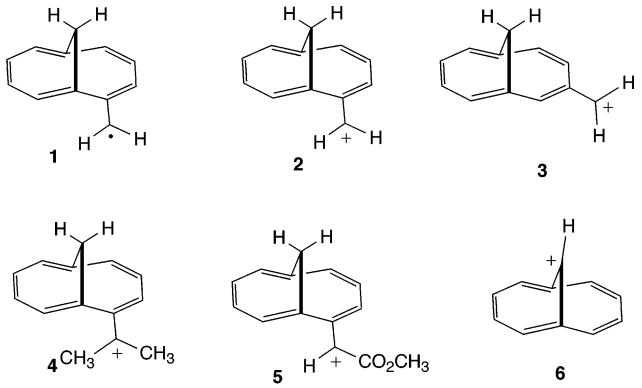
2-Chloromethyl and 3-chloromethyl-1,6-methano[10]annulene systems solvolyze in methanol to give simple substitution products. Solvent effect studies and the special salt effect support the involvement of cationic intermediates stabilized by the 1,6-methano[10]annulene group. Rate data indicate that the degree of cation stabilization greatly exceeds that of naphthyl groups. B3LYP/6-31G* computational studies also suggest that the cationic intermediates are greatly stabilized by the 1,6-methano[10]annulene. By way of contrast to these findings, solvolytic and computational studies indicate that the 11-(1,6-methano[10]annulenyl) cation is a destabilized analogue of the cycloheptatrienyl cation. There are no favorable interactions with the annulene ring. Distortions from planarity prevent charge delocalization as in the analogous aromatic cycloheptatrienyl cation.

Introduction

The 1,6-methano[10]annulene system, first prepared by Vogel in 1964, is an example of an aromatic group possessing 10 π-electrons.[1] NMR as well as chemical reactivity criteria confirm the aromatic nature of this group.[2] Recently we have determined that the 1,6-methano[10]annulene group is a potent radical stabilizing group, which far surpasses the ability of phenyl and naphthyl to stabilize free radicals.[3] Our methylenecyclopropane rearrangement probe was used to determine the γ^+ value for the 1,6-methano[10]annulene group, and computational studies supported the suggestion that radicals such as **1** were remarkably stabilized. 1,6-Methano[10]annulene substituted carbenes have also been thermally generated utilizing the appropriate tosylhydrazone salts as precursors.[4] However, little is known about the cation stabilizing ability of the 1,6-methano-[10]annulene system. We have studied the carbocations **2**−**6** by solvolytic methods, and we now report on the stabilities of these cations.



Results and Discussion

1,6-Methano[10]annulenyl Cations. The 2-substituted chloride **8** was prepared as previously described[5,6] from the corresponding alcohol **7**, and the isomeric 3-substituted chloride **10** was prepared in an analogous fashion from alcohol **9**.[7] These chlorides were solvolyzed in methanol at 25.0 °C, where both of these substrates readily react. The methyl ether substitution products **11** and **12** were the sole products formed in these reactions. Rate data are reported in Table 1, as well as data on chloride **13** and mesylates **16** and **17** for comparison purposes. The effect of solvent on reaction rate of chloride **8** was also determined. The rate was too fast to measure in the more highly ionizing solvent CF_3CH_2OH, and therefore chloride **8** was studied in 90% aqueous methanol, EtOH, and *i*-PrOH, where rates were slow enough to be conveniently measured. There are large rate increases as solvent ionizing power is increased, and the Winstein−Grunwald *m* value is 1.28 (r = 0.997). This solvent effect is consistent with solvolysis of **8** by a cationic mechanism.

Data in acetic acid also strongly implicate a cationic intermediate in acetolysis of **8**. The reaction of 2.5 mM **8** in CD_3CO_2D (containing no buffering base) does not go to completion but reaches an equilibrium position con-

(1) (a) Vogel, E.; Roth, H. D. *Angew. Chem. Int. Ed. Engl.* **1964**, *3*, 228. (b) Vogel, E.; Klug, W.; Breuer, A *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VI, p 721.

(2) Dorn, H. C.; Yannoni, C. S.; Limbach, H. H.; Vogel, E. *J. Phys. Chem.* **1994**, *98*, 11628.

(3) Creary, X.; Miller, K. *Org. Lett.* **2002**, *4*, 3493.

(4) Jones, W. M.; LaBar, R. A.; Brinker, U. H.; Gebert, P. H. *J. Am. Chem. Soc.* **1977**, *99*, 6379.

(5) Neidlein, R.; Zeiner, H. *Chem. Ber.* **1982**, *115*, 3353.

(6) Kitching, W.; Olszowy, H. A.; Schott, I.; Adcock, W.; Cox, D. P. *J. Organomet. Chem.* **1986**, *310*, 269.

(7) Nelson, P. H.; Bartsch, G. A.; Untch, K. G.; Fried, J. H. *J. Med. Chem.* **1975**, *18*, 583.

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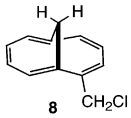
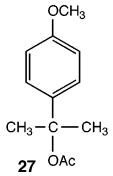
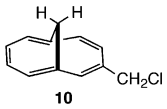
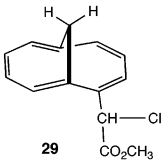
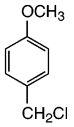
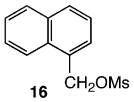
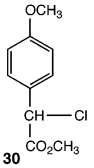
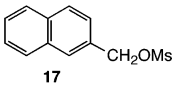
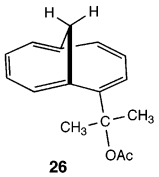
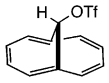
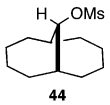
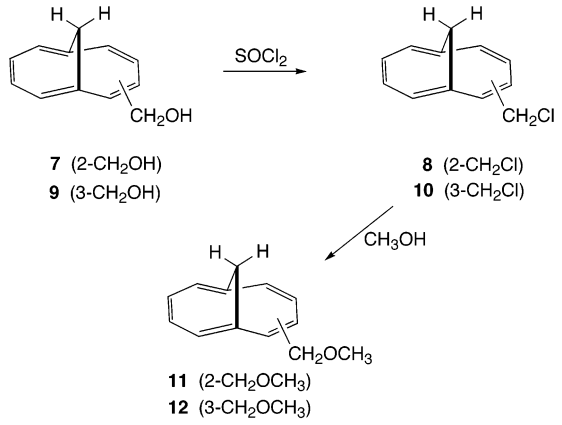
TABLE 1. Solvolysis Rates at 25.0 °C

Compound	Solvent	k (s^{-1})	Compound	Solvent	k (s^{-1})
 **8**	CH_3OH	5.63×10^{-3}	 **27**	CH_3OD	3.87×10^{-5}
	90% CH_3OH	3.36×10^{-2}			
	EtOH	2.75×10^{-4}			
	i-PrOH	2.86×10^{-5}			
 **10**	CH_3OH	6.10×10^{-5}	 **29**	CD_3OD	2.78×10^{-3a}
				CD_3OD	2.06×10^{-3b}
 **13**	CH_3OH	3.10×10^{-4}			
 **16**	CH_3OH	1.25×10^{-3}	 **30**	CH_3OH	8.24×10^{-5}
 **17**	CH_3OH	2.40×10^{-4}			
 **26**	CH_3OD	1.47×10^{-5}	 **42**	CF_3CH_2OH	4.89×10^{-4}
				DMSO-d_6	5.83×10^{-6}
			 **44**	CF_3CH_2OH	6.04×10^{-4}

[a] Fast isomer. [b] Slow isomer.



7 (2-CH_2OH) **8** (2-CH_2Cl)
9 (3-CH_2OH) **10** (3-CH_2Cl)
11 (2-CH_2OCH_3)
12 (3-CH_2OCH_3)

taining 52% of the acetate substitution product and 48% unreacted chloride **8**. This equilibrium position is approached in a first-order fashion. The reaction is subject to a special salt effect when lithium perchlorate is added to the CD_3CO_2D, i.e., there are large rate increases as perchlorate concentration is increased. The ^1H NMR spectra shown in Figure 1 demonstrate the effect of lithium perchlorate on the extent of reaction of **8** over 15 min at 25 °C. In pure CD_3CO_2D, the acetate product is barely visible after 15 min and the reaction approaches equilibrium with a half-life of 526 min. A significant rate increase can be seen in 0.01 M $LiClO_4$, where the half-life for approach to equilibrium is now 50 min. With 0.1 M $LiClO_4$ added to the solution, the reaction has almost reached the equilibrium position after 15 min and the half-life for approach to equilbrium is only 2.8 min. Such large rate increases with only small changes in perchlorate ion concentration (special salt effect) were first observed by Winstein and are suggestive of the interception of an ion pair by replacement of chloride ion with perchlorate ion at the solvent separated ion-pair stage.[8]

The remarkably fast solvolysis rates of the primary chlorides **8** and **10** are indicative of an unusually large cation stabilizing effect of the 1,6-methano[10]annulene system on both cations **2** and **3**. However, the stabilization of cation **2** appears to be slightly larger than that of cation **3**. The chloride **8** is even more reactive than *p*-methoxybenzyl chloride, **13**, despite the potent cation stabilizing ability of the *p*-methoxy substituent. Both chlorides **8** and **10** are far more reactive than the naphthyl analogues **14** and **15**. In fact chlorides **14** and **15** are quite unreactive in methanol, and mesylates **16** and **17** were the derivatives studied in order to achieve convenient reactivity. The relative rate data shown are approximations assuming that mesylates are 3×10^4 times more reactive than chlorides.[9]

(8) Winstein, S.; Robinson, G. C. *J. Am. Chem. Soc.* **1958**, *80*, 169.
(9) Noyce, D. S.; Virgilio, J. A. *J. Org. Chem.* **1972**, *37*, 2643.

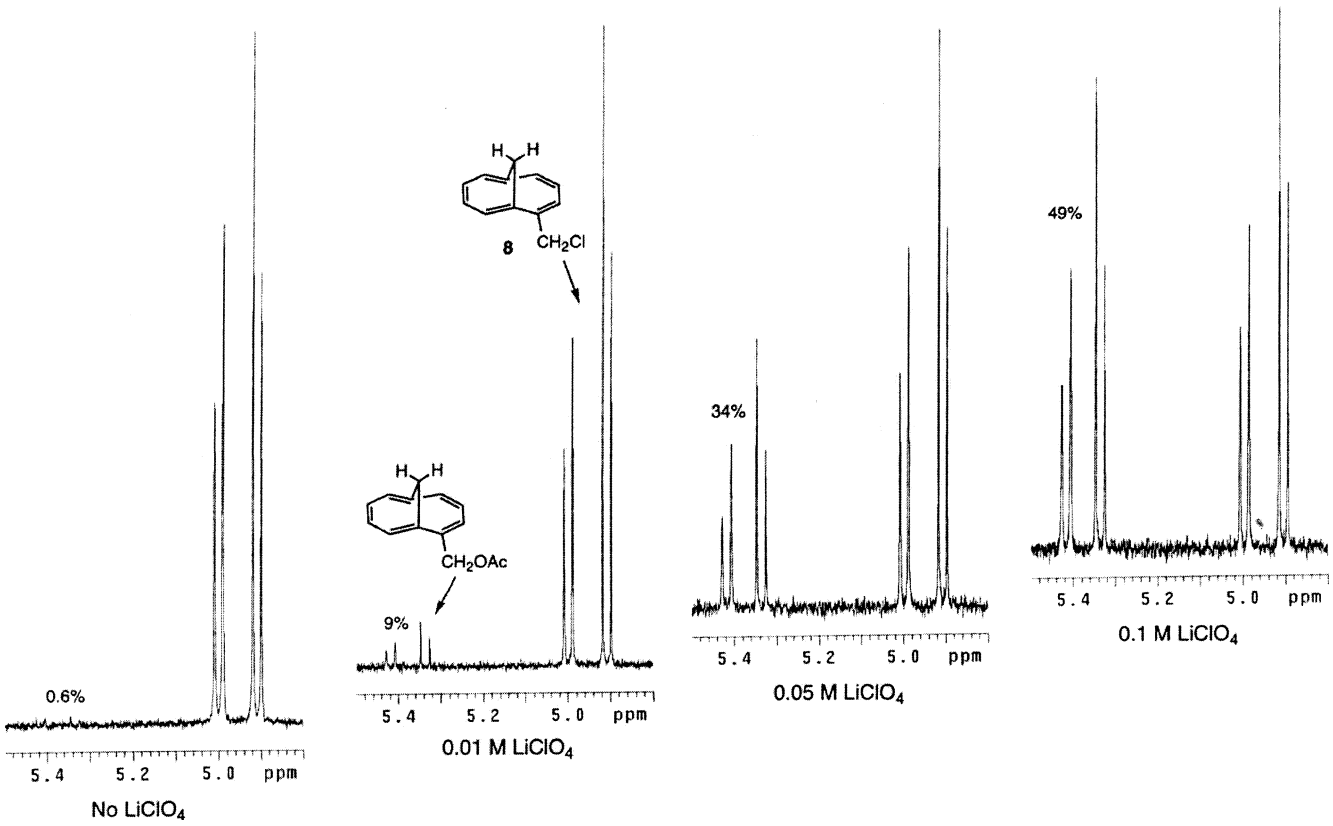
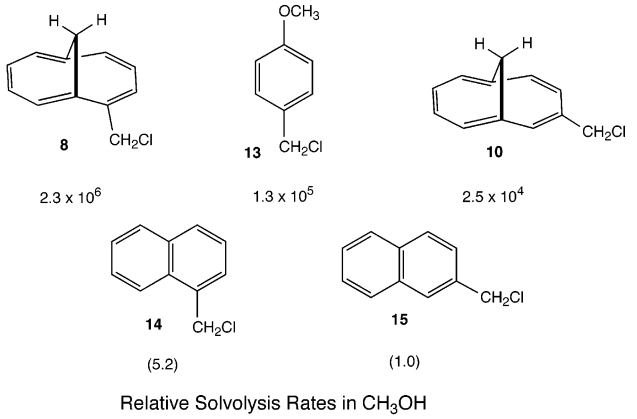
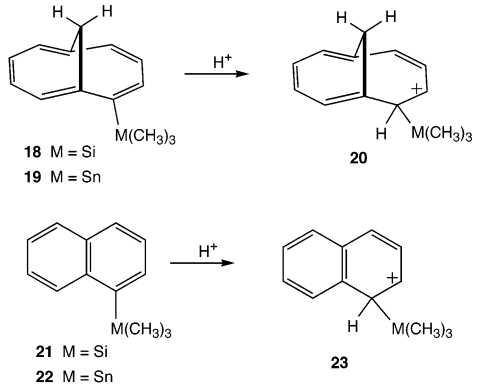


FIGURE 1. ^{1}H NMR spectra of **8** in CD_3CO_2D containing varying amounts of $LiClO_4$ after 15 min at 25 °C.





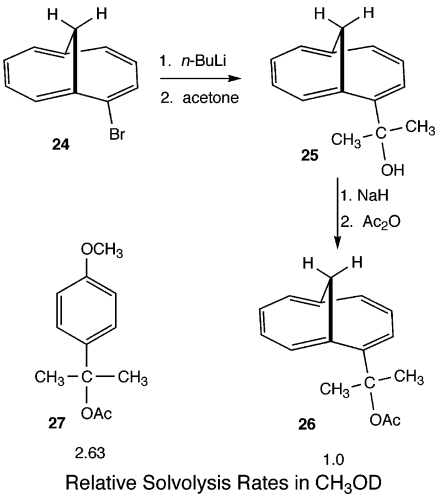
What is the origin of the high reactivity of chlorides **8** and **10**? A previous study on rates of protiodemetalation of substrates **18** and **19** showed that desilylation occurred 35 times faster in the 1,6-methano[10]annulene systems than in the analogous naphthyl systems **21**.[6] Protiodestannylation of **19** occurred 700 times faster than in **22**.[6] The implication is that the intermediate cations **20** in this electrophilic aromatic substitution reaction are more effectively stabilized by the annulene system than the cations **23** are stabilized by the naphthyl system. These findings complement our solvolysis rate data, which also suggest that 1,6-methano[10]annulene stabilization of carbocations greatly surpasses naphthyl stabilization.

The extraordinary solvolysis rate of chloride **8** indicates that cation **2** is even more stable than the *p*-methoxybenzyl cation. We were therefore interested in a more quantitative measure of the cation stabilizing ability of the 1-annulenyl group in terms of the γ^+ value (group σ^+ value).[10] The acetate **26** was prepared from the alcohol **25**, which was in turn available from reaction of 2-lithio-1,6-methano[10]annulene with acetone. Both **26** and the related substrate *p*-methoxycumyl acetate, **27**, solvolyze readily in methanol at room temperature to form the corresponding methyl ether products. To our initial surprise, **26** was 2.63 times less reactive than the *p*-methoxy analogue **27**, despite the fact that chloride **8** is 18 times *more* reactive than *p*-methoxy benzyl chloride, **13**. This implies that the 1,6-methano[10]annulene system ($\gamma^+ = -0.69$)[11] is now less cation stabilizing than the *p*-anisyl group ($\gamma^+ = -0.78$). There are two possible

(10) (a) Peters, E. N.; *J. Am. Chem. Soc.* **1976**, *98*, 5627. (b) Peters, E. N. *J. Org. Chem.* **1977**, *42*, 1419.

(11) γ^+ for the 1,6-methano[10]annulene group is calculated from the rate of methanolysis of **26** and assuming a ρ^+ value of −4.82 in methanol.

explanations for this reduced 1,6-methano[10]annulene effect in solvolysis of **26**. The first is reduced conjugation. Twisting of the 1,6-methano[10]annulene group out of conjugation in the 3° cation **4** due to steric factors may account for the reduced cation stabilizing influence. This possibility is addressed in the computational section. The possibility also exists that there is less demand for 1,6-methano[10]annulene stabilization in the 3° cation **4** derived from **26**. Hence the response is less than that of the *p*-methoxyphenyl group. This latter explanation would require that the ability of the 1,6-methano[10]-annulene group to respond to electron demand is much more variable than that of the *p*-methoxyphenyl group.



Attention was next turned to the electron-deficient cation **5**, where the formally electron-withdrawing CO_2CH_3 group is attached to the cationic center.[12] The precursors to this cation were the chlorides **29**, which were available from the α-ketoester **28**. Reduction of **28** with borohydride followed by reaction with thionyl chloride gave an inseparable mixture of diastereomeric chlorides **29** (1.7:1 ratio). These chlorides are quite reactive, undergoing solvolysis in methanol readily at room temperature at comparable rates. In fact, the rates of solvolyses of chlorides **29** in methanol differ little from that of chloride **8** despite the presence of the cation destabilizing CO_2CH_3 group. This rate behavior contrasts with that of previously studied systems **31**−**34**, where the effect of the CO_2CH_3 group is to retard solvolysis rate by a significant factor.[13]

Examination of the solvolysis products suggests a reason for the very small effect of the carbomethoxy group (relative to hydrogen) on the rate of solvolysis of **29**. While solvolyses of **8** and **26** gave simple substitution products, chlorides **29** give a major product **35**, where methanol is captured at the 5-position of the 1,6-methano[10]annulene ring. Also produced are minor unidentified products. The structure of this "aromaticity-disrupted" product rests on a number of features in the ^{1}H NMR spectrum as well as comparison with the calculated[13] (B3LYP/6-31G*/

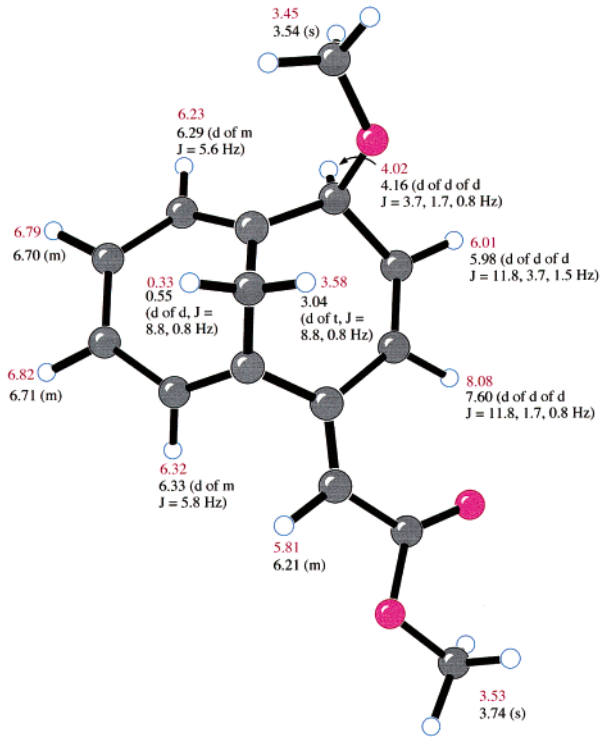
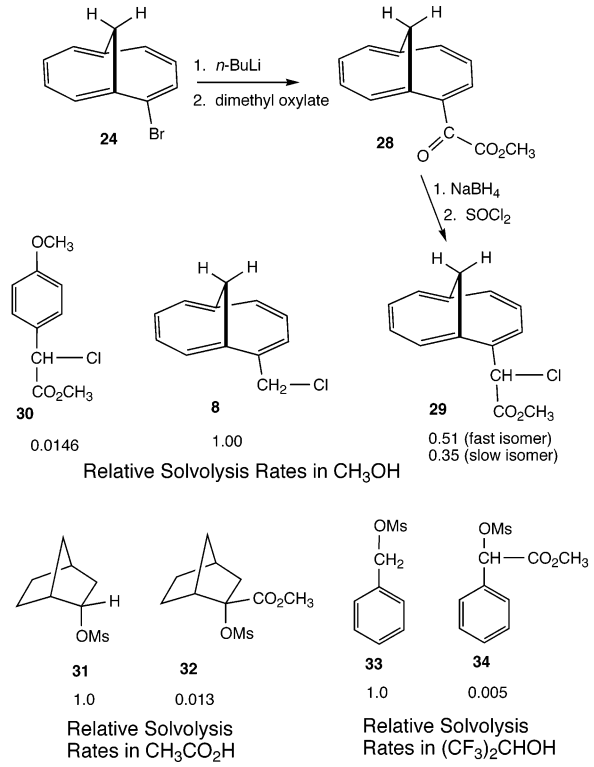


FIGURE 2. ^{1}H NMR Spectral Data for **35**. B3LYP/6-31G*/GIAO calculated values are in red.



GIAO) NMR spectrum. These are shown in Figure 2. One of the C-11 hydrogens is in the shielding region of the cycloheptatriene system and appears upfield at δ 0.55. The other hydrogen at δ 3.04 is in the deshielding region of the cycloheptatriene and is further desheilded by the exocyclic double bond. The stereochemistry of the meth-

(12) For a review and leading references on carbocations containing formal electron-withdrawing groups, see: Creary, X. *Chem. Rev.* **1991**, *91*, 1625.

(13) Creary, X.; Geiger, C. C. *J. Am. Chem. Soc.* **1982**, *104*, 4151.

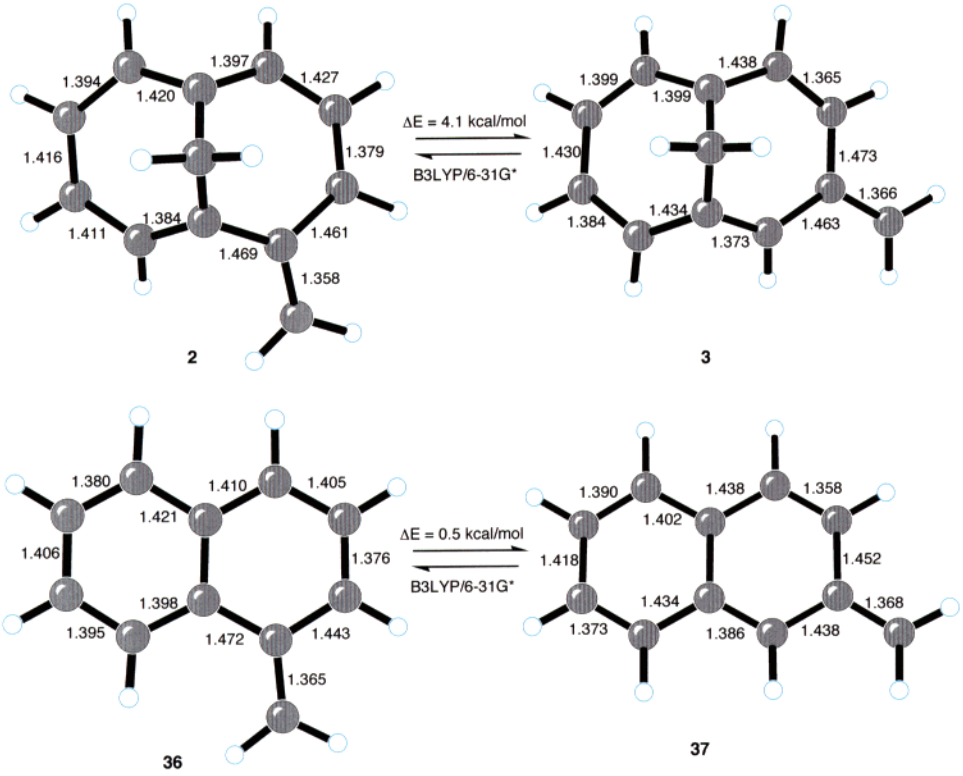
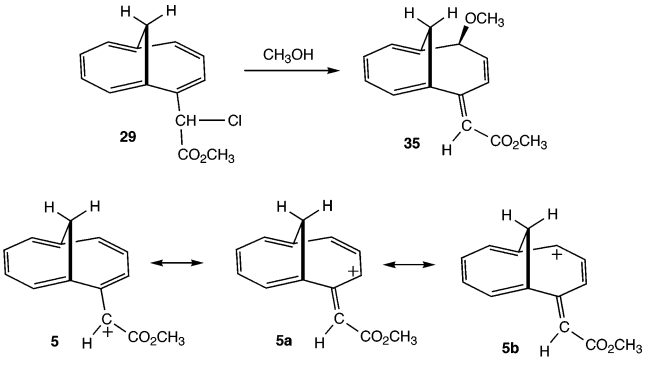


FIGURE 3. B3LYP/6-31G* relative energies of 2- and 3-substituted 1,6-methano[10]annulyl and naphthyl cations.

oxy group is established by the observation of W-coupling (0.8 Hz) of the C-5 hydrogen (δ 4.16) to the C-11 hydrogen at δ 0.55.



This product **35** implies unusually large charge delocalization into the aromatic annulene ring of the intermediate carbocation **5**. This is a result of the increased demand for charge delocalization as a result of the electron-withdrawing nature of the carbomethoxy group. The loss of aromaticity when methanol is trapped at the C-5 position is consistent with the reduced aromaticity of 1,6-methano[10]annulene system relative to benzenoid systems.[15] In other words, the price paid for loss of aromaticity in **35** is not unreasonable.

Computational Studies on 1,6-Methano[10]annulenyl Cations. Computational studies[14] have been carried out at the B3LYP/6-31G* level on cations **2** and **3** as well as on naphthyl analogues **36** and **37** (Figure 3). In line with our rate data is the finding that cation **2** is 4.1 kcal/mol more stable than cation **3**.

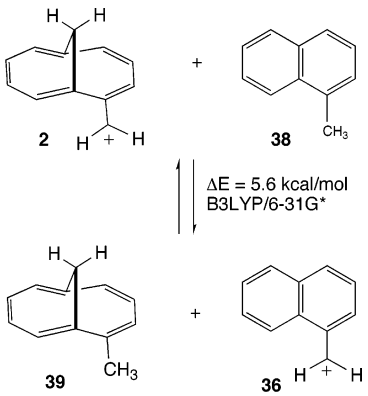
Isodesmic calculations suggest that the 2-(1,6-methano-[10]annulenyl) cation **2** is also 5.6 kcal/mol more stable than the 1-naphthyl cation **36** and 23.5 kcal/mol more stable than the unsubstituted benzyl cation, $PhCH_2^+$. This is a conjugation phenomenon, as can be clearly seen by examining bond lengths from the cationic center to the aromatic ring.

The pertinent bond length in the benzyl cation is 1.371 Å, and the shrinkage to 1.358 Å in cation **2** is consistent with increased conjugation and subsequent delocalization of charge into the annulene ring of **2**. Cation **3** is still extensively stabilized by the annulene ring, but bond lengths again suggest that delocalization is not as effective as in cation **2**. Bond lengths in cations **2** and **3** closely parallel those in the naphthyl analogues **36** and **37**, respectively, such that **2** and **3** can be considered "homonaphthyl" cations.

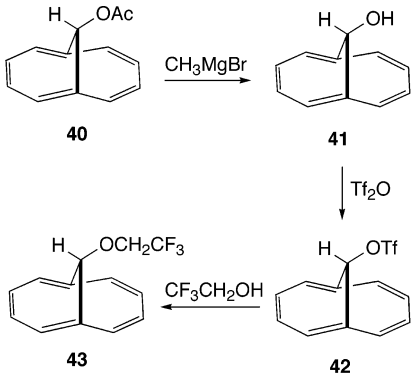
11-(1,6-Methano[10]annulenyl) Cation. The carbocation **6**, with charge at the 11-position, was also of interest. Is there any interaction of the cationic center with the aromatic annulene system? Is neighboring group

(14) Frisch, M, J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, Jr., J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I. Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.

(15) Roth, W. R.; Böhm, M.; Lennartz, H. W.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 1007.

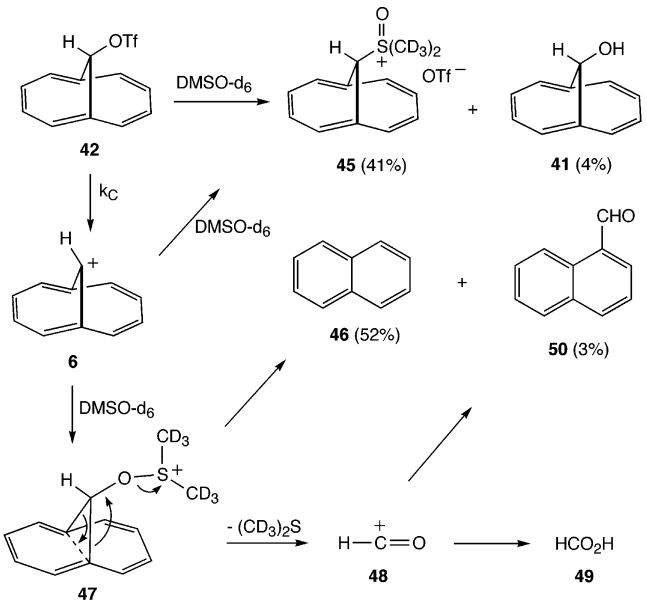


participation an important feature in generation of this cation? Is this cation related to the cycloheptatrienyl cation? Answers to these questions were sought by examining the chemistry of triflate **42**. The preparation of **42** utilized the acetate **40**, which is available from a silver acetate assisted solvolysis reaction of 11-bromo-1,6-methano[10]annulene in acetic acid.[16] This silver-assisted reaction may well involve the carbocation **6**, or at least a transition state with cationic character at the 11-position. The acetate **40** was converted to the alcohol **41** by reaction with methylmagnesium bromide. Conversion of **41** to the corresponding mesylate derivative was straightforward, but this derivative proved to be quite unreactive under solvolytic conditions. Therefore **41** was converted to the triflate derivative **42**.



Solvolysis of **42** in trifluoroethanol occurred at a convenient rate at 25 °C to give the substitution product **43**. Rate data for **42** are given in Table 1 along with data for the saturated substrate **44** for comparison purposes. The mesylate **44** also reacts at a convenient rate at 25 °C. If one corrects for the triflate/mesylate rate ratio,[17] then triflate **42** is approximately 10^5 times less reactive than the saturated analogue. It therefore appears that, on the basis of solvolysis rate data, the carbocation **6** derived from triflate **42** has no unusual stabilizing features. In fact, it is substantially destabilized relative to the saturated analogue.

We have recently reported that the aprotic solvent DMSO can be a reasonable solvent for generation of carbocationic intermediates from certain mesylates, chlorides, and trifluoroacetates.[18] As in polar protic solvents such as trifluoroethanol and acetic acid, carbocation intermediates formed in DMSO-d_6 can rearrange, suffer proton elimination, or undergo solvent capture. The triflate **42** undergoes an interesting pseudo-first-order reaction when dissolved in DMSO-d_6 at room temperature. When the reaction is monitored by ^{1}H NMR, the minor product **45** (41%) builds up with the disappearance of triflate **42**. An unstable product, presumably the oxosulfonium ion **47**, can also be detected. This product converts to the major product, naphthalene (52%), under the reaction conditions, and at the same time, formic acid appears. Also formed in this reaction are small amounts of 1-naphthaldehyde, **50** (3%), and the alcohol **41** (4%). A mechanistic scheme that accounts for these observations involves an ionization process in DMSO-d_6 to give the cation **6**. Capture of the DMSO-d_6 solvent at sulfur gives product **45**, whereas capture at oxygen gives the unstable oxosulfonium ion **47**. This intermediate can lose dimethyl sulfide and fragment to naphthalene and the formyl cation, **48**, which is the source of the formic acid via the trace of water present in the DMSO-d_6. The formyl cation can also serve to produce the trace of 1-naphthaldehyde. The alcohol **41** could also be derived from the oxosulfonium ion **47** on reaction with the trace of water present. We have previously shown that this is a facile reaction of other oxosulfonium ions with traces of water present in DMSO-d_6.[18]



Computational Studies on the 11-(1,6-Methano-[10]annulenyl) Cation. Density functional calculations (B3LYP/6-31G*) have also been carried out on cation **6** in order to provide additional insight. Cations **51**−**53** were also examined for comparison purposes. The relative energies of these cations were evaluated via the isodesmic reaction shown and are listed under the corresponding cation in Figure 4. In agreement with the solvolytic rate data, cation **6** is substantially less stable than the saturated analogue **51**.

(16) Vogel, E.; Weyres, F.; Leper, H.; Rautenstrauch, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 732.

(17) Triflates are approximately 10^5 times more reactive than mesylates or tosylates under solvolytic conditions; see: Su, T. M.; Sliwinski, W. F.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1969**, *91*, 5386.

(18) Creary, X.; Burtch, E. A.; Jiang, Z. *J. Org. Chem.* **2003**, *68*, 1117.

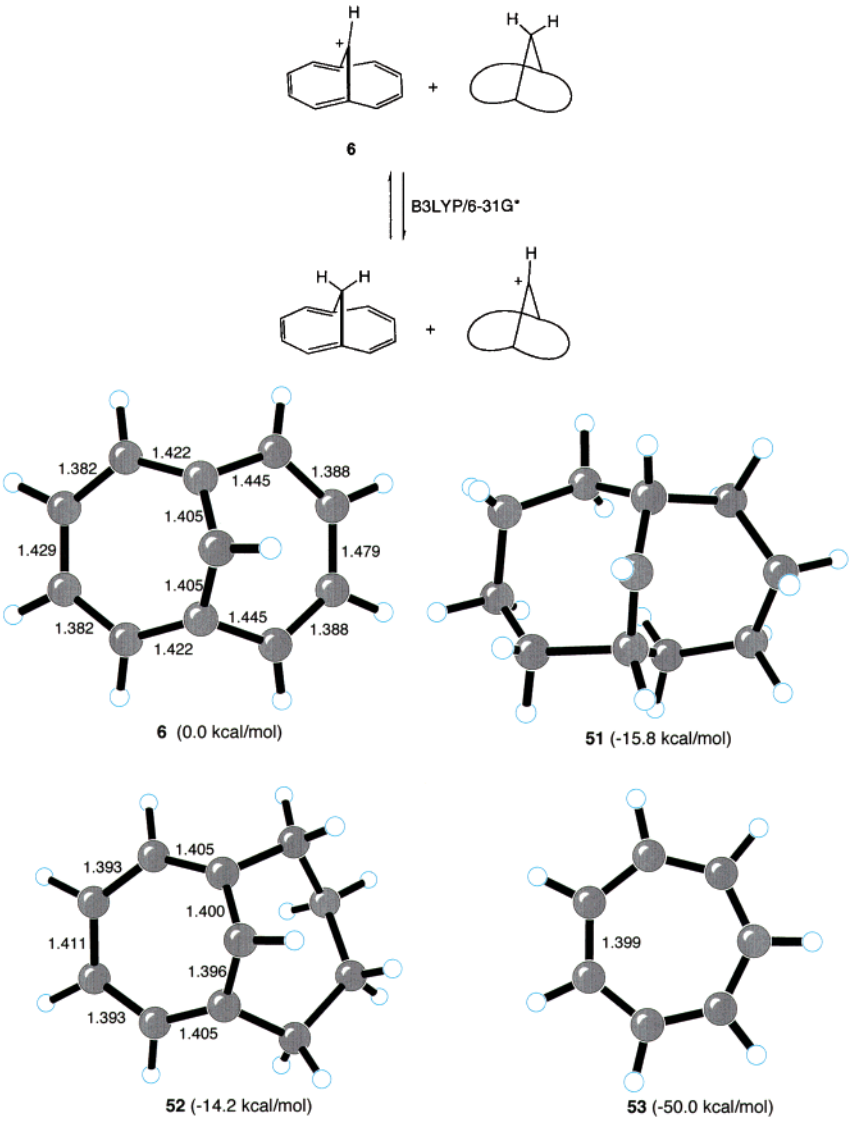
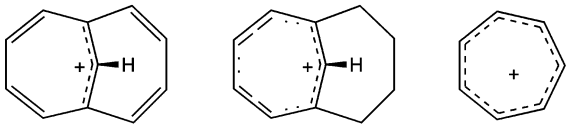


FIGURE 4. B3LYP/6-31G* relative energies of the 11-(1,6-methano[10]annulyl) cation (**6**) and analogues.

Structural information is also informative. Unlike the saturated system **51**, the cationic center of **6** is not completely planar and the C11 hydrogen is tilted significantly toward one of the CH═CH−CH═CH bridges. The same tilt is observed in cation **52**, which is formally a cycloheptatrienyl cation bridged by a saturated four-carbon fragment. Cation **52** is also 14.2 kcal/mol more stable than cation **6**, and bond lengths in the conjugated 7-carbon fragment are more equivalent than in **6**. However, delocalization is not as complete as in the cycloheptatrienyl cation, **53**, where the bond lengths are equivalent. The cation **52** still maintains a portion of its stabilization due to aromaticity, but stabilization is weakened by the four-carbon bridge. On the other hand, although cation **6** might resemble the cycloheptatrienyl cation at first glance, it is a deformed entity lacking the remarkable properties of the authentic, aromatic cycloheptatrienyl cation **53**. It is, in actuality, a distorted allylic cation, with miniscule delocalization into the unsaturated 4-carbon bridges. It also has none of the delocalized properties of the 7-norbornadienyl cation.[19]



Conclusions

Solvolysis rate data indicate that 2- and 3-substituted 1,6-methano[10]annulyl cations (**2** and **3**) are remarkably stabilized by the annulene ring, with the 2-substituted system **2** being more stabilized than the 3-substituted system **3**. These solvolysis studies, along with B3LYP/6-31G* computational studies, confirm that stabilization of these cations greatly exceeds that of naphthyl analogues. Solvolytic studies also show that charge in the "electron-deficient" carbocation **5** is extensively delocalized into the methanoannulene ring, resulting in a

(19) Lustgarten, R. K.; Brookhart, M.; Winstein, S. *J. Am. Chem. Soc.* **1972**, *94*, 2347 and references therein.

nonaromatic solvent capture product. On the other hand, solvolytic and computational studies indicate that the 11-(1,6-methano[10]annulyl) cation, **6**, is destabilized relative to analogues. There is a distinct lack of charge delocalization in **6** involving the unsaturated bridges. Although there is some structural resemblance to the aromatic cycloheptatrienyl cation, in actuality, distortions from planarity preclude any such aromatic stabilization of **6**.

Experimental Section

Preparation of 2-Chloromethyl-1,6-methano[10]annulene (8).[5,6] To a stirred solution of 131 mg of 2-hydroxymethyl-1,6-methano[10]annulene (**7**)[5,6] in 3 mL of anhydrous ether containing 100 mg of Na_2CO_3 was added 230 mg of thionyl chloride. The mixture was stirred for 1 h and filtered, and the ether was removed using a rotary evaporator. The crude 2-chloromethyl-1,6-methano[10]annulene **8** (134 mg; 92%) was used without further purification. ^{1}H NMR ($CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 1 H), (7.42, m, 2 H), 7.16 (m, 3 H), 7.03 (t, J = 9.0 Hz, 1 H), 4.93 (d, J = 12 Hz, 1 H), 4.80 (d, J = 12 Hz, 1 H), −0.36 (d, J = 9.3 Hz, 1 H), −0.50 (d, J = 9.3 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 136.8, 130.3, 128.4, 128.1, 127.3, 127.0, 126.9, 126.3, 116.6, 113.2, 44.8, 35.3.

Preparation of 3-Chloromethyl-1,6-methano[10]annulene (10).[6,7] A solution of 31 mg of 3-hydroxymethyl-1,6-methano[10]annulene (**9**).[7,20] in 1 mL of anhydrous ether containing 50 mg of Na_2CO_3 was stirred as 54 mg of $SOCl_2$ was added. After 1.5 h the mixture was filtered, and the solvent was removed using a rotary evaporator. The crude 3-chloromethyl-1,6-methano[10]annulene **10** (33.3 mg; 97%) was used without further purification. ^{1}H NMR ($CDCl_3$) δ 7.48−7.36 (m, 4 H), 7.14−7.04 (m, 3 H), 4.77 (d, J = 11 Hz, 1 H), 4.70 (d, J = 11 Hz, 1 H), −0.30 (d, J = 9 Hz, 1 H), −0.36 (d, J = 9 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 135.0, 130.3, 129.4, 129.3, 128.8, 127.4, 126.9, 126.8, 115.0, 113.7, 51,2, 35.3.

Preparation of Mesylate 16. A solution of 441 mg of 2-hydroxymethylnaphthalene and 415 mg of mesyl chloride in 5 mL of methylene chloride was cooled to −25 °C, and 423 mg of triethylamine in 1 mL of CH_2Cl_2 was added dropwise. The mixture was slowly warmed to room temperature and diluted with ether, and cold water was added. The mixture was rapidly transferred to a separatory funnel, and the organic extract was washed with cold water, dilute HCl, and saturated NaCl solution. The solution was dried over $MgSO_4$ and filtered, and the solvent was removed using a rotary evaporator to give 536 mg (81%) of mesylate **16** as a light yellow oil. Mesylate **16** decomposes on standing at room temperature and was stored in ether solution at −20 °C. ^{1}H NMR ($CDCl_3$) δ 8.10 (m, 1 H), 7.98−7.82 (m, 2 H), 7.66−7,40 (m, 4 H), 5.70 (s, 2 H), 2.80 (s, 3 H). ^{13}C NMR ($CDCl_3$) δ 133.7, 1431.5, 130.7, 128.85, 128.81, 128.76, 127.2, 126.4, 125.1, 123.3, 70.0, 38.4.

Preparation of Mesylate 17. Silver mesylate (240 mg) was added to a solution of 150 mg of 3-chloromethylnaphthalene in 3 mL of ether. The mixture was refluxed for 26 h. After dilution with ether, the mixture was filtered, and the ether was removed using a rotary evaporator to give 174 mg (94%) of mesylate **17** as a light yellow oil. Mesylate **17** decomposes on standing at room temperature and was stored in ether solution at −20 °C. ^{1}H NMR ($CDCl_3$) δ 87.94−7.80 (m, 4 H), 7.60−7.46 (m, 3 H), 5.42 (s, 2 H), 2.91 (s, 3 H). ^{13}C NMR ($CDCl_3$) δ 133.4, 132.9, 130.7, 128.8, 128.4, 128.1, 127.7, 126.9, 126.6, 125.7, 71.8, 38.3.

Preparation of Alcohol 25. To a solution of 2-bromo-1,6-methano[10]annulene (**24**)[21] (351 mg, 1.59 mmol) in anhydrous THF (4 mL) under nitrogen at −78 °C was added *n*-butyllithium (1.2 mL, 1.91 mmol) in hexanes dropwise. After the addition was complete, the solution was stirred at −78 °C for 20 min, and a solution of acetone (460 mg, 7.94 mmol) in anhydrous THF (2 mL) was added dropwise. The solution was stirred at −78 °C for 30 min, then slowly warmed to room temperature, quenched with water, and diluted with ether. The organic phase was separated, washed with saturated NaCl solution, dried over a mixture of Na_2SO_4 and $MgSO_4$, and filtered, and the solvent was removed by rotary evaporator. The crude residue was chromatographed on 30 g of silica gel. Elution with hexanes separated hydrocarbon impurities. Gradient elution with 15−20% ether in hexanes gave alcohol **25** (111 mg, 35%) as a yellow solid, mp 78−79 °C. ^{1}H NMR ($CDCl_3$) δ 8.02 (d, J = 8.5 Hz, 1 H), 7.44 (d, J = 7.8 Hz, 1 H), 7.40 (d, J = 9.0 Hz, 1 H), 7.27−7.15 (m, 3 H), 7.01 (t, J = 9.2 Hz, 1 H), 1.85 (s, 3 H), 1.60 (s, 3 H), −0.47 (d of t, J = 9.4, 1.4 Hz, 1 H), −0.67 (d of d, J = 9.4, 0.9 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 149.7, 129.6, 128.7, 127.7, 126.8, 126.5, 126.1, 123.5, 117.3, 112.8, 75.2, 36.0, 33.2, 32.7. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 84.01; H, 8.00.

Preparation of Acetate 26. A suspension of 92 mg of a 60% dispersion of sodium hydride in mineral oil (2.30 mmol) was placed in a flask under nitrogen, and the mineral oil was removed by successive washing with hexanes. The hexanes were then decanted, and the last traces were removed by a stream of nitrogen. A solution of alcohol **25** (115 mg, 0.57 mmol) in anhydrous THF (6 mL) was added. The mixture was refluxed for 2 h and cooled, and acetic anhydride (88 mg, 0.86 mmol) was then added. The solution was stirred for an additional 2 h at room temperature, then diluted with ether, and washed with water and saturated sodium chloride solution. The organic phase was separated, dried over a mixture of Na_2SO_4 and $MgSO_4$, and filtered, and the solvent was removed by rotary evaporator to give 151 mg of a 56:44 mixture of acetate **26** and starting alcohol **25**. This mixture was used for kinetic studies without further purification. ^{1}H NMR of **26** ($CDCl_3$) δ 7.76 (d, J = 8.8 Hz, 1 H), 7.42 (d, J = 9.0 Hz, 1 H), 7.37 (d, J = 8.8 Hz, 1 H), 7.27−7.07 (m, 3 H), 6.99 (t, J = 9.0 Hz, 1 H), 2.20 (s, 3 H), 2.09 (s, 3 H), 1.40 (s, 3 H), −0.38 (d of m, J = 9.3 Hz, 1 H), −0.75 (d of d, J = 9.3, 1.0 Hz, 1 H).

Preparation of Ketoester 28.[22] To a solution of 2-bromo-1,6-methano[10]annulene (**24**) (200 mg, 0.9 mmol) in anhydrous THF (3 mL) at −85 °C under nitrogen was added 0.9 mL of 1.6 M *n*-butyllithium (1.4 mmol) in hexanes dropwise. After the addition was complete, the solution was kept at −85 °C for 30 min, and then a solution of 128 mg of dimethyl oxalate (1.1 mmol) in 2 mL of anhydrous THF was added dropwise. After 30 min at −85 °C the solution was slowly warmed to room temperature. The mixture was quenched with water and diluted with ether. The organic phase was separated, washed with saturated sodium chloride solution, dried over a mixture of Na_2SO_4 and $MgSO_4$, and filtered, and the solvent was removed using a rotary evaporator. The crude residue was chromatographed on 10 g of silica gel. The α-ketoester **28** (86 mg, 42%) eluted with 4−5% ether in hexanes. ^{1}H NMR ($CDCl_3$) δ 8.26 (d, J = 8.8 Hz, 2 H), 7.73 (d, J = 8.8 Hz, 2 H), 7.72 (d, J = 9.5 Hz, 2 H), 7.44 (d, J = 8.6 Hz, 1 H), 7.35 (t, J = 9.2 Hz, 2 H), 7.23 (t, J = 9.0 Hz, 1 H), 7.13 (t, J = 9.2 Hz, 1 H), 3.99 (s, 3 H), −0.25 (d of m, J = 9.0 Hz, 1 H), −0.28 (d of m, J = 9.0 Hz, 1 H). ^{13}C NMR ($CDCl_3$) δ 186.4, 165.2, 137.4, 134.4, 132.3, 130.8, 130.4, 128.4, 127.6, 124.6, 117.2, 113.7, 52.7, 35.8. Exact mass (EI) calcd for $C_{14}H_{12}O_3$ 228.0796, found 228.0787.

Preparation of Chlorides 29. To a suspension of sodium borohydride (15 mg, 0.37 mmol) in methanol (3 mL) under nitrogen was added dropwise a solution of α-keto ester **28** (85 mg, 0.37 mmol) in methanol (1 mL). After the addition was completed, the solution was stirred at room temperature for 90 min and diluted with ether, and the resulting solution was washed with water and saturated sodium chloride solution.

(20) Vogel, E.; Sombroek, J. *Tetrahedron Lett.* **1974**, *17*, 1627.
(21) Vogel, E.; Böll, W. A.; Biskup, M. *Tetrahedron Lett.* **1966**, 1569.
(22) Creary, X. *J. Org. Chem.* **1987**, *52*, 5026.

The organic phase was separated, dried over a mixture of Na_2SO_4 and $MgSO_4$, and filtered, and the solvent was removed by rotary evaporator. The crude residue was chromatographed on 8 g of silica gel. Elution with 15% ether in hexanes gave 58 mg (69%) of a 1.8:1 mixture of diastereomeric alcohols. The mixture of alcohols was not separated. ^{1}H NMR of alcohol mixture ($CDCl_3$) δ 7.70−7.00 (m, aromatic), 5.57 (s, CH), 3.69 (s, OCH_3), 3.66 (s, OCH_3), −0.38 to −0.58 (m, CH_2).

To a solution of the mixture of alcohols prepared above (51 mg, 0.22 mmol) in 3 mL of anhydrous ether was added 35 mg of sodium carbonate and 40 mg of thionyl chloride. After 30 h of stirring at room temperature, an additional 27 mg of thionyl chloride was added, and stirring was continued for an additional 24 h. The mixture was filtered, and the solvent was removed by rotary evaporator to give 48 mg (87%) of a 1.7:1 mixture of diastereomeric chlorides **29**. This mixture was used without further purification in kinetic studies. ^{1}H NMR of chlorides **29** ($CDCl_3$) δ 7.75−7.07 (m, aromatic), 5.91 (s, CH), 5.90 (s, CH), 3.78 (s, CH_3), 3.71 (s, CH_3), −0.43 to −0.53) (m, CH_2). ^{13}C NMR of chlorides **29** ($CDCl_3$) δ 169.1, 168.8, 134.3, 134.1, 131.1, 130.8, 128.9, 128.8, 127.83, 127.75, 127.66, 127.36, 127.33, 127.30, 127.28, 127.0, 126.9, 126.6, 117.6, 117.3, 112.9, 112.2, 58.3, 56.6, 53.5, 53.3, 35.3, 35.3.

Preparation of Triflate 42. A solution of 96 mg of 11-hydroxy-1,6-methano[10]annulene[16] and 91 mg of 2,6-lutidine in 3 mL of methylene chloride was cooled to −20 °C, and 213 mg of triflic anhydride was added dropwise. The mixture was slowly warmed to room temperature, and cold water was added. The mixture was rapidly transferred to a separatory funnel using ether, and the organic extract was washed with cold water, dilute NaOH solution, and saturated NaCl solution. The organic extract was dried using $MgSO_4$ and filtered, and the solvent was removed using a rotary evaporator to give 161 mg (91%) of triflate **42**, mp 71−73 °C. ^{1}H NMR ($CDCl_3$) δ 7.49 (m, 2 H), 7.30 (m, 2 H), 7.24 (m, 2 H), 7.21 (m, 2 H), 2.31 (s, 1 H). ^{13}C NMR ($CDCl_3$) δ 128.5, 128.1, 126.1, 125.3, 118.1 (q, J = 320 Hz), 115.97, 79.1. Exact mass (EI) calcd for $C_{12}H_9F_3OS$ 290.0225, found 290.0207.

Preparation of Mesylate 44. A solution of 226 mg of 11-hydroxybicyclo[4.4.1]undeca-2,4,8-triene[23] in 8 mL of ether containing 35 mg of 10% Pd/C was hydrogenated at 50 psi for 4.5 h. The solution was filtered, and the solvent was evaporated using a rotary evaporator. The crude residue was purified by chromatography on 15 g of silica gel to give 178 mg (79%) of 11-hydroxybicyclo[4.4.1]undecane, mp 64−66 °C. ^{1}H NMR ($CDCl_3$) δ 4.17 (m, 1 H), 2.25 (m, 2 H), 1.40−1.90 (m, 16 H). ^{13}C NMR ($CDCl_3$) δ 77.7, 43.0, 30.9, 29.2, 26.1, 25.7. Exact mass (EI) calcd for $C_{11}H_{20}O$ 167.1436, found 167.1413.

A solution of 178 mg of 11-hydroxybicyclo[4.4.1]undecane and 182 mg of mesyl chloride in 2 mL of CH_2Cl_2 was cooled to −15 °C, and a solution of 182 mg of triethylamine in 1 mL of CH_2Cl_2 was added dropwise. The mixture was warmed to room temperature and diluted with ether, and water was added. The mixture was transferred to a separatory funnel, and the organic phase was washed with dilute HCl solution and saturated NaCl solution and dried over $MgSO_4$. The solvent was removed using a rotary evaporator to give 252 mg (97%) of mesylate **44**, mp 52−54 °C. ^{1}H NMR ($CDCl_3$) δ 5.09 (t, J = 4.2 Hz, 1 H), 3.01 (s, 3 H), 2.49 (m, 2 H), 1.40−1.90 (m, 16 H). ^{13}C NMR ($CDCl_3$) δ 90.0, 41.9, 38.6, 30.3, 29.1, 25.7, 25.4.

Solvolysis of 2-Chloromethyl-1,6-methano[10]annulene (8) in Methanol. A solution of 82 mg of **6** in 3 mL of methanol containing 66 mg of 2,6-lutidine was stirred at room temperature for 4 h. The methanol was removed using a rotary evaporator, and the residue was taken up into ether, washed with dilute HCl solution and saturated NaCl solution, and dried over $MgSO_4$. After filtration, the solvent was removed using a rotary evaporator, and the residue was chromatographed on 8 g of silica gel. The methyl ether **11** (73 mg; 92%) eluted with 5% ether in hexanes. ^{1}H NMR of **11** ($CDCl_3$) δ 7.70 (d, J = 8 Hz, 1 H), 7.42, (m, 2 H), 7.16 (m, 2 H), 7.08 (d, J = 9 Hz, 1 H), 7.01 (t, J = 9 Hz, 1 H), 4.81 (d, J = 13 Hz, 1 H), 4.52 (d, J = 13 Hz, 1 H), 3.485 (s, 3 H), −0.34 (d, J = 9 Hz, 1 H), −0.50 (d, J = 9 Hz, 1 H). ^{13}C NMR of **9** ($CDCl_3$) δ 138.6, 129.3, 128.1, 127.2, 127.0, 126.8, 126.5, 125.9, 115.9, 113.8, 73.8, 58.2, 35.4. Exact mass (EI) calcd for $C_{13}H_{14}O$ 186.1045, found 186.1031.

Solvolysis of 2-Chloromethyl-1,6-methano[10]annulene (8) in CD_3CO_2D containing $LiClO_4$. The solvent was removed from a 25-μL sample of a 0.05 M chloride **8** in ether using a rotary evaporator. The residue was dissolved in 0.50 mL of CD_3CO_2D containing the appropriate amount of $LiClO_4$. The solution was transferred to an NMR tube, and the tube was placed in a temperature-controlled probe of a 600 mHz NMR spectrometer at 25.0 °C. The reaction was monitored periodically over two half-lives by integration of the signals at δ 5.38 (acetate product) and δ 4.95 (unreacted chloride **8**). Rate constants for approach to equilibrium were calculated by standard least-squares methods using measured infinity values. Figure 1 shows typical spectra after 15 min at 25 °C.

Solvolysis of 3-Chloromethyl-1,6-methano[10]annulene (10) in Methanol. A solution of 12 mg of **10** in 2 mL of 0.05 M of 2,6-lutidine in methanol was stirred at room temperature for 3 days. The mixture was taken up into ether, washed with water, dilute HCl solution, and saturated NaCl solution, and dried over $MgSO_4$. After filtration, the solvent was removed using a rotary evaporator and the residue was chromatographed on 10 g of silica gel. The methyl ether **12** (11 mg; 91%) eluted with 2% ether in hexanes. ^{1}H NMR of **12** ($CDCl_3$) δ 7.46−7.38 (m, 4 H), 7.13−7.04 (m, 3 H), 4.65 (d, J = 11 Hz, 1 H), 4.50 (d, J = 11 Hz, 1 H), 3.41 (s, 3 H), −0.32 (d of t, J = 9, 1 Hz, 1 H), −0.38 (d of t, J = 9, 1 Hz, 1 H). ^{13}C NMR of **10** ($CDCl_3$) δ 135.8, 129.3, 129.0, 128.6, 128.4, 126.304, 126.297, 126.2, 114.7, 114.1, 78.5, 57.9, 35.3. Exact mass (EI) calcd for $C_{13}H_{14}O$ 186.1045, found 186.1029.

Solvolysis of Chlorides 29 in Methanol. To a solution of 5 mg of 2,6-lutidine in 3 mL of methanol was added 8 mg of the mixture of chlorides **29**. The resulting solution was kept at room temperature for 2 h. The methanol was then removed using a rotary evaporator, and the residue was taken up into ether, washed with water and saturated sodium chloride solution, and dried over a mixture of Na_2SO_4 and $MgSO_4$. After filtration, the solvent was removed using a rotary evaporator, and the residue was filtered through a short pad of silica gel. Elution with 10% ether in hexanes gave 7 mg (90%) of methyl ether **35**. ^{1}H NMR ($CDCl_3$) δ 7.60 (d of d of d, J = 11.8, 1.7, 0.8 Hz, 1 H), 6.71 (m, 1 H), 6.70 (m, 1 H), 6.33 (d of m, J = 5.8 Hz, 1 H), 6.29 (d of m, J = 5.6 Hz, 1 H), 6.21 (m, 1 H), 5.98 (d of d of d, J = 11.8, 3.7, 1.5 Hz, 1 H), 4.16 (d of d of d, J = 3.7, 1.7, 0.8 Hz, 1 H), 3.74 (s, 3 H), 3.54 (s, 3 H), 3.04 (d of t, J = 8.8, 0.8 Hz, 1 H), 0.55 (d of d, J = 8.8, 0.8 Hz).). ^{13}C NMR of **35** ($CDCl_3$) δ 166.6, 151.1, 132.8 (d, J = 159 Hz), 127.7 (d, J = 159 Hz), 127.4 d, J = 159 Hz), 124.5 (d, J = 157 Hz), 123.2 (d, J = 164 Hz), 121.8 (d, J = 157 Hz), 114.0 (d, J = 161 Hz), 99.7, 99.0, 78.9 (d, J = 143 Hz), 56.7 (q, J = 141 Hz), 51.4 (q, J = 146 Hz), 29.2. Exact mass (EI) calcd for $C_{15}H_{16}O_3$ 244.1100, found 244.1125.

Solvolysis of Triflate 42 in CF_3CH_2OH. A solution of 15 mg of triflate **42** in 1.6 mL of 0.05 M 2,6-lutidine in trifluoroethanol was stirred at room temperature for 20 h. The mixture was taken up into ether, washed with water, dilute HCl solution, and saturated NaCl solution, and dried over $MgSO_4$. After filtration, the solvent was removed using a rotary evaporator, and the residue was chromatographed on 5 g of silica gel. The trifluoroethyl ether **43** (11 mg; 92%) eluted with 5% ether in hexanes. ^{1}H NMR of **43** ($CDCl_3$) δ 7.37 (m, 2 H), 7.21 (m, 2 H), 7.10 (m, 2 H), 7.06 (m, 2 H), 3.03 (q, J = 9 Hz, 2 H), 1.34 (s, 1 H). ^{13}C NMR of **43** ($CDCl_3$) δ 126.74, 126.65, 126.1, 124.1, 123.4 (q, J = 279 Hz), 117.2, 73.9, 63.9 (q, J = 35 Hz). Exact mass (EI) calcd for $C_{13}H_{11}F_3O$ 240.0762, found 240.0749.

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Solvolysis of Triflate 42 in DMSO-d_6. A solution was prepared by dissolving 5 mg of triflate **42** in 1.0 mL of DMSO-d_6, and the solution was transferred to an NMR tube. The reaction was monitored by 600 mHz ^{1}H NMR at room temperature. The major product, naphthalene **46**, was identified by spectral comparison with an authentic sample, as were formic acid, **49**, alcohol **41**, and 1-naphthaldehyde, **50**. Small amounts of the unstable oxosulfonium ion intermediate **47** (δ 7.63, 7.45, 2.24) grow in with time at room temperature. The minor product **45** (δ 7.87, 7.78, 7.28, 7.20, 1.63) also appears at room temperature. After 64 h at room temperature, the mixture was heated at 55−60 °C for 3 h. The ^{1}H NMR spectrum now showed no remaining **42** or **47** and the products **41**, **45**, **46**, and **50** in a 4:41:52:3 ratio.

Kinetic Studies. Rates of reaction of 2-chloromethyl-1,6-methano[10]annulene, **8**, *p*-methoxybenzyl chloride, **13**, mesylate **16**, and mesylate **17** in methanol (3×10^{-4} M in 2,6-lutidine) were determined using the UV spectroscopic method previously described.[24] The reactions of **8**, **16**, and **17** were monitored at 270 nm while the reaction of **13** was monitored at 246 nm. Rates of reaction of 3-chloromethyl-1,6-methano-[10]annulene, **10**, chloride **30**, triflate **42**, and mesylate **44** were monitored by the NMR spectroscopic method previously described.[25] The rate of reaction of triflate **42** in DMSO-d_6 was monitored using the ^{19}F NMR method previously described.[26] Rates of reaction of acetates **26** and **27** (CH_3OD) as well as chlorides **29** (CD_3OD containing 0.05 M 2,6-lutidine) were determined by ^{1}H NMR spectroscopy. Rate constants were calculated using standard least-squares methods and represent an average of duplicate runs. Typical data given in Table 1 are ±2%.

Computational Studies. Ab initio molecular orbital calculations were performed using the Gaussian 98 series of programs.[14] Structures were characterized as minima via frequency calculations that showed no negative frequencies.

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Supporting Information Available: B3LYP calculated structures, energies, and Cartesian coordinates of **2**, **3**, **4**, **6**, **35**−**37**, and **51**−**53** and ^{1}H and ^{13}C NMR spectra of compounds **11**, **12**, **28**, and **42**−**44**. This material is available free of charge via the Internet at http://pubs.acs.org.

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