zoate chromophores, it does not provide a conclusive assignment in the absence of a rigorous theoretical treatment. The chiral effect of the tetrahydrobenzo[*a*]pyrene chromophore on that of the *N,N*-dimethylaminobenzoyloxy groups would be eliminated if the 4,5- and 11,12-double bonds in **4** were reduced to produce an octahydrobenzo[*a*]pyrene (biphenyl) chromophore (**5**). The resulting isolated exciton chirality interaction between the two *N,N*-dimethylaminobenzoyloxy chromophores in such a diester of **5** would provide an unambiguous basis for configurational assignment. After examination of a wide variety of reduction conditions on **4** and its esters, catalytic hydrogenation of the diacetate of (−)-**4** (70 mg) in THF with 50 psi of H_2 in the presence of 10% Pd–C and a trace amount of concentrated HCl for 7 days, followed by reacetylation of the crude product, allowed isolation of 12 mg of *trans*-7,8-dihydroxy-4,5,7,8,9,10,11,12-octahydrobenzo[*a*]pyrene (**5**) as its diacetate.[11] The diacetate was subsequently converted to the bis-*p*-*N,N*-dimethylaminobenzoate of **5** (12 mg) for which a clear pair of CE centering at 316 nm was observed (Figure 2). This requires 7*S*,8*S*-absolute stereochemistry as shown and provides an unequivocal assignment for each series (Table I).

Preliminary studies of the metabolism-induced mutagenicity[3a] of (+)- and (−)-**3** as well as their individual tumorogenicity[12] indicate that these enantiomers have different biological activity. Racemic diol epoxides **1** and **2** alkylate the exocyclic N^2-amino group of guanosine[5b,d] in poly(G) by cis and trans addition at C-10 and alkylate the phosphate backbone.[5d] Exposure of bovine bronchial explants to BP has allowed identification of a single enantiomer of diol epoxide **2** as a trans-adduct at the N^2-amino group of guanine in the RNA of these cells as one of the hydrocarbon adducts formed.[5c] Comparison of the chromatographic mobility of the guanosine adducts from (+)- and (−)-diol epoxides **1** and **2** has allowed assignment of absolute stereochemistry to the eight possible adducts.[13] Examination of the RNA from the skins of mice treated topically with BP has provided evidence that both cis and trans adducts of (+)-diol epoxide **1** and (+)-diol epoxide **2** are important metabolites in the binding of BP to RNA in vivo.[13] Interestingly, both of these diol epoxides formed by skin have the 9*R*,10*R*-configuration at the epoxide moiety.

Note Added in Proof. Nakanishi et al.[15] have examined the CD spectrum of the bis-*p*-*N,N*-dimethylaminobenzoate of (−)-**3** and have assigned the same absolute configuration as does the present study. Kapitalnik et al.[16] have found that racemic diol epoxide **2** is highly carcinogenic when compared to BP.

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(7) Esterification of (±)-*trans*-7,8-dihydroxy-7,8,9,10-tetrahydrobenzo[a]-pyrene (**4**) with 1.1 mole equiv of (−)-MTPA chloride in pyridine/CH_2Cl_2 at room temperature gave a ca. 1:1 mixture of 7- and 8-mono-(−)-MTPA esters which were separated by column chromatography on silica gel with 5–20% THF in hexane as eluent. The diastereomeric pair of 7-mono-MTPA esters of **4** (isomer with k' = 15, H_7 δ 6.59 and H_8 4.30 with $^3J_{7,8}$ = 6.0 Hz; isomer with k' = 20, H_7 δ 6.59 and H_8 4.30 with $^3J_{7,8}$ = 7.0 Hz) was readily distinguished from the 8-mono-MTPA diastereomers (mixture, H_7 δ 5.20 and H_8 5.48) by NMR spectroscopy (220 MHz, $CDCl_3$). The order of elution of the 7-MTPA diastereomers of (±)-**4** inverts in CH_2Cl_2 based chromatography systems.

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(10) The diacetate of **4** has UV absorptions (MeOH) at 343, 329, 313, and 277 nm with extinction coefficients of 40 800, 29 400, 12 100, and 35 900, respectively.

(11) The structure of the (+)-diacetate of **5** (mp 186–187 °C) was assigned from its mass spectrum (M^+ 376 by CI with NO–N_2) and NMR spectrum (220 MHz, CCl_4): δ (ppm) 1.96 (3 H, s, OAc), 2.04 (3 H, s, OAc), 2.10 (2 H, m, H_9), 2.60–2.95 (10 H, br s, H_4, H_5, H_{10}, H_{11}, and H_{12}), 5.00 (1 H, m, H_8), 5.90 (1 H, d, H_7), and 6.80–7.20 (4 H, m, aromatic) with $^3J_{7,8}$ = 6.0 Hz. The UV spectrum (MeOH) showed λ_{max} at 275, 285, and 297.5 nm at long wavelength.

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Solvolysis of 2-Aryl-2-bicyclo[2.1.1]hexyl *p*-Nitrobenzoates. Evidence for the Absence of σ-Participation by the Application of the Tool of Increasing Electron Demand

Sir:

Solvolysis of 2-aryl-2-bicyclo[2.1.1]hexyl *p*-nitrobenzoates provides a value for ρ^+ of −4.31, even more negative than the ρ^+ observed in the solvolysis of 2-aryl-*endo*-norbornyl *p*-nitrobenzoates (ρ^+ = −3.72), a system where σ-participation is believed to be absent. Consequently, application of the tool of increasing electron demand to the bicyclo[2.1.1] system does not support the presence of significant σ-participation. Moreover, extrapolation of the data from the tertiary 2-aryl-2-bicyclo[2.1.1]hexyl derivatives to the parent secondary system fails to reveal any enhancement in rate of the secondary derivative attributable to σ-participation. It is concluded that

Table I. Solvolysis of 2-Aryl-2-bicyclo[2.1.1]hexyl *p*-Nitrobenzoates and Related Derivatives in 80% Aqueous Acetone[a]

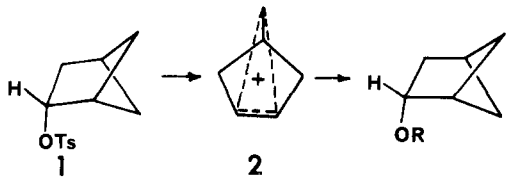
2-Aryl or 2-R	$k_1 \times 10^6$, s^{-1}			$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu
	T_2, °C	T_1, °C	25 °C		
p-CH_3O			289		
p-H	93.7 (75)	4.87 (50)	0.154[b]	25.9	−3.0
p-CF_3	58.0 (125)	5.40 (100)	3.99×10^{-4} [b]	27.5	−9.5
3,5-$(CF_3)_2$	24.0 (150)	2.29 (125)	3.69×10^{-6} [b]	30.9	−7.3
2-Methyl	138 (150)	14.0 (125)	3.19×10^{-5} [b]	30.0	−5.7
2-Hydrogen	17.0 (75)[c]		7.33×10^{-13} [d]		

[a] The reproducibility of the measured rate constants has been established in successive determinations as ±1%. The reproducibility of ρ^+ is ±2%, an uncertainty in the reported value of −4.31 ± 0.07. [b] Extrapolated from data at higher temperatures. [c] Acetolysis of tosylate (ref 3c). [d] Calculated by comparing the rate with *endo*-2-norbornyl tosylate (0.33), extrapolating to 25 °C assuming the same entropy of activation for both compounds, and then converting the 25 °C rate constant ($k_1 = 2.24 \times 10^{-8}$ s^{-1}) to *p*-nitrobenzoate using the factor 3.27×10^{-11} (ref 14).

σ-participation is not a significant factor in the solvolysis of the 2-aryl-2-bicyclo[2.1.1]hexyl *p*-nitrobenzoates and in the parent system itself.

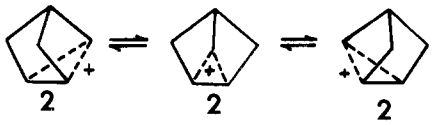
Numerous systems have been assigned nonclassical structures in recent years. However, it has proven extraordinarily difficult to confirm such assignments.[1] The nature of the 2-bicyclo[2.1.1]hexyl cation is of special interest in view of its relationship to the norbornyl cation. MINDO/3 calculations indicate that the strain in 2-bicyclo[2.1.1]hexyl cation makes this an especially favorable case for a σ-bridged species.[2] However, even here the experimental data are conflicting.

The early studies of Meinwald and co-workers on the 2-bicyclo[2.1.1]hexyl derivatives revealed that the rearrangement in this system is degenerate. It was argued that the rate of solvolysis of **1** is greater than might be expected for a classical ion.[3] This led to the suggestion that the species formed on ionization might be a bridged ion (**2**) (eq 1). From a study



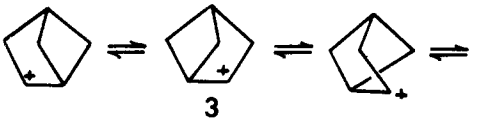
(1)

of the ^1H NMR spectrum of the ion derived from 2-chlorobicyclo[2.1.1]hexane in superacid media, Wiberg and co-workers concluded that the rearrangement in this system involves equilibration of a set of three equivalent bridged ions (eq 2).[4]



(2)

On the other hand, Olah, Liang, and Jindal have recently examined ^1H and ^{13}C spectra of the 2-bicyclo[2.1.1]hexyl and the tertiary methyl and phenyl cations under stable ion conditions.[5] They conclude from their NMR observations that these ions must be essentially classical in nature, involving in the parent system rapid equilibration (eq 3) between a set of six equivalent cations (**3**).[5]



(3)

In view of these results, we decided to apply the tool of increasing electron demand to this system. Recently we have provided unambiguous evidence for carbon participation in the

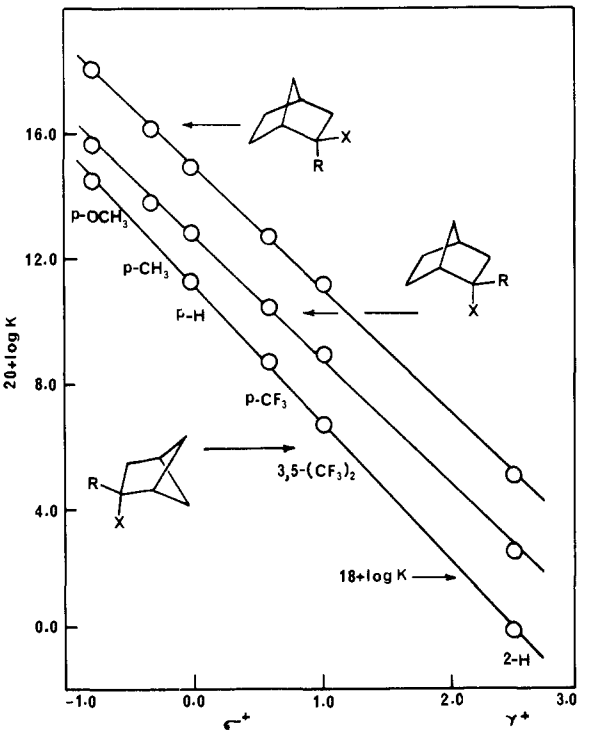


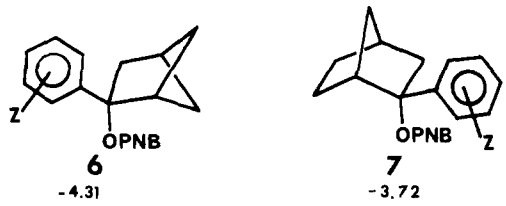
Figure 1. Correlation of the rates of solvolysis of the tertiary *exo*- and *endo*-2-aryl-2-norbornyl and 2-aryl-2-bicyclo[2.1.1]hexyl *p*-nitrobenzoates with the secondary. (The data points for the 2-aryl-2-bicyclo[2.1.1]hexyl system are displaced downward by 2 units to minimize overlap with the *endo*-norbornyl points.)

Coates cation (**4**) by the application of this tool.[6] On the other hand, in 2-norbornyl, the tool has failed to reveal such participation (**5**).[7]

Accordingly, we undertook to synthesize the 2-aryl-2-bicyclo[2.1.1]hexyl *p*-nitrobenzoates (**6**) with representative substituents in the aryl ring (Z = *p*-CH_3O, *p*-H, *p*-CF_3, and 3,5-$(CF_3)_2$). The addition of the appropriate Grignard reagents to bicyclo[2.1.1]hexan-2-one[8] afforded the corresponding tertiary alcohols, converted to the *p*-nitrobenzoates (**6**) by treating their lithium salts with *p*-nitrobenzoyl chloride.[9] The rates of solvolysis of the *p*-nitrobenzoates were determined in 80% aqueous acetone utilizing the standard titrimetric procedure.[9] The pertinent rate data are summarized in Table I.

The system (**6**) reveals excellent log k-σ^+ relationship.[10] The aryl derivatives yield a value of ρ^+ −4.31 (correlation coefficient 0.999).

If the strained cyclobutane moiety facilitates solvolysis by σ-participation, ρ^+ in this system should be more positive than in the 2-aryl-*endo*-norbornyl derivatives (**7**). However, this is not observed. Indeed, ρ^+ is more negative, indicating the unimportance of σ-participation in this system.



6 −4.31 **7** −3.72

The question next arises as to whether bridging can be absent in the tertiary derivatives examined, but present in the secondary. The observed rate of solvolysis for 2-bicyclo[2.1.1]-hexyl tosylate (**1**) fails to exhibit any enhancement in rate attributable to σ-participation. Thus the rate of acetolysis for **1** is reported to be 1.7×10^{-5} s^{-1} at 75 °C.[11] This is three times slower than the rate for *endo*-norbornyl tosylate and 1000 times slower than that for *exo*-norbornyl tosylate, a molecule to which it is structurally related. With $\nu_{C=O}$ 1764 cm^{-1},[12] application of the Foote–Schleyer correlation does not reveal any enhanced rate attributable to significant σ-participation.[1,13] Finally, extrapolation of the data from tertiary 2-bicyclo[2.1.1]hexyl derivatives (**6**) to the secondary using the recently developed substituent constant for hydrogen[14] fails to reveal any enhanced rate for the secondary derivative attributable to the incursion of σ-participation (Figure 1). (The calculated value is 19.5×10^{-19} s^{-1}, as compared to the observed value, 7.33×10^{-19}.)

It is, of course, hazardous to extrapolate conclusions based on solvolytic data to stable ion conditions,[15] or to the gas phase[16] (and vice versa). However, with this reservation in mind, it is evident that our results and conclusions are in better agreement with the position reached by Olah[5] than with that of Wiberg[4] or of Dewar.[2]

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Direct Substitution of Hydroxyl Groups of Allyl Alcohols with Alkyl Groups by the Reaction of Lithium Allyloxyalkylcuprates with *N,N*-Methylphenylaminotriphenylphosphonium Iodide. Regio- and Stereoselective Olefin Synthesis

Sir:

The allylic unit[1] is a common structural feature of many compounds of natural origin, and the most important synthon for such units are allyl alcohols. We wish now to report a novel and efficient method for direct substitution of a hydroxyl group of alcohols with alkyl or aryl groups of the corresponding organolithium compounds in a single step as depicted in eq 1. The reaction appears to be general and particularly efficient for regio- and stereoselective synthesis of olefins from allyl alcohols.

$$R^1OH \xrightarrow[4.\ [Ph_3PN(CH_3)Ph]^+I^-\ (1)]{1.\ CH_3Li,\ 2.\ CuI,\ 3.\ R^2Li} R^1\text{-}R^2 \qquad (1)$$

N,N-Methylphenylaminotriphenylphosphonium iodide (**1**)[2] is a versatile reagent for regio- and stereoselective syntheses of amines and sulfides from alcohols. Nucleophilic attack of amines or sulfides toward a key intermediate of aminophosphonium salt (**2**) seems to proceed like an S_N2 type reaction.[3] When methylmetallic reagents such as methyllithium, methylcopper, and lithium dimethylcuprate were allowed to react with **2**, methylation products were obtained in less than 15% yield along with *N,N*-methylphenylamines (85–99%), indicating that the nucleophilic character of *N*-methylanilide toward the alkoxy group of **2** is stronger than that of the methyl

$$\underset{\uparrow}{[ROPPh_3]}^+[N(CH_3)Ph]^-$$
$$HY \qquad 2$$

moiety. We chose to investigate mixed cuprates[4] as alkylating agents since we anticipated that *N*-methylanilide in the mixed cuprates bonds to copper tightly, and, consequently, inhibiting the nucleophilic attack toward the α-carbon of the alkoxy group. Indeed, the reaction of lithium geranylalkoxymethylcuprate with **1** gave methylation products, (**6E**)-2,6-dimethyl-2,6-nonadiene (**3**) and 3,3,7-trimethyl-1,7-octadiene (**4**) in 90% yield (**3**/**4** = 50/50); *N,N*-methylphenylgeranylamine was not present. High regioselectivity (**3**/**4** = 93/7) was obtained upon treatment with 3 equiv of methyllithium (entry 6)[5] Although the detailed structure of the alkylating reagents remains obscure, admixture of lithium alkoxylalkylcuprate and alkyllithium is presumably a bulky, highly reactive cuprate having the stoichiometry $R^1OCuR^2_3Li_3$ analogous to Me_3CuLi_2 or Me_4CuLi_3.[6]

Table I summarizes the representative examples. Alkylation and arylation proceed well (entries 1, 3–8, 12, 14–17) and require no comment except that secondary butyllithium provides the corresponding alkene without difficulty (entry 8).[1b] The versatility of the organolithium compounds evidently enhances the synthetic utility of the reaction. Thus, reaction of geranyl alcohols with methallyllithium (entry 9) or 1-hexynyllithium (entry 10) gave the corresponding 1,5-diene or 4-ene-1-yne, respectively, with complete regioselectivity. Further, reaction with a molar equivalent of 2-lithio-1,3-dithiane (entries 2, 11, 13) gave a valuable intermediate, 2-allyl-1,3-dithiane. Importantly, the substitution at the allylic position proceeds with inversion of configuration. Thus, reaction of *trans*-4-*tert*-butyl-2-cyclohexen-1-ol[7] (*trans*-**5**) with methyllithium under the present reaction conditions gave *cis*-3-*tert*-butyl-6-methyl-1-cyclohexene[8] (**6**) stereoselectively in 75% isolated yield (entry 15).[9]

Naturally, simple alcohols can be converted into hydrocarbons in high yields. Thus, α-methylbenzyl alcohol and cyclopropylcarbinol can be converted into 2-phenylbutane (65%