Regarding Polarizability Effects of Hydrocarbon Substituents on Base Strengths in Solution[1]

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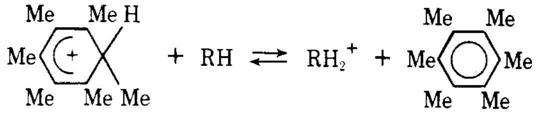
Hydrocarbon substituent effects play many and varied roles in chemistry. In spite of much effort, the understanding of these effects has remained a substantial challenge.[2] In proton-transfer (and similar) equilibria, the substitution of hydrogen by alkyl groups is expected to act to stabilize positive charge. No exceptions are known in gas-phase proton-transfer equilibria.[3] In solution, there are numerous exceptions, even when the alkyl substituent is introduced at relatively large distances from the site of protonation. For example, a 4-methyl substituent decreases (not increases) the basicity of quinuclidine by 0.11 pK_a units in water.[4]

We wish to report important new comparisons of hydrocarbon substituent effects on proton-transfer equilibria in the gas phase and in aqueous solution. These comparisons establish that the intrinsic ability of hydrocarbon substituents to stabilize positive charge by polarizability,[5,6] inductive, and conjugative interactions is observed with appropriate carbon bases almost quantitatively in aqueous solutions. That is, for proton-transfer reactions such as eq 1, the effects of hydrocarbon substituents in B are influenced in a very minor way by aqueous solvent. The result has important consequences in showing that polarizability effects of hydrocarbon substituents can be a major effect, even *in aqueous solution* in appropriate cases (e.g., reaction 1). In other words, polarizability effects cannot be regarded as an isolated curiosity of gas-phase chemistry.[7]


(1)

The latter impression has arisen because, for example, the phenyl (or cyclohexyl) substituent in anilinium ion (or cyclohexylammonium ion) stabilizes the gaseous cation by polarization by about 7 kcal/mol more than does a methyl substituent in methylammonium ion.[3] In aqueous solution, however, there is little or no such effect.[3] Polarizability effects of hydrocarbon substituents in ammonium (and oxonium[8]) ions are generally virtually completely attenuated by hydroxylic (or other hydrogen-bond acceptor) solvents.[3] The dispersal to solvent of cationic charge through the formation of hydrogen bonds between the hydrogen-bond acceptor solvent and the NH^+ and OH^+ solvation sites has been proposed to account for the high degree of attenuation of hydrocarbon substituent polarizability effects in these ions.[3,7-10] Inductive (dipolar) and conjugative effects of hydrocarbon substituents are less attenuated by such solvation interactions,[3,11,12] since the stabilization by polarization falls off especially rapidly with the distance of charge dispersal ($1/r^4$ in the simple electrostatic model[5,6]).

Our present results are of interest in providing critical new evidence for the above concept of substituent–solvent interactive effects. It has been well recognized[13] that delocalized aryl carbocations and their unsaturated hydrocarbon precursors form weak to negligible hydrogen bonds to acceptors, e.g., $(H_2O)_n$. Thus the principal mechanism of cationic charge dispersal to aqueous solvent is evidently absent for such cations. The expected consequence is indeed that which is observed for reaction 1; namely, the hydrocarbon subsituent effect (polarizability, inductive, and conjugative effects in total) is nearly the same in the aqueous solution as is observed in the gas phase.

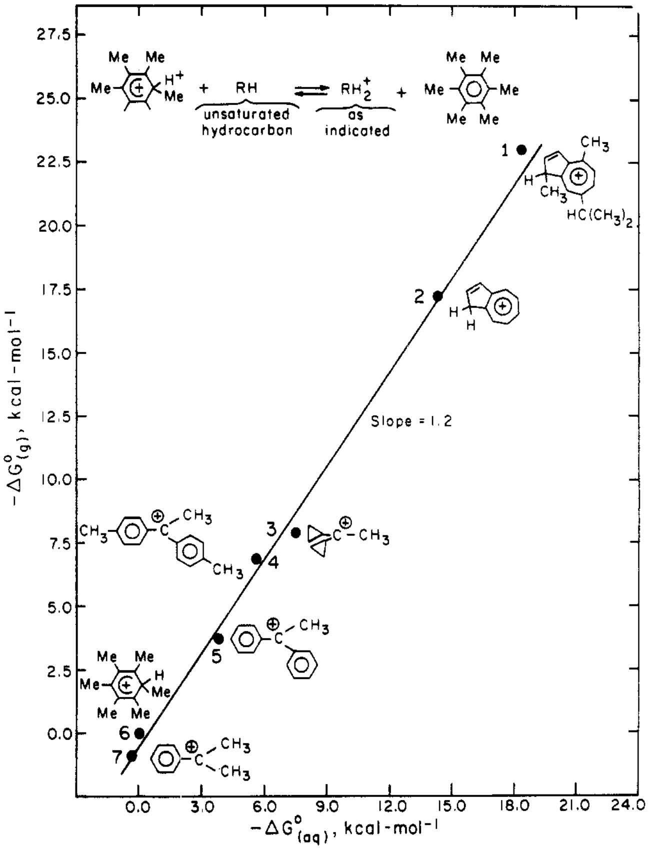


Figure 1. Comparison of gaseous and aqueous phase base strengths of hydrocarbon bases.

The present report represents an extension, now including alkyl substituents (points 1 and 4 in Figure 1) and cyclopropyl substituents (point 3 in Figure 1), of our earlier report[14] that carbon bases (which protonate to give delocalized aryl carbocations) are accompanied by structural effects on protonation which are approximately quantitatively equal in the gas phase and in aqueous solution. The results are shown in Figure 1, which plots for reaction 1 $\Delta G^\circ_{(g)}$ vs. $\Delta G^\circ_{(aq)}$. The linear regression line has a slope of 1.2, which is not significantly different from unity in view of uncertainties in acidity function behavior (specifically between H'_R[15] and H_c[16]) on which the $\Delta G^\circ_{(aq)}$ values are based.[17] It should be noted, however, for the pair guaiazulene and azulene, which both protonate in dilute acid, that there is very little uncertainty of this nature. The $\Delta G^\circ_{(aq)}$ value for 1,1-dicyclopropylethylene is based upon our UV measurements in H_3PO_4 (pK_{R+} + −7.5) using the H'_R scale reported by Arnett.[18]

The results for the 1,1-dicyclopropylethylene are significant in the present context. In the gas phase cyclopropylamine is 3.1 kcal/mol stronger base than aniline.[19] In aqueous solution the cyclopropylamine is not relatively less basic, but is in fact 6.1 kcal/mol stronger than aniline. However, as shown in Figure 1, 1,1-dicyclopropylethylene is approximately a 4 kcal/mol stronger base than 1,1-diphenylethylene in the gas phase and *in aqueous solution.* It is generally accepted that the base strength of aniline is decreased by 5–6 kcal/mol by conjugation in the free-base form.[3] In aqueous solution, the principal cause of the 6.1 lower basic strength of aniline than cyclopropyl amine may be attributed to this conjugation, since there is little preferential stabilization by polarization of the hydrated anilinium ion over that of the hydrated cyclopropylammonium ion.

In the gas phase, however, anilinium ion is more stabilized than cyclopropylammonium ion by the polarization effect, which tends to offset the "resonance" effect in aniline. Thus there is a substantial increase ($\sim$3 kcal) in the gas-phase base strength of aniline compared to cyclopropylamine. In the carbocations, greater polarization stabilization by phenyl than cyclopropyl also presumably occurs (as well as the π electron delocalization, which favors the dicyclopropylethyl cation), but in the absence of the hydrogen-bonding solvation the relative combination of polarization and resonance effects in the carbocations is not changed in solution compared to the gas phase.

Finally, we call attention to the wide variety of sizes, shapes, and carbon content (8–17) of the carbocations involved in Figure 1, as well as the nearly 25-kcal range of structural effects, as evidence supporting the ideas expressed on cation solvation. The methods used for the gas-phase equilibrium constant determinations have been described in detail.[21]

Registry No.—1,2,3,4-Tetramethylbenzene, 488-23-3; hexamethylbenzene, 87-85-4; guaiazulene, 489-84-9; azulene, 275-51-4; 1,1-dicyclopropylethylene, 822-93-5; 1,2-di-*p*-tolylethylene, 2919-20-2; 1,1-diphenylethylene, 530-48-3; (1-methylethenyl)benzene, 98-83-9.

References and Notes

(1) This work was supported in part by a grant from the Public Health Service.

(2) Cf., for example, F. G. Bordwell, G. E. Drucker, and G. J. McCallum, *J. Org. Chem.*, **41**, 2786 (1976).

(3) For a review, cf. R. W. Taft in "Proton Transfer Reactions", E. F. Caldin and V. Gold. Ed., Chapman and Hall, London, 1975, Chapter 2.

(4) C. A. Grob and M. G. Schlageter, *Helv. Chim. Acta*, **59**, 264 (1971).

(5) J. I. Brauman, J. M. Riveros, and L. K. Blair, *J. Am. Chem. Soc.*, **93**, 3914 (1971).

(6) D. H. Aue, H. M. Webb, and M. T. Bowers, *J. Am. Chem. Soc.*, **98**, 311 (1976).

(7) This conclusion was first clearly recognized by E. M. Arnett and J. F. Wolf, *J. Am. Chem. Soc.*, **95**, 978 (1973), for alkyl substituent effects in phosphonium and sulfonium ions in fluorosulfuric acid solutions; cf. also E. W. Bittner, E. M. Arnett, and M. Saunders, *ibid.*, **98**, 3734 (1976).

(8) (a) E. M. Arnett and G. Scorrano, *Adv. Phys. Org. Chem.*, **13**, 83 (1976); (b) R. W. Taft, J. F. Wolf, J. L. Beauchamp, G. Scorrano, and E. M. Arnett, *J. Am. Chem. Soc.*, submitted for publication.

(9) Cf. E. M. Arnett in ref. 3, Chapter 3.

(10) Similar considerations may prevail for anions. J. E. Bartmess and R. T. McIver, Jr., *J. Am. Chem. Soc.*, in press, have recently presented evidence that alkyl polarizability effects dominate in the relative enthalpies of ionization of alkyl mercaptans in water, but that these effects contribute little to the corresponding quantities for ionization of alcohols in water. The poorer dispersal of charge from mercaptide than alkoxide ions through hydrogen bond acceptor interactions with water appears to be a reasonable interpretation.

(11) (a) D. H. Aue, H. M. Webb, M. T. Bowers, C. L. Liotta, C. J. Alexander, and H. D. Hopkins, Jr., *J. Am. Chem. Soc.*, **98**, 854 (1976); (b) E. M. Arnett, B. Chawla, L. Bell, M. Taagepera, W. J. Hehre, and R. W. Taft, *ibid.*, in press.

(12) The polarizability and inductive effects of alkyl groups on the gas-phase basicities of amines are correlated by σ_I values, cf. R. W. Taft and L. S. Levitt, *J. Org. Chem.*, **42**, 916 (1977). This consideration makes it difficult to readily dissect their relative contributions, or, in fact, to learn whether these effects are parallel or opposed in a given type of ion.

(13) R. W. Taft, *J. Am. Chem. Soc.*, **82**, 2965 (1960).

(14) J. F. Wolf, P. G. Harch, and R. W. Taft, *J. Am. Chem. Soc.*, **97**, 2904 (1975).

(15) N. C. Deno, P. T. Groves, and G. Saines, *J. Am. Chem. Soc.*, **81**, 5790 (1959).

(16) R. T. Regan, *J. Am. Chem. Soc.*, **91**, 5506 (1969).

(17) Cf. footnote 7 of ref. 11.

(18) E. M. Arnett and G. W. Mach, *J. Am. Chem. Soc.*, **88**, 1177 (1966).

(19) Aniline protonates preferentially at nitrogen in aqueous solution and in the gas phase, although in the latter the preference over p-C protonation is only a few kilocalories per mole, cf. S. K. Pollack, J. L. Devlin III, K. D. Summerhays, R. W. Taft, and W. J. Hehre, *J. Am. Chem. Soc.*, **99**, 4583 (1977).

(20) J. S. Christensen, R. M. Izatt, D. P. Wrathall, and L. D. Hansen, *J. Chem. Soc. A*, 1215 (1969).

(21) (a) M. T. Bowers, D. H. Aue, H. M. Webb, and R. T. McIver, Jr., *J. Am. Chem. Soc.*, **93**, 4313 (1971); (b) J. F. Wolf, R. H. Staley, I. Koppel, M. Taagepera, R. T. McIver, Jr., J. L. Beauchamp, and R. W. Taft, *ibid.*, **99**, 5417 (1977).

Approaches to the Mitomycins. Photochemistry of Aminoquinones

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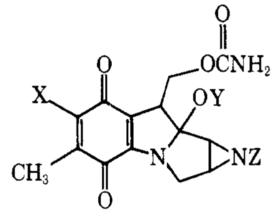
The mitomycin antibiotics (**1**) have been the subject of a wide variety of synthetic endeavors.[1] Very little experimentation has been described that deals with the problem of the introduction of oxygen functionality at the α carbon of the pyrrolidine ring. Toward this goal, we have examined a method for obtaining α-oxygenated aminohydroquinones that was discovered by Cameron and Giles.[2] Readily prepared aminoquinones are photooxidized by an intramolecular oxygen insertion, e.g., **2** → **3**.



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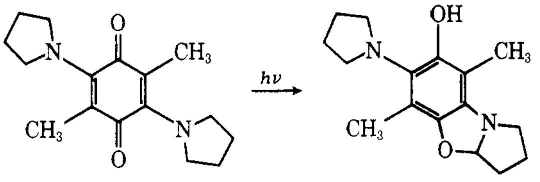
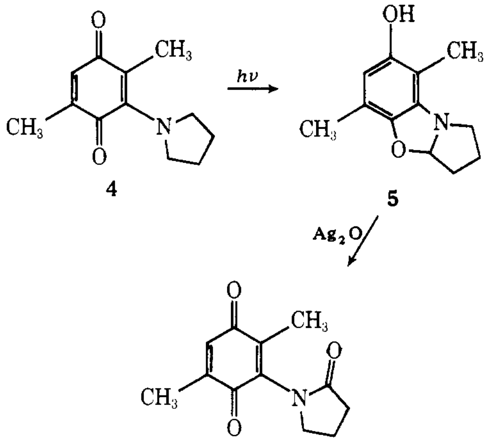


2 **3**

In our work, a model aminoquinone **4** was prepared by using a tenfold dilution of the conventional conditions for the condensation of pyrrolidine and xyloquinone to form a bis adduct. The photolysis of **4** with a sunlamp to produce **5** proceeded cleanly, although isolation of **5** in high yield was not possible.



4 **5** **6**

These insertion products are characterized by the appearance of a downfield methine hydrogen in their NMR spectra and the disappearance of quinone carbonyls in their IR spectra. Oxidation of photoproduct **5** with silver oxide yielded pyrrolidone–quinone **6**, a derivative with the heterocyclic α carbon in the desired oxidation state. Lactam **6** was characterized by its unambiguous NMR, by its carbonyl band at 5.78 μm, and by its UV $\lambda_{\max}$ 273 nm. This maximum is shifted almost 30 nm to longer wavelength compared to **4**, presumably because of lesser stabilization of the ground state of the chromophore.