23 H), 3.52–4.27 (m, 2 H), 5.03–5.68 (m, 3 H), 6.0 (s, 3 H); IR (mull) 3480, 3340, 3140, 2720, 2640, 2560, 1725, 1675, 1265, 1250, 1090, 1075, 970 cm^{-1}; mass spectrum, calcd for $C_{29}H_{55}Si_3O_4$ [$M^+ - CH_3$ for the tris(trimethylsilyl) derivative] *m/e* 551.3408, found *m/e* 551.3387 (other ions at *m/e* 566, 495, 476, 405, 386, 73); $[\alpha]_D$ +91° (*c* 0.964, CH_3OH). Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 71.80; H, 9.68.

Compound **2** was also identical by TLC with authentic material (mixture melting point 60–61.5 °C).[6a,21]

Acknowledgment. Helpful discussions with Professor D. J. Cram and Dr. D. R. Morton are gratefully acknowledged. I also thank Mr. P. A. Meulman and Mr. R. J. Wnuk for infrared and mass spectra and Dr. A. Scott for the preparation of intermediates.

Registry No. 2, 69552-46-1; **2** bis(tetrahydropyranyl) ether, 71845-98-2; **2** tris(trimethylsilyl) derivative, 70398-64-0; **3a**, 70870-92-7; **3b**, 69552-54-1; **3b** bis(trimethylsilyl) derivative, 70398-74-2; **4**, 37517-42-3; **5**, 76794-00-8; **6**, 76794-01-9; **7**, 76794-02-0; **8**, 76794-03-1; **9**, 76794-04-2; dimethyl methylphosphonate, 756-79-6; (4-carboxybutyl)triphenylphosphonium bromide, 17814-85-6; (5*Z*)-6a-carba-PGI_2 bis(tetrahydropyranyl) ether, 76822-29-2.

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(24) Since the completion of this work the synthesis of 5-methyl-6-oxobicyclo[3.3.0]oct-1-en-3-one has been reported utilizing an intramolecular Wittig reaction of a stabilized phosphorane with potassium carbonate at 40 °C: Trost, B. M.; Curran, D. P. *J. Am. Chem. Soc.* **1980**, *102*, 5699. Since a stabilized phosphorane is generally less nucleophilic than the corresponding β-ketophosphonate anion, this route would probably not be effective for the formation of bicyclo[3.3.0]octenone **7**.

(25) For a very recent review of the intramolecular Wittig reaction see: Becker, K. B. *Tetrahedron* **1980**, *36*, 1717.

Cation–Anion Combination Reactions. 19.[1] Some Reactions of Ortho-Substituted Triarylmethyl Cations in Water

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Received December 17, 1980

As a part of our general studies of electrophile–nucleophile reactions,[1] we have studied the reactions of two tri-ortho-substituted triarylmethyl cations with several nucleophiles in aqueous solution. The results are reported in the present paper.

Experimental Section

Synthesis of Tris(2,4-dimethoxyphenyl)methyl Alcohol. To a solution of 0.094 mol of phenyllithium in ca. 50 mL of absolute ether was added 0.092 mol of 2,4-dimethoxybromobenzene (Aldrich) in ca. 30 mL of ether. The resulting solution was stirred at room temperature for 4 h, and then a solution of 0.025 mol of dimethyl carbonate in ca. 10 mL of ether was added dropwise. The reaction mixture was heated to reflux for ca. 20 min and then cooled to ice bath temperature. Excess lithium reagent and salts were decomposed by the addition of ca. 75 mL of 6 M acetic acid followed by 25 mL of concentrated ammonium hydroxide. The aqueous layer was separated and washed with several portions of ether, and the combined ether solutions were then washed with dilute sodium carbonate and dried over potassium carbonate. The ether was removed on a rotary evaporator and the remaining oil was dissolved in the minimum amount of hot ethanol. On cooling, the ethanol solution yielded crystals which were recrystallized once from ethanol and then once from acetone to give ca. 3.5 g of purified product, mp 153.0–153.5 °C (lit.[2] mp 149 °C). The ^1H NMR spectrum of the material in $CDCl_3$ solution showed the methoxy singlets at 3.42 and 3.73 ppm, the OH singlet at 5.2 ppm, and the aromatic multiplets at 6.3–7.1 ppm, with the expected relative intensities. A solution of the compound in 0.1 M HCl showed absorbance peaks at 552 nm (ϵ 3.1 × 10^4 M^{-1} cm^{-1}), 415 (1.4 × 10^4), and 277 (1.9 × 10^4), and a strong shoulder at ca. 515 nm (3.0 × 10^4).

Synthesis of Tris(2-methyl-4-methoxyphenyl)methyl Alcohol. The Sandmeyer reaction of 2-methyl-4-methoxyaniline[3] was used for the preparation of 2-methyl-4-methoxybromobenzene.

To ca. 30 g of the aryl bromide in 60 mL of anhydrous ether under argon was slowly added a 10% excess of *n*-butyllithium in hexane at 0 °C. The solution was allowed to stand at ice-bath temperature for ca. 1 h, and then a solution of 6 g diethyl carbonate in ether was added dropwise over the period of 0.5 h. The reaction mixture was stirred at 0 °C for ca. 1.25 h. Water was then added, the layers were separated, and the ether layer was washed with water and then dried over potassium carbonate. The carbinol crystallized from the remaining hexane when most of the ether had been removed by evaporation, giving ca. 3.0 g of a slightly red solid. The product was repeatedly recrystallized from hexane, mp 172–173 °C. Anal. Calcd for $C_{25}H_{28}O_4$: C, 76.50; H, 7.19. Found: C, 76.35; H, 7.20. The ^1H NMR spectrum of the compound in $CDCl_3$ solution showed the methyl singlet at 2.17 ppm, the methoxy singlet at 3.77 ppm, the OH singlet at 2.71 ppm, and the aromatic multiplet at 6.4–6.8 ppm, with the expected relative intensities. A solution of the carbinol in 0.1 M HCl showed absorbance peaks at 512 nm (ϵ 6.1 × 10^4 M^{-1} cm^{-1}) and 265 (1.6 × 10^4).

Rate and Equilibrium Studies. All measurements were carried out at room temperature of 23 ± 1 °C.

The pK_R measurements for both cations utilized cation concentrations of 1–2 × 10^{-6} M and 10-cm pathlength spectrophotometer cells. Absorbances of the solutions at the wavelength of maximum absorbance were measured with a Cary Model 14 spectrophotometer. For the tris(2,4-dimethoxyphenyl)methyl cation, both chloroacetic acid and succinic acid buffers were used with ionic strengths ranging from 0.01 to 0.1 M. There was no detectable effect of buffer or ionic strength change on the equilibrium. All of the measurements showed a precision of ca. ±0.04 p*K* units. For the tris(2-methyl-4-methoxyphenyl)methyl cation, both chloroacetic acid and citric acid buffers were utilized. Again there was no detectable effect of buffer change or ionic strength change (0.01–0.1 M) on the equilibrium, and the precision was ca. ±0.04 p*K* units.

With the exceptions of the reactions of water and hydroxide ion with tris(2-methyl-4-methoxyphenyl)methyl cation, reaction kinetics were studied by stop-flow spectrophotometry, using techniques analogous to those reported in earlier papers.[1] The extreme insolubility of the tris(2-methyl-4-methoxyphenyl)methyl alcohol caused problems at the concentrations necessary for accurate stop-flow measurements (ca. 10^{-5} M). The reactions of the corresponding cation with water and hydroxide ion were, therefore, studied in 10.0-cm cells, using the Cary Model 14 spectrophotometer. It was possible to begin observation within ca. 15 s of mixing the cation solution, and, even in the fastest reactions studied, this was no more than one half-life of the reaction.

The reactions of both cations were followed by observations of the visible absorbance peaks of the cations and, in separate experiments, the ultraviolet absorbance peaks. The spectra of the reaction solutions immediately after reaction showed no evidence for formation of quinoid structures.

The rate and equilibrium constants obtained are reported in Table I.

Results

Previous work[1] and literature reports[4] concerning reactions of ortho-substituted triarylmethyl cations had led us to expect some difficulties from reactions of nucleophiles

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(1) For the previous paper in this series, see C. D. Ritchie and T. C. Hofelich, *J. Am. Chem. Soc.*, **102**, 7039 (1980).

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Table I. Rate and Equilibrium Constants for Reactions in Water[a]

	$(o,p\text{-di-MeO})_3$trityl cation		$(o\text{-Me},p\text{-MeO})_3$trityl cation	
nucleophile	$\log k$[b]	$\log K$[c]	$\log k$[b]	$\log K$[c]
water	0.30 ± 0.04	-3.24 ± 0.04	-2.00 ± 0.04	-3.80 ± 0.04
OH^-	1.24 ± 0.04	10.76 ± 0.04	1.00 ± 0.04	10.20 ± 0.04
glycinate	3.80 ± 0.04		0.73 ± 0.04	-7.4 ± 0.3
$H_2NCH_2CH_2NH_2$	2.96 ± 0.04		0.52 ± 0.04	-7.6 ± 0.3
CN^-	1.53 ± 0.04			

[a] All reactions at 23 ± 1 °C and ionic strengths from 0.01 to 0.1 M. [b] Rate constant for the water reaction is in units of seconds^{-1}; all others are in units of molar^{-1} seconds^{-1}. [c] Equilibrium constants for the water and amine reactions are for $Ar_3C^+ + BH \rightleftharpoons Ar_3CB + H^+$. Those for hydroxide ion reactions are for $Ar_3C^+ + OH^- \rightleftharpoons Ar_3COH$ and are in units of molar^{-1}.

at the para positions of the cations studied here. No evidence for such reactions was found; all reactions showed excellent pseudo-first-order kinetics for changes in absorbances in both the visible and ultraviolet spectra, no appreciable formation of absorbance above 350 nm was observed, and the pK_R measurements indicated a clean conversion of the cations to carbinols. Some initial difficulties with reactions of the tris(2-methyl-4-methoxyphenyl)methyl cation proved to be due to sample impurities and extreme insolubility of the carbinol in aqueous solutions. The first source of difficulty was removed by careful, repeated, recrystallizations of the carbinol sample, and the second was eliminated by using cation concentrations of ca. 10^{-6} M for studies of the carbinol-forming reactions.

The reactions of both cations with nucleophiles were found to be accurately first order with respect to nucleophile concentration (with the exception of water, of course). No evidence for kinetic terms second order with respect to amine concentrations[5] was found for amine reactions.

Considerable effort was expended in a search for general-base catalysis of the reaction of water with the tris(2,4-methoxyphenyl)methyl cation by Dabco (1,4-diazabicyclo[2.2.2]octane). We were unable to detect any such catalysis at Dabco concentrations up to 0.25 M. Since we would certainly have observed any increase in rate greater than 10%, the Dabco general-base catalysis of water reaction must have a rate constant less than 0.8 $M^{-1}\,s^{-1}$, and the ratio of "uncatalyzed" to Dabco-catalyzed rate constants must be greater than unity.

Discussion

In the previous paper of this series, we reported[1] that the introduction of a single *o*-methylsulfonyl group on a triarylmethyl cation caused no change in the relative rates of reactions of nucleophiles with the cation but did lead to a substantial decrease in rate of reactions of all nucleophiles. These observations are in accord with the expectation that nucleophiles will attack the unhindered face of the cation, with the ortho group on the opposite face exerting its influence by hindering the compression of the aryl rings on going from trigonal cation to tetrahedral product.

For the present cations, with ortho groups on all three rings, one expects, on the basis of statistics, models, and precedence,[4] that the most stable conformation will have two of the groups on one face, with the third on the opposite face. This expectation provides the simplest rationalization of the observed rates of reactions of nucleophiles with the tris(2-methyl-4-methoxyphenyl)methyl cation. Both glycinate and ethylenediamine react more slowly than hydroxide ion with this cation, whereas these amines react faster than hydroxide ion (by factors of 4 to 10) with trianisylmethyl cation,[5] Malachite Green,[1] or aryltropylium cations.[6] The relative reactivities of hydroxide ion and water with this cation are almost identical with those for trianisylmethyl cation in accord with previous observations of an absence of steric influence on the relative reactivities of these reactants.[1] It is also interesting to note that the effect of introducing the three *o*-methyl groups onto the trianisylmethyl cation is nearly the same on the equilibrium constants as on the rate constants for water and hydroxide ion reactions; the pK_R is increased by 3 units and the log *k*'s are decreased by 2.9–3.2 units.

A much more complex situation exists for reactions of the tris(2,4-dimethoxyphenyl)methyl cation. The most immediately striking point is that hydroxide ion reacts only 8.7 times faster than does water (ratio of the second-order to pseudo-first-order rate constants). This is the smallest rate ratio for reactions of these nucleophiles of which we are aware; the ratio is usually greater than 10^3. Just as striking, on further examination, is the observation that $k_{\text{glycinate}}/k_{OH^-} = 10^{2.6}$ for the present cation but is only ca. 7 for the trianisylmethyl cation. Ethylenediamine reacts nearly a factor of ten more slowly than does glycinate with the present cation, whereas the two amines react at nearly the same rates with other triarylmethyl cations,[6] including the tris(2-methyl-4-methoxyphenyl)methyl cation of the present study.

The reactions of water with triarylmethyl cations generally show general-base catalysis, with the rate constant for Dabco-catalyzed reaction ca. 10 greater than that for the "uncatalyzed" reaction.[7] We were unable to detect general-base catalysis for the reaction of water with the tris(2,4-dimethoxyphenyl)methyl cation and can set an upper limit of unity on the ratio of Dabco-catalyzed and "uncatalyzed" rate constants.

Any postulate of involvement of the *o*-methoxy groups as intramolecular general-base catalysts for either the water or amine reactions discussed above can be discarded on the basis of Jencks' rules.[8] We are, in fact, unable to offer any consistent rationalizations of the rates of reactions of the tris(2,4-dimethoxyphenyl)methyl cation with nucleophiles. We can point out, however, that the fact that cyanide ion reacts faster than hydroxide ion with this cation, whereas the reverse is true for other cations and neutral electrophiles,[1] indicates that the high k_{nuc}/k_{OH^-} ratios discussed above may be at least partially due to an "abnormally" low hydroxide ion rate constant. We also offer the purely ad hoc suggestion that the *o*-methoxyl groups may be influencing the water structure in the immediate vicinity of the reaction site.

Acknowledgment. This work was supported by grants from the National Institutes of Health, Public Health

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Service (GM 12832), and from National Science Foundation (CHE77-24701A). We also acknowledge the aid of Dr. Joe Murphy in carrying out some early experiments and of Dr. T. C. Hofelich for considerable consultative aid in the later stages of this work.

Registry No. 2,4-Dimethoxybromobenzene, 17715-69-4; 2-methyl-4-methoxybromobenzene, 27060-75-9; tris(2,4-dimethoxyphenyl)methyl alcohol, 76832-37-6; tris(2-methyl-4-methoxyphenyl)methyl alcohol, 76832-38-7; (*o*,*p*-di-MeO)$_3$trityl cation, 14426-26-7; (*o*-Me,*p*-MeO)$_3$trityl cation, 76832-39-8.

Conformational Analysis. 40. Conformation of 1-Methyl-1-phenylcyclohexane and the Conformational Energies of the Phenyl and Vinyl Groups[1]

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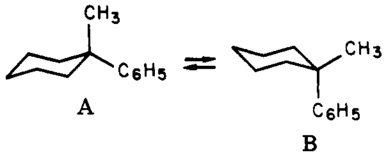
Received November 26, 1980

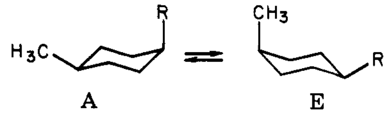
In 1971 Allinger and Tribble[2] calculated, using a force-field approach, that in 1-methyl-1-phenylcyclohexane (1, Scheme I) the conformational energies[3] of methyl (1.7 kcal/mol) and phenyl (3.0 kcal/mol) should not be additive, the conformation with the larger phenyl group in the axial position being preferred at equilibrium by 0.9 kcal/mol. This comes about because the most stable conformation of the axial phenyl group (phenyl perpendicular to the bisector plane of the cyclohexane chair) is not perturbed by introduction of a geminal methyl substituent, whereas considerable perturbation occurs upon introduction of geminal methyl into equatorial phenylcyclohexane whose phenyl substituent is (in the absence of the geminal methyl) most stable in the bisector plane of the cyclohexane chair. The Allinger–Tribble prediction was in qualitative agreement with contemporary NMR data[4] but was not quantitatively borne out by low-temperature proton NMR work subsequently carried out with 1-methyl-1-phenyl-4,4-dimethoxycyclohexane.[5] This work[5] indicated a preference for the axial phenyl group of only 0.34 kcal/mol. However, the experimenters stated:[5] "Whether this discrepancy is due to the presence of the *gem*-dimethoxy group or to some computational insufficiency remains a moot point".

In view of the importance of the prevalence of axial phenyl over geminal methylene in a number of alkaloids of the mesembrine[6] and amarillidacea[7] families, which we are presently investigating, we felt that confirmation of the result of Anteunis' group[5] by low-temperature ^{13}C NMR spectroscopy was desirable. At the same time we decided to reinvestigate the conformational energy of the phenyl group itself, since three discrepant values, 2.0,[8] 2.6,[9] and 3.0 kcal/mol,[10] were in the literature. Although the last $-\Delta G^\circ$ value is the now generally accepted one,[3] it is the composite (at 25 °C) of a rather larger $-\Delta H^\circ$ of 3.61 kcal/mol and an unexpectedly large $-\Delta S^\circ$ of 2.09 gibbs that is not anticipated by the force-field calculations which predict uniquely stable conformations for both equatorial and axial phenylcyclohexane.[2]

Scheme I



Scheme II



2, R = C_6H_5
3, R = $CH{=}CH_2$

Finally we have investigated the conformational energy of the vinyl ($CH_2{=}CH{-}$) group which could previously be obtained,[5,11] only by assuming the very additivity of ΔG° values in geminally substituted compounds which is absent in the 1-phenyl-1-methyl case; the two values so computed were 1.5 kcal/mol[5] and 1.4 kcal/mol.[11]

Results

The room-temperature ^{13}C NMR spectral data of 1 is given in Table I (entry 1) as are the low-temperature spectral data of conformers A and B (Scheme I) at −100 °C (entries 2, 3). The two conformational isomers are present in quite unequal amounts and the configurational assignment can be readily made from the upfield shift of the methyl in conformer A and the ipso carbon of the phenyl in B. Measurement of relative areas of various peaks[12] (Table II) gives a K of 2.53 ± 0.33 and $-\Delta G^\circ$ of 0.32 ± 0.04 kcal/mol, favoring conformer B. This result is in excellent quantitative agreement with that of Anteunis' group,[5] whose equilibrium measurement was evidently not perturbed by the presence of the dimethyl ketal function at C(4). The force-field calculations[2] are thus only qualitatively correct in that they overestimate the axial preference of phenyl by nearly 0.6 kcal/mol.

The conformational equilibria in phenyl- and vinylcyclohexanes are too one-sided to be measured directly. We therefore turned to a technique previously used by one of us[13] as well as Booth,[14] involving determination of the conformational equilibrium in a *cis*-4-methylcyclohexyl-R instead of in cyclohexyl-R itself (cf. Scheme II). The technique is particularly attractive since additivity in such 1,4-disubstituted systems does seem to obtain in the cases where it has been tested[13,14] and since a very accurate determination of the conformational energy of the methyl group used as counterpoise—1.74 ± 0.06 kcal/mol—is now available.[15]

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