The proton-transfer reactions of the solvent-free hydroxide and methoxide ions were all observed to proceed rapidly with rate constants $\gtrsim 10^{-9}$ cm^3 molecule^{-1} s^{-1}.[5] Solvation of the bare ions was observed to result either in a slight or a dramatic reduction in the rate of reaction, the latter occurring in some instances already after the addition of just one molecule of solvent. This remarkable divergence in behavior can be accounted for by a careful consideration of the degree of stabilization of the bare ions by solvation.[6] The solvent-free reactions are all exoergic: they span ranges in $-\Delta G°$ (i.e., relative intrinsic acidity) from 10.3 to 36.9 kcal mol^{-1} for the reactions with OH^- and from 0.2 to 26.8 kcal mol^{-1} for the reactions with CH_3O^-.[1,7] The free energies of solvation of the reactant ions act to decrease the reaction exoergicities and can lead to changes in the sign of $\Delta G°$ (reversals in relative acidity) and therefore changes in the preferred direction of reaction unless they are offset by the solvation energies of the conjugate bases produced.[8]

The carbanions produced by the deprotonation of allene and toluene, the acids closest in intrinsic acidity to water and methanol, are expected to have free energies of solvation insufficient to compensate for the high solvation free energies of OH^- and CH_3O^-.[9] The sharp (3 orders of magnitude) drop in the rate of deprotonation observed upon the addition of just one molecule of solvent is therefore a manifestation of a reversal in the relative acidity of these two carbon acids and water or methanol.

The addition of one methanol molecule to CH_3O^- causes an immediate reversal in the relative acidity of methanol and acetylene; reaction 4 was not observed. In contrast, the reversal in

$$CH_3O^-\cdot CH_3OH + C_2H_2 \not\rightarrow C_2H^-\cdot CH_3OH + CH_3OH \qquad (4)$$

the relative acidity of water and acetylene is delayed by one solvent molecule; reaction 5 was observed to occur rapidly. Apparently

$$OH^-\cdot H_2O + C_2H_2 \rightarrow C_2H^-\cdot H_2O + H_2O \qquad (5)$$

the lower free energy of hydration by one water molecule expected for C_2H^- is compensated for by the higher relative intrinsic acidity of water and acetylene.[10]

For the deprotonation of acetone by OH^- and CH_3O^-, both reversals also occur, but they are delayed by one additional molecule of solvent; the sharp decline in the rate occurs at n = 3 and 2, respectively.[11]

No reversals are observed for the deprotonation of nitromethane, hydrogen cyanide, and ethanol; reaction 2 remains rapid up to the addition of three solvent molecules.[12] The intrinsic acidities of nitromethane and hydrogen cyanide are sufficiently high to offset the weaker anion–solvent interactions expected for $CH_2NO_2^-$ and CN^-.[13] In comparison, the intrinsic acidity of ethanol is relatively close to that of water and methanol, but in this case the order of acidity is preserved up to the addition of three solvent molecules by the strong solvation of $C_2H_5O^-$.[14]

The trends in the rates of the acid–base reactions of type 2 identified in this study are consistent with rate measurements made in solution[15] and with known solution acidities. Indeed, they provide a vivid confirmation of expectations on the basis of measurements made in solution. The approach which has been developed should be applicable to the investigation of transitions in the relative acidity of other acid pairs and with solvents other than water and methanol. However, a clear pattern has already emerged from the measurements reported here which may well be representative of the general transition in the rates of reactions of type 2 between the gas phase and solution.

Acknowledgment. We thank the Natural Sciences and Engineering Council of Canada for financial support.

Registry No. Allene, 463-49-0; toluene, 108-88-3; ethanol, 64-17-5; acetylene, 74-86-2; acetone, 67-64-1; nitromethane, 75-52-5; hydrogen cyanide, 74-90-8; hydroxide ion, 14280-30-9; methoxide ion, 3315-60-4.

(5) These large rate constants correspond to proton transfer at essentially every collision.

(6) The rate of proton transfer can be expected to remain high upon solvation if the reaction remains exoergic. Conversely, a sharp drop in the rate can be anticipated if solvation renders the reaction endoergic.

(7) The intrinsic acidity of allene has been established in our laboratory from a measurement of the equilibrium constant for its deprotonation by CH_3O^-.

(8) Exoergicity will be preserved upon solvation if the free energy of solvation of the conjugate base produced is comparable to or greater than the free energy of solvation of the reactant base or if a lower free energy of solvation of the product base is offset by the exoergicity of the unsolvated reaction.

(9) The free energies of solvation of OH^- by H_2O and CH_3O^- by CH_3OH are approximately 19 and 17 kcal mol^{-1}, respectively. The failure to observe reaction 2 for n = 1 implies free energies of solvation for $C_3H_3^-$ and $C_6H_5CH_2^-$ by H_2O and CH_3OH less than approximately 9 and 17 kcal mol^{-1}, respectively. The free energy of hydration of OH^- was taken from: Kebarle, P. *Annu. Rev. Phys. Chem.* **1977**, *28*, 445. The free energy of solvation of CH_3O^- by CH_3OH was deduced from the results reported in ref 2.

(10) The observation of reaction 5 implies a free energy of hydration for C_2H^- greater than approximately 3.5 kcal mol^{-1}. The equilibrium constant for this reaction appeared to be $\gtrsim 8 \times 10^2$ which raises the lower limit for the hydration free energy to ~7.5 kcal mol^{-1}. Failure to observe the corresponding methanol reaction sets an upper limit of 13 kcal mol^{-1} to the solvation free energy of C_2H^- by CH_3OH.

(11) The decays observed for the $OH^-\cdot(H_2O)_2$ and $OH^-\cdot(H_2O)_3$ ions and their deuterated versions suggest that the reaction with n = 2 may be close to isoergic while the reaction with n = 3 may be only slightly endoergic.

(12) The slight decrease in the rate constants with added solvent observed for the reactions with HCN and CH_3NO_2 corresponds approximately to the decrease in the collision rate constant as calculated from the AADO theory (Su, T.; Su, E.C.F.; Bowers, M. T. *J. Chem. Phys.* **1978**, *69*, 2243). A similar situation exists in the case of ethanol except at the higher values of n where the rate constant appears to drop somewhat faster, presumably because the reactions become nearly isoergic. Our measurements indicate that the equilibrium constant for reaction 2 with B^- = CH_3OH, S = CH_3OH, and AH = C_2H_5OH diminishes as n increases to a value of ~1 for n = 3.

(13) In fact, the solvent-free reactions are sufficiently exoergic to allow at least the first solvent molecule to be "boiled off".

(14) When the free energies of solvation of the two bases are nearly equal, as is the case here for $OH^-/C_2H_5O^-$ and $CH_3O^-/C_2H_5O^-$, the reversal in relative acidity may be shifted to much higher additions of solvent. The location of these reversals are more accessible to experiments carried out at lower temperatures since solvent binding energies become progressively smaller as n increases.

(15) For example, the reaction between OH^- and HCN is rapid in aqueous solution, $k = 3.7 \times 10^9$ l mol^{-1} s^{-1}, while the reaction with CH_3COCH_3 is much slower, $k = 2.7 \times 10^{-1}$ l mol^{-1} s^{-1} (Eigen, M., *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1).

Stereo- and Regiocontrolled Synthesis of Methyl *N*-Acetyl-α-D-sibirosaminide

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The unique antitumor antibiotic sibiromycin[2] is a glycoside comprising a pyrrolo[1,4]benzodiazapene aglycon, sibiromycinone, and an unusual amino sugar sibirosamine, **8a**. Parker[3] has made significant synthetic advances toward the aglycon, and a synthesis of methyl *N*-acetyl-α-D-sibirosaminide (**8b**) was reported by Dyong and Shulte[4] while our work was in progress. In this communication

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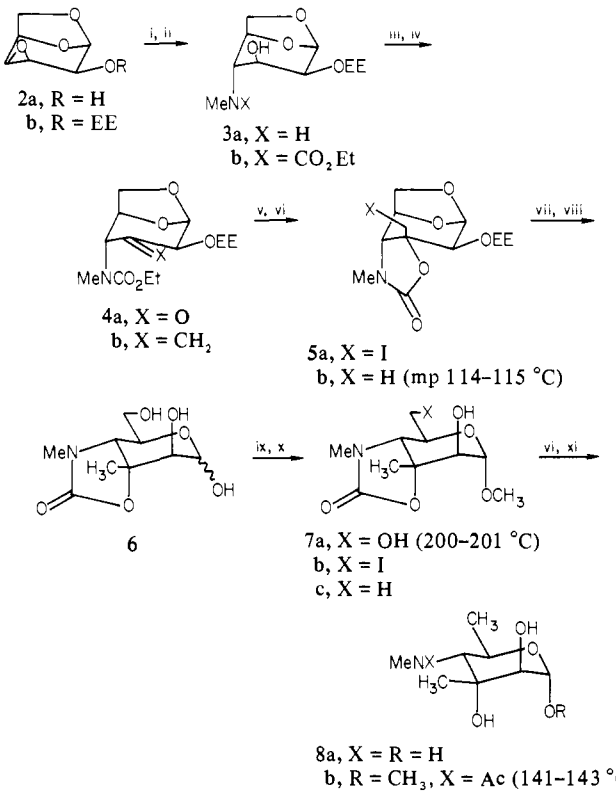
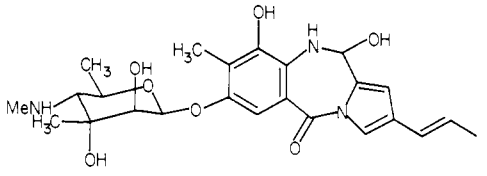
Scheme I[a]



[a] (i) $MeNH_2$/EtOH/heat; quantitative. (ii) EtOCOCl, 93%. (iii) Collin's, 82%. (iv) $Mg(Hg)CH_2I_2$, benzene ether,[16] 35%. (v) Iodonium dicollidine perchlorate[18,19]/CH_2Cl_2/room temperature/18 h, 68%. (vi) $Bu_3SnH/(PhCOO)_2$, 88%. (vii) 10% H_2SO_4 in Ac_2O/40 °C/0.5 h, 93%. (viii) NaOMe, 84%. (ix) MeOH/Dowex (H^+)/reflux/48 h, 93%. (x) TsCl/pyridine, then NaI, 73%. (xi) 5% KOH, then Ac_2O/MeOH, 71%.

we describe an alternative synthesis of this important amino sugar derivative in which all reactions were found to proceed in high yields with a single unfortunate exception, this being also the only stage at which chromatographic fractionation was necessary.



1

As in Dyong's synthesis,[4] our starting material was a derivative of D-mannose, but the precise choice of precursor has been found to have a crucial and unpredictable bearing upon the success of several transformations. Concurrently with the synthesis outlined below, we examined an approach based upon an α-D-mannopyranoside having the $^4C_1$ conformation[5] and found that we were frequently confronted with problems of regio- and/or stereocontrol in key reactions. The 1,6-anhydro system used for the synthesis below has the pyrano ring in $^1C_4$ conformation,[5] and this provided a much more reliable template, the [3.2.1] bicyclic skeleton eliciting complete stereo- and regiocontrol.

The starting material for our synthesis was the 1,6:3,4-dianhydro-β-D-talopyranose (**2a**) which is obtained from D-mannosan (1,6-anhydro-β-D-mannopyranose),[6] according to the procedure of Hann and Hudson.[9] Ammonolysis of the protected form **2b** with methylamine gave the oily amine **3a** quantitatively, and this was converted directly into the urethane **3b**, also an oil. Collins' oxidation afforded the ketone **4a**[10] in 82% yield which was completely free of the hydrated form, judging from the absence of hydroxyl absorptions in the infrared spectrum.

Carbonyl groups flanked by O and/or N substituents are known to react poorly with unstabilized Wittig reagents,[11] and **4a** proved to be no exception, giving nine products with methylenetriphenylphosphorane, none of which was **4b**. The olefination reactions of Johnson[12] and Chan[13] also failed. Finally success was had with the Cainelli reagent,[15] and although we were able to reduce the volume of the magnesium amalgam to one-sixth of that prescribed,[16] the yield of **4b**[10] could not be raised above 35%, marking this step as the low point of the synthesis. A major contaminant seemed to be the alcohol resulting from reduction of ketone **4a**.[17]

Our key reaction for achieving stereocontrolled oxyamination was now applied.[18] Treatment of **4b** with iodonium dicollidine perchlorate[19] in methylene chloride at room temperature overnight led to the iodourethane **5a** in 68% yield, and reduction gave the crystalline *C*-methyl derivative **5b**[10,20] in 88% yield.

In the hope of obtaining the triol **6** directly, we treated **5b** with 0.5 N HCl under reflux overnight, but the only reaction was cleavage of the ethoxyethyl group. However, treatment with 10% sulfuric acid in acetic anhydride gave the triacetate, and deacetylation afforded **6**[10] in 80% overall yield. Upon refluxing the solution with methanol and Dowex (H^+) resin for 48 h, an α,β mixture of anomers was obtained from which the α-form **7a**[10,21] crystallized spontaneously.

The primary alcohol of **7a** could be converted directly into the iodide **7b** in 53% yield by using the Mitsunobo reaction;[22] however, the traditional two-step sequence involving sulfonation followed by iodionlysis gave a better overall yield of 73%. Reduction to the 6-deoxy product **7c**[10,23] was quantitative, and hydrolysis with 5% potassium hydroxide followed by N-acetylation gave **8b**. This product had identical melting point, mixed melting point (141–143 °C), and 200–MHz NMR spectrum as a sample obtained from Professor Dyong's laboratory. Doubling up of the NMR spectrum of **8b** reveals a 9:1 mixture of amide rotomer conformers.

Acknowledgment. We are grateful to the National Cancer Institute (U.S.) (CA 28193) and the Natural Sciences and Engineering Research Council of Canada for financial support and

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(24) We have been informed recently by Professor Parker of Brown University that she has reexamined the structure of sibirosamine obtained by degradation of the antibiotic and has concluded that the configuration at C3 is opposite to that originally assigned (Mesentsev, A. S.; Kulyaeva, V. V. *Tetrahedron Lett.* **1973**, 2225) and synthesized by Dyong[4] and, now, by us. We are grateful to Professor Parker for informing us of this development prior to publication.

Professor Heesing, a colleague of the late Professor Dyong, for a sample of **8b**.

Registry No. 2a, 34147-09-6; **2b**, 80471-15-4; **3a**, 80462-77-7; **3b**, 80462-78-8; **4a**, 80462-79-9; **4b**, 80462-80-2; **5a**, 80462-81-3; **5b**, 80462-82-4; **6**, 80462-83-5; **7a**, 80462-84-6; **7b**, 80462-85-7; **7c**, 80462-86-8; **8b**, 78013-88-4; D-mannosan, 14168-65-1.

Photooxidation of Water by *p*-Benzoquinone

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There is strong interest in understanding photosynthesis, and in aqueous photosynthetic-like systems utilizing light for chemical purposes.[1-3] Naturally occurring quinones play an essential role in electron transport in bacterial reaction centers,[4,5] photosystem II of green plants,[6] and mitochondria.[7] Therefore it seems important to understand the aqueous photoredox behavior of the simplest quinone, *p*-benzoquinone (BQ). Using the technique of transient spontaneous Raman spectroscopy, we report here two- and apparently one-photon photooxidation of water by BQ without catalysis.

Our apparatus and methods have been recently described.[8,9] A 266-nm pulse (10 Hz) photolyzes the flowing sample, and a Raman spectrum is generated by a time-delayed 416-nm pulse. The pulses have $\simeq$10-ns widths, and sensitivity is enhanced by extensive averaging with gated, multichannel optical detection. BQ (freshly sublimed) solutions were studied within a few minutes of preparation.

Aqueous BQ (pH $\simeq$6.0) has its $S_0 \rightarrow S_1$ ($n-\pi^*$) transition maximum ($\epsilon \simeq 20\ M^{-1}\ cm^{-1}$) near 430 nm.[10] An energetic 416-nm pulse by itself has the potential to both make transient species and generate their Raman spectra. Figure 1 shows spectra as a function of 416-nm pulse energy *without* prior 266-nm excitation. At least three different species appear to be present. Peaks labeled S_0 are assigned to S_0 BQ as they scale approximately linearly with pulse energy and agree with S_0 vibrational frequencies.[11] Peaks labeled T_1, and $Q^{-}\cdot + QH\cdot$, vary together as a higher (approximately second) power of energy. These peaks represent transient species created by absorption of one photon, with a second photon required for Raman scattering. These species appear within the pulse width and cannot be bimolecular BQ reaction products.

$Q^{-}\cdot$ refers to the semiquinone radical anion, which can be made independently by MnO_2 oxidation of aqueous hydroquinone at neutral pH.[12] The $Q^{-}\cdot$ spectrum thus generated[13] (Figure 2a) agrees with a $Q^{-}\cdot$ spectrum recently obtained via pulsed radiolysis.[14] QH· is protonated $Q^{-}\cdot$. Previous studies have shown that $Q^{-}\cdot$ (pK_a = 4.1) protonates in acidic solution.[15] Figure 2b shows a QH· 416-nm spectrum observed at long delay time Δt after photolysis of acidic hydroquinone.[13] In agreement with these assignments, we observe a smooth transformation of $Q^{-}\cdot$ into QH· at long Δt as a function of pH.

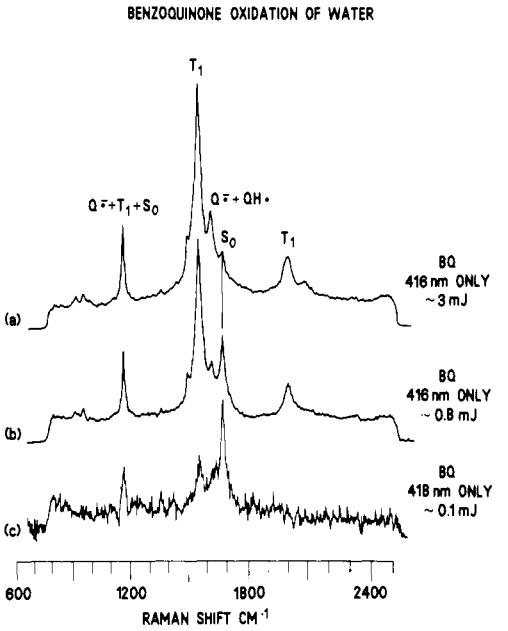

Figure 1. 416-nm Raman spectra, as function of pulse energy, of an aqueous solution of BQ (3×10^{-2} M, pH $\simeq$6). Transient species produced and probed by the same laser pulse are the lowest $n\pi^*$ triplet of BQ (T_1) and apparently semiquinone radicals $Q^{-}\cdot$ + QH·. The ground-state vibrations are labeled S_0. Trace a, taken at 3-mJ, 416-nm power, is an average of 600 laser pulses; trace b, taken at 0.8-mJ laser power, is an average of 3000 laser pulses (vertical axis is expanded by 2×); trace c, taken at 0.1-mJ laser power, is an average of 12 000 laser pulses (vertical axis is expanded by 8×).

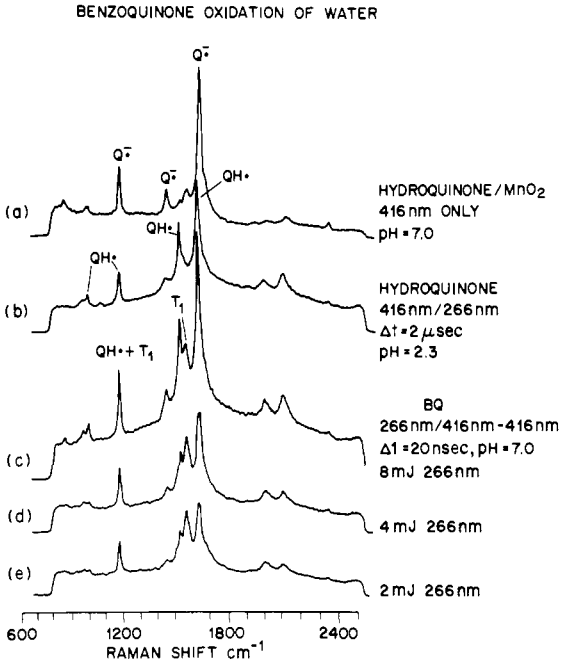

Figure 2. (a) Raman spectrum of 1×10^{-2} M neutral pH aqueous solution of hydroquinone passed over powdered MnO_2 (416-nm laser only); all peaks are assigned to $Q^{-}\cdot$; (b) Raman spectrum of aqueous hydroquinone (1×10^{-2} M; pH 2.3) 2 μs after 266-nm photolysis; all peaks assigned to QH·; (c)-(e) Raman spectra of 5×10^{-3} M aqueous BQ solution taken 20 ns following 266-nm excitation, as a function of 266-nm pulse energy. The contribution of the 416-nm laser to transient production has been approximately subtracted so that peaks are due mainly to 266-nm excitation. Trace b was taken at 8-mJ, 266-nm power; trace c, 4 mJ; trace d, 2 mJ.

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