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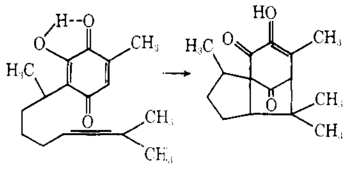
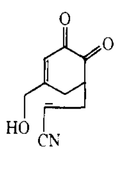

i ii


iii

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(11) The precise order of events in the formation of **7** is not known (i.e., whether lactonization occurs before or after ketone attack by a second pyrone molecule).

Equilibria and Rates in the Reaction of *o*-Methyl Malachite Green with Sulfite Ions[1]

Jack Hine* and V. Thiagarajan

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

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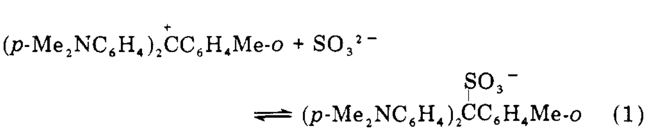
A study of the reaction of the *o*-methyl malachite green cation (M^+) with sulfite ions was initiated as part of an extension of earlier work on rate–equilibrium correlations in Lewis acid–base reactions.[2] We were not able to obtain the



$$(p\text{-}Me_2NC_6H_4)_2\overset{+}{C}C_6H_4Me\text{-}o + SO_3^{2-} \rightleftharpoons (p\text{-}Me_2NC_6H_4)_2\overset{SO_3^-}{C}C_6H_4Me\text{-}o \qquad (1)$$

additional data to permit us to draw broader generalizations, but the rate and equilibrium constants obtained are described here.

Results

Equilibrium Constants. Equilibrium in eq 1 was studied by absorbance measurements on mixtures of known concentrations of M^+ and SO_3^{2-} at 25 °C and ionic strength 0.5. Inasmuch as the pK values of HM^{2+} and M^+ at 20 °C and ionic strength 0.5 have been reported to be 1.31 and 9.07, respectively,[3] we took the concentrations of HM^{2+} and MOH to be negligible over the pH range 4.8–7.2 over which we made measurements. The sulfite adduct was assumed to be present in forms with and without an amino group protonated ($HMSO_3$ and MSO_3^-, respectively). If A is the absorbance of a solution of M^+, A_s is the absorbance of an equilibrium mixture of C mL of this solution and B mL of sulfite solution, and M_t is the concentration of M^+ in the original solution, then the total concentration of adduct is given by eq 2.

$$[MSO_3^-] + [HMSO_3] = \left(\frac{C}{B + C} - \frac{A_s}{A}\right) M_t \qquad (2)$$

$$[M^+] = M_t A_s / A \qquad (3)$$

$$K(1 + [H^+]/K_a) = \frac{AC}{A_s(B + C)[SO_3^{2-}]} - \frac{1}{[SO_3^{2-}]} \qquad (4)$$

The equilibrium concentration of M^+ is given by eq 3. Division of eq 2 by eq 3 and then by $[SO_3^{2-}]$ and rearrangement gives eq 4, in which K_a is the acidity constant of $HMSO_3$ and K is the equilibrium constant for addition of sulfite ions to M^+. Over the pH range 4.8–7.2 58 points were taken, with A_s/A ranging from 0.21 to 0.95. The concentrations of hydrogen and sulfite ions were calculated from the pH ($-\log a_{H^+}$), an acidity constant of 1.96×10^{-7} M for bisulfite ions interpolated from data at surrounding ionic strengths,[4] and ionic activity coefficients calculated from the Davies equation.[5] The equilibrium concentrations of sulfite ions ranged from 1.6×10^{-5} to 0.013 M. Equation 4 was solved for A_s and then K and K_a were calculated by an unweighted nonlinear least-squares method.[6] The values (± standard deviations) of 173 ± 2 M^{-1} and $(1.3 \pm 0.1) \times 10^{-6}$ M for K and K_a, respectively, fit the observed A_s values with a standard deviation of 0.010.

Rate Constants. Stopped flow kinetic runs were made using about 2×10^{-5} M M^+ and 0.005–0.05 M total sulfite over the pH range 6.16–7.58. In each run the approach to equilibrium was first order in $[M^+]$. Each first-order rate constant (k_{obsd}) is equal to the sum of a forward first-order rate constant (k_f) and a reverse first-order rate constant (k_r). Equation 5 allows for an uncatalyzed and an acid-catalyzed addition of sulfite ions to M^+.

$$k_f = k_0[SO_3^{2-}] + k_h[H^+][SO_3^{2-}] \qquad (5)$$

Equation 6 then follows from the principle of microscopic reversibility.

$$k_r = \frac{k_f}{K[SO_3^{2-}](1 + [H^+]/K_a)} \qquad (6)$$

Combination of eq 5 and 6 gives eq 7.

$$k_{obsd} = (k_0 + k_h[H^+]) \times \left([SO_3^{2-}] + \frac{1}{K(1 + [H^+]/K_a)}\right) \qquad (7)$$

Least-squares treatment of 52 k_{obsd} values, using the reciprocal of the standard deviation as the weighting factor, gave k_0 and k_h values (± standard deviations) of 24.5 ± 0.2 $M^{-1}\,s^{-1}$ and $(1.3 \pm 0.1) \times 10^7$ $M^{-2}\,s^{-1}$, respectively.

Discussion

The K_a value obtained corresponds to a pK_a value of 5.88 ± 0.04 or 5.58 on a per amino group basis. This is not far from the value 5.627 reported at 25 °C for the conjugate acid of *N*,*N*-dimethyl-*p*-toluidine,[7] a reasonable model compound for the sulfite ion adduct of M^+. The equilibrium constant K is smaller by more than 5000-fold than the value $>10^6$ M^{-1} reported[8] for malachite green itself at 23 °C and ionic strength 0.001. Under the same conditions the rate constant for reaction of malachite green cations with sulfite ions was reported[8] to be 4000 $M^{-1}\,s^{-1}$, which is 160 times as large as our value at 25 °C and ionic strength 0.5. A considerably smaller rate constant (280 $M^{-1}\,s^{-1}$) for the reaction of malachite green with sulfite has been reported[9] at 30 °C and ionic strength 1.0, but little experimental detail was given. Ritchie and Virtanen noted that the difference in rate constants reported is about that expected from the Debye–Hückel limiting law, which gives a log $v_\pm$ value of −1.1 for a 2:1 salt at ionic strength 1.0. However, the limiting law is not applicable at ionic strengths this large, and a survey of data on more than 50 2:1 and 1:2 salts[10] showed that all the experimentally determined log $v_\pm$ values at ionic strength 1.0 were between −0.04 and −0.7. Regardless of the exact value of the rate constant, it seems clear that introduction of an *o*-methyl substituent into malachite green decreases both the rate constant and eqiulibrium constant for combination with sulfite ions and that the decrease in the equilibrium constant is larger.

The acid catalysis of the combination of M^+ with sulfite ions that gives rise to the k_h term in the kinetic equation presumably comes from the combination of sulfite ions with HM^{2+}. If this is the case, then k_h is equal to k_2/K_{hm}, where K_{hm} is the acidity constant of HM^{2+} and k_2 is the rate constant for combination of sulfite ions with HM^{2+}. If pK_{hm} has the same value at 25 °C that it does at 20 °C (1.31),[3] then k_2 is equal to 6.4×10^5 M^{-1} s^{-1}.

Experimental Section

***o*-Methyl Malachite Green Perchlorate.** The leuco base was prepared from *o*-tolualdehyde and *N*,*N*-dimethylaniline as described by Esktröm[3] but the product obtained by recrystallization from absolute ethanol melted at 102 °C, as reported by Noelting and Gerlinger,[11] instead of 86–87 °C, as reported by Ekström. Lead dioxide oxidation using hydrochloric acid[3] gave a solution that yielded the carbinol base upon treatment with sodium hydroxide. Repeated recrystallization from benzene–heptane gave a brick-red solid melting at 130 °C, which reacted with 1 equiv of dilute aqueous perchloric acid to give a blue-green solution. Concentration of this solution and cooling gave golden needles of the perchlorate, which melted at 220 °C after four recrystallizations from water. Elemental analyses for C, H, N, and Cl were satisfactory. ^1H NMR in acetone-d_6 showed the aromatic protons at δ 6.45–7.35, the *N*-methyl protons at 3.38, and the *C*-methyl protons at 2.98 ppm, with relative peak areas of 4:2:1.

Equilibrium Measurements. Stock solutions of M^+ were prepared by dissolving about 0.01 g of the perchlorate in 10 mL of methanol and diluting to 250 mL with water, all under nitrogen. Enough potassium chloride to give an ionic strength of 0.5 plus 5 mL of stock solution of M^+ were diluted to 50 mL. The absorbance of 2.5 mL of this solution at 25 °C in a 1-cm quartz cuvette under nitrogen was determined at the 620-nm absorption maximum. Then various amounts of fresh sodium sulfite–bisulfite buffer solutions were added and the absorbance was measured again. Duplicate solutions were prepared outside the spectrophotometer and their pHs were measured using a Radiometer pH meter (PHM 26) and glass electrode. The sulfite solutions, which are very easily oxidized by air, were kept under nitrogen and their sulfite content was determined by iodimetric titration at the time of the spectral measurements.

Kinetic Measurements. In a typical run 2×10^{-5} M M^+ was placed in one syringe and a sodium sulfite–bisulfite buffer solution was placed in the other syringe of a Durrum-Gibson stopped flow spectrophotometer. Each solution contained enough potassium chloride to give an ionic strenght of 0.5 and each had been kept under nitrogen. Absorbance values (4000) obtained at intervals of 0.001 s were stored in a Nicolet digital oscilloscope, Model 1090. Every fortieth value was then transferred to the memory of an interfaced Hewlett-Packard calculator, Model 9830A. Of the resulting values, 25, spaced as evenly as possible in absorbance units between the maximum and minimum values, were then used in a least-squares determination of the first-order rate constant and initial and infinite absorbances. Other aspects of the experiment were similar to those used in the equilibrium measurements.

Registry No.—$(p\text{-Me}_2NC_6H_4)_2C^+C_6H_4Me\text{-}o$, 34074-05-0; SO_3^{2-}, 14265-45-3; *o*-methyl malachite green perchlorate, 63658-42-4; *o*-tolualdehyde, 529-20-4; *N*,*N*-dimethylaniline, 121-69-7.

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Mechanism of the Reaction of Diazomethane with Weak Acids[1a]

Maurice M. Kreevoy*[1b] and Stephen J. Thomas

Chemical Dynamics Laboratory, University of Minnesota, Minneapolis, Minnesota 55455

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In spite of the broad synthetic utility of the reaction of diazomethane with acids[2] and the intense interest in the mechanism of such reactions,[3-5] the parent compound, diazomethane, appears, up until now, to have had only little quantitative study.[6] The present paper describes the kinetics, products, and mechanism of acidolysis of diazomethane at high pH in phenol–phenate buffer solutions, in a solvent composed of 80% dimethyl sulfoxide (DMSO) and 20% water by weight.

Results

The acid-dissociation constant of phenol in 80% DMSO–20% water was determined from eight separate indicator measurements[8] of the H^+ concentration in solutions of known phenol:phenate ratios, using 2,4-dinitrodiphenylamine as the indicator. These give an average value of $4.3 \pm 0.6 \times 10^{-13}$ M for the acid-dissociation constant of phenol in this solvent. The cited uncertainty is the probable error of the mean. When diazomethane is added to phenol–phenate buffer solutions, containing ~0.1 M phenol and ~0.03 M phenate, the products produced are methanol (isolated as its 3,5-dinitrobenzoate) and anisole. The isolated yields were low, particularly in the case of the methanol derivative. This is thought to be related to the inherent difficulty of isolating small quantities of such materials from large volumes of solvent, rather than to the intrusion of other products. The percentage yields were also not accurately known because the amount of diazomethane added could only be approximated.

When the products are isolated from similar buffer solutions in which the H_2O was replaced with D_2O, all three hydrogens of the methyl group are replaced with deuterium, in both the methanol and the anisole. For comparison, diazomethane was also added to the same solvent mixture acidified with 0.1 M trifluoromethanesulfonic acid. In that case only methanol was produced, and, if the H_2O was replaced with D_2O, monodeuteriomethanol was obtained. These results are consistent with previous observations.[9]

The rate of consumption of diazomethane was measured spectrophotometrically in 27 different buffer solutions in the DMSO–water solvent at 25.0 °C. The initial diazomethane concentration was about 0.02 M in each case. The phenol concentrations ranged from 0.03 to 0.15 M; the phenate concentrations ranged from 0.02 to 0.10 M. The ionic strength was maintained at 0.2 M with tetraethylammonium perchlorate. After each measurement of rate was complete, the H^+ concentration was measured by the indicator method[8] and ranged from 1 to 3×10^{-12} M. In each case the consumption of diazomethane was accurately described by the rate law for exponential decay.[10] The pseudo-first-order rate constants k_1