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-Me$_2$NC$_6$H$_4$)$_2$C$^+$C$_6$H$_4$Me-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]

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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

**Table I. Rate Parameters for the Reaction of Phenol–
Phenate Buffers with Diazomethane in 80% DMSO–20%
H_2O**

Parameter	Value[a]
k_H	$4.4 \pm 0.5 \times 10^8$ M^{-1} s^{-1}
k_{HA}	$6.6 \pm 0.9 \times 10^{-3}$ M^{-1} s^{-1}
k_0	$1.5 \pm 1.1 \times 10^{-4}$ s^{-1}

[a] The uncertainties are the standard errors of the best
values.

were obtained graphically. These k_1 values, which cover a
range of a factor of 3, were fitted to eq 1.

$$k_1 = k_H(H^+) + k_{HA}(HA) + k_0 \qquad (1)$$

The HA in this case is phenol. The three paramenters k_1, k_{HA},
and k_0 were adjusted so as to minimize $\Sigma(k_1^{calcd} - k_1^{obsd})^2$,
using a digital computer.[11] The average discrepancy between
calculated and observed rate constants is 6.5%. The multiple
regression coefficient is 0.94. The addition of neither square
terms nor cross terms improved the fit given by eq 1. The
parameters and their uncertainties are given in Table I.

Both k_H and k_{HA} seem to be real, beyond reasonable
question. On the other hand, both the reality and the physical
meaning of k_0 are uncertain. We tried to measure k_1 in 0.1 M
KOH, in the same solvent, but could not, as the absorbance
did not decrease during the period over which k_1 was normally
measured (several hours). In a much longer period (several
days) qualitative changes in the spectrum of the solution were
noted, indicating reactions other than hydrolysis. Such re-
actions would be too slow to account for k_0 in any event. The
latter may represent the rate of loss of diazomethane by co-
distillation with the nitrogen which is being evolved from a
solution in which diazomethane is reacting with acid. In any
event, k_0 appears not to be a catalytic coefficient for the H_2O
portion of the solvent.

Discussion

The foregoing results are consistent with the mechanism
shown in Scheme I. In the buffered solutions OH$^-$, and
probably phenate as well, abstract protons from CH$_3$N$_2^+$ more
rapidly than they attack carbon, so CH$_3$N$_2^+$ is in equilibrium
with the starting materials and becomes completely deuter-
ated before being converted to products if the mobile protons
are deuterium. If proton transfer were rate determining, there
would be no obvious reason for the observation of fully deu-
terated products. The mechanism can be characterized as A2.
In the absence of strong bases, nucleophilic attack is, appar-
ently, faster than proton abstraction, so the protonation of
diazomethane is irreversible.[7] If the mobile protons are re-
placed with deuterons, the product is monodeuterated because
there is no reversion from CH$_3$N$_2^+$. The mechanism can be
characterized as A-S$_E$2. A similar mechanistic change has been
observed for the acid-catalyzed hydrolysis of diazoacetate
ion[12] although, in that case, the mechanism was A1 rather than
A2 in the more basic solutions.

The catalytic coefficients, k_H and k_{HA}, are $k_{H_2O}^N \cdot K_{CH_3N_2^+}$
and $K_{HA}k_A^{-N}/K_{CH_3N_2^+}$, respectively, where $k_{H_2O}^N$ and k_A^{-N}
are the rate constants for nucleophilic attack of water and A$^-$,
respectively, on CH$_3$N$_2^+$.[13] (The activity of water is incorpo-
rated in k_{H_2O}.) The ratio $k_A^{-N}/k_{H_2O}^N$ is only 34, which is
rather small considering the very substantial difference in
basicity but reasonable in view of the strongly spontaneous
nature of the reactions involved.[14] Similar results, that is, an
A-2 mechanism but low selectivity among nucleophiles, have
previously been obtained with ethyl diazoacetate,[15] dia-
zoacetone,[15] and two alkylsulfonyldiazomethane[16] reac-
tions.

Scheme I

$$CH_3N_2^+ \xrightleftharpoons{K_{CH_3N_2^+}} CH_2N_2 + H^+$$

$$\downarrow H_2O \text{ or } A^-$$

$$(CH_3OH \text{ or } CH_3A) + N_2$$
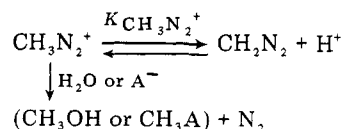
If eq 1 contained a term for H_2O acting as an acid, the rate
constant k_{H_2O} would be given by $k_{OH}^{-N}K_w/K_{CH_3N_2^+}$ where
k_{OH}^{-N} is the rate constant for OH$^-$ acting as a nucleophile and
K_w is the autoprotolysis constant of water in the present sol-
vent mixture (4×10^{-19}).[8] In view of the small difference be-
tween k_A^{-N} and $k_{H_2O}^N$ it is hardly likely that k_{OH}^{-N} would be
larger than k_A^{-N} by more than a factor of 10^2. The value of
k_{H_2O} would then be ~10^{-6} s^{-1}, which is unobservably small
in the present set of experiments and smaller than k_0 by a
factor of 10^2. This confirms our conclusion that k_0 cannot be
identified with k_{H_2O}.

Experimental Section

Gaseous diazomethane was prepared by dropping concentrated
aqueous potassium hydroxide onto either *N*-methyl-*N*-nitrosourea
or *N,N'*-dimethyl-*N,N'*-dinitrosoterephthalamide.[17] (The latter gave
more satisfactory results.) The product gases were swept through a
potassium hydroxide drying tube into a vessel containing 15 mL of
the DMSO–water solvent which was cooled with an ice–water bath
and stirred magnetically to facilitate transfer across the gas–liquid
interface. The yield of collected diazomethane was around 40%.
Portions of the resulting solution (1 mL) were added to 2 mL of buffer
in the same solvent to initiate a rate measurement. Analytical reagent
grade phenol was purchased from Mallinckrodt. 3,5-Dinitrobenzoyl
chloride was purchased from Eastman Kodak Co. and recrystallized
from petroleum ether. Yellowish needles were obtained with mp, on
various occasions, between 64 and 69 °C (lit.[18,19] 74 and 69–70 °C).
Methyl 3,5-dinitrobenzoate and its trideuterio analogue were pre-
pared in the usual way.[20] They had mp 107.5–108.0 and 108.0–108.5
°C, respectively (lit.[21,22] mp 108 °C). The tetradeuteriomethanol used
to make trideuteriomethyl 3,5-dinitrobenzoate was purchased from
Aldrich Chemical Co. and used without purification. The derivative
showed no band for methyl protons in its NMR spectrum. Bromo-
benzene was purchased from Eastman Kodak Co. and was used
without further purification. All other materials used have been
previously described.[8,23]

For a typical product isolation, 15 mL of diazomethane solution in
DMSO was prepared in the usual way. This solution also contained
enough tetraethylammonium perchlorate to bring the final solution
to an ionic strength of 0.2 M. This DMSO solution was allowed to
come to 25.0 °C in a thermostat and then 4 mL of aqueous phenol-
phenate buffer was rapidly added, with stirring, to bring the solution
back to 25 °C as quickly as possible. (There is some heat evolution
when water is mixed with DMSO, and 10–20% of the reaction inevi-
tably took place at temperatures several degrees above 25 °C.) The
reaction was allowed to proceed for 1 h (~ 6 half-lives) and then the
products were separated using countercurrent extraction between
cyclohexane and water. (The first two portions of water were made
basic with KOH.) The cyclohexane extracts were combined and dried
over magnesium sulfate, and the cyclohexane was distilled off. A little
carbon tetrachloride was added for ease of handling and IR and NMR
spectra were obtained. In the case of material produced from H_2O,
these were identical with spectra of genuine anisole. The aqueous
layers were combined (these also contained the DMSO) and 4 mL was
removed by distillation. This was mostly water but contained most
of the methanol that had been formed and a trace of DMSO. To the
aqueous distillate was added 8 mL of 3% 3,5-dinitrobenzoyl chloride
in bromobenzene, and methyl ester was prepared as in a Schotten–
Baumann reaction.[24] The bromobenzene was then removed under
vacuum, using a rotary evaporator, and the solid residue was thor-
oughly leached with aqueous, 2%, sodium carbonate. Finally, the
product was twice recrystallized from aqueous alcohol. The IR and
NMR spectra of material prepared in this way from H_2O were iden-
tical with the spectra of authentic methyl 3,5-dinitrobenzoate. Ma-
terial prepared from D_2O gave NMR and IR spectra very similar to
those obtained from authentic trideuteriomethyl 3,5-dinitrobenzoate.
In the NMR spectrum of anisole made from D_2O, the sharp singlet
at 3.72 ppm (from tetramethylsilane) was replaced by a broad, low
intensity peak. Six integrations of this peak and the aromatic peaks
(three times up field, three times down) gave an average ratio of 0.036

with an averge deviation from the mean of 0.003 and a probable error of 0.001. The sharp singlet at 4.07 ppm in the NMR spectrum of methyl 3,5-dinitrobenzoate prepared from D_2O undergoes a similar transformation, in this case giving 0.060 of the intensity of the aromatic peaks. For both products this leads to the conclusion that they are 94% deuterated in their methyl groups.

The deuterium content of the water was determined by following the procedure described above up to the countercurrent extraction. The reaction mixture was then acidified with a small volume of strong acid in D_2O. From this solution 2.5 mL of water was distilled, bp 102–110 °C, contaminated with a little DMSO. The deuterium content of this water was found to be 97%.[25] This is not thought to be significantly different from the 94% deuteration of the two products.

Diazomethane shows a very broad, low-intensity absorption in the visible and near-ultraviolet, with an ill-defined maximum, λ_{max}, somewhere between 350 and 400 nm and a maximum extinction coefficient of around 6. This is the band which is responsible for its yellow color. In determining rate constants it was necessary to monitor the diazomethane concentration at a wavelength somewhat above λ_{max}, in order to avoid interference from UV-absorbing substances which build up with time in these reaction mixtures; 410 nm was used.

Registry No.—Diazomethane, 334-88-3; phenol, 108-95-2.

References and Notes

(1) (a) This work was supported, in large part, and publication costs assisted by the National Science Foundation through Grants CHE76-01181 and GP-31360X to the University of Minnesota. (b) M. M. Kreevoy was a guest of the Physical Chemistry Laboratory, Oxford, while he was preparing this paper. He wishes to thank the members of that laboratory, particularly Dr. W. J. Albery, for their warm hospitality.
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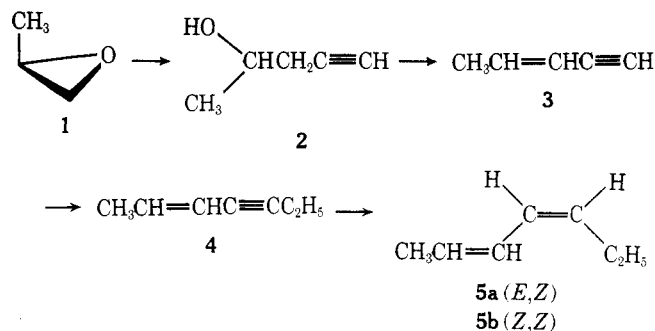## A Convenient Synthesis of (E,Z)- and (Z,Z)-6-Deuterio-2,4-heptadiene

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The successful elucidation of the mechanistic details of any reaction depends initially upon the reliability of available

Scheme I

synthetic procedures. This is especially obvious when the specific introduction of an isotopic label is desired.

For the detailed investigation of the rearrangement chemistry of 2,4-heptadiene, we required the 6-deuterio analogue (**10**). In this note we present the conceptually simple yet operationally challenging synthesis of this specifically labeled hydrocarbon.

Results and Discussion

Our approach to the synthesis of (E,Z)-6-deuterio-2,4-heptadiene (**10a**) involved the intermediate preparation of 6-deuterio-2-hepten-4-yne (**9**). Preliminary results (Scheme I) indicated this to be a rational approach: ethynylation of propylene oxide (**1**),[3] followed by tosylation of the resulting alcohol (**2**) and base-catalyzed elimination gave a 55:45 mixture of the known[4] (E)- and (Z)-3-penten-1-ynes (**3**); alkylation of **3** with ethyl bromide, followed by catalytic hydrogenation over freshly prepared Lindlar catalyst[5,6] or, alternatively, hydralumination[6,7] with diisobutylaluminum hydride in hexane and subsequent hydrolysis gave (E,Z)- and (Z,Z)-2,4-heptadiene (**5**) in 29% isolated yield based on 3-penten-1-yne (**3**), or 7.4% based on starting propylene oxide (**1**).

Careful gas chromatographic monitoring of the hydralumination reaction revealed a significant difference in the rates of reaction for the individual 2-hepten-4-yne diastereomers. The hydralumination of the E diastereomer of **4** is so much more rapid than the corresponding addition to the Z diastereomer that early hydrolysis of the reaction mixture constitutes a highly stereoselective synthesis of (E,Z)-2,4-heptadiene (**5a**). If the bulky diisobutylaluminum group adds preferentially to C-4 of **4**,[8] it should encounter less steric hindrance when adding to the E diastereomer; however, the exact regiochemistry of this addition has not yet been determined.[16]

In order to utilize this synthetic sequence for the preparation of **10**, the starting 6-deuterio-2-hepten-4-yne (**9**) was secured through the reaction of acetic anhydride with the Grignard reagent from 3-penten-1-yne (**3**),[9] diisobutylaluminum hydride reduction of the resulting 2-hepten-4-yn-6-one (**6**),[10] mesylation,[11] and lithium aluminum deuteride reduction[12] as depicted in Scheme II. Hydrogenation of the labeled enyne **9** over freshly prepared Lindlar catalyst[5] in scrupulously dried cyclohexane afforded the title compound (**10**) in 25% yield based on starting 3-penten-1-yne (**3**). The product was obtained as a mixture of E,Z and Z,Z diastereomers which could be separated by preparative gas chromatography. Mass spectrometric analysis revealed the product to be >98% d_1.

Experimental Section

^1H NMR spectra were obtained on a Varian T-60 instrument. Infrared spectra were recorded on a Beckman IR-20 spectrophotometer. Mass spectra were secured on a Finnigan 1015D quadrupole mass spectrometer with a variable leak inlet, an ion source temperature of 55 °C, an ionization potential of 70 eV, and, for chemical ionization spectra, a reagent gas pressure of 1.0 Torr. Analytical and preparative