Methylthio Group Migration in the Acid-Catalyzed Hydrolysis of S-Methyl Phenyldiazothioacetate. Kinetics and Mechanism of the Reaction

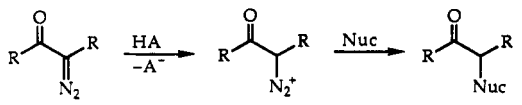
J. Jones, Jr.,† and A. J. Kresge*

Department of Chemistry, University of Toronto, Toronto, Ontario M5S 1A1, Canada

Received February 2, 1993

The acid-catalyzed hydrolysis of *S*-methyl phenyldiazothioacetate, $C_6H_5C(=N_2)COSCH_3$, in aqueous solution at 25 °C was found to occur with the hydronium ion isotope effect $k_{H^+}/k_{D^+} = 3.08$ and to give a Bronsted relation, based on carboxylic acid catalysts, whose exponent is $\alpha = 0.70$. This is taken to mean that the reaction occurs by rate-determining proton transfer to the diazo carbon atom. The principal product of the reaction, however, is α-(methylthio)-α-phenylacetic acid, $C_6H_5CH(SCH_3)CO_2H$, which must be formed by 1,2-shift of the methylthio group. An argument is presented which suggests that this shift is accompanied by a rate acceleration and that it consequently must take place in the rate-determining step of the reaction.

The acid-catalyzed decomposition of α-diazocarbonyl compounds is a much-studied reaction that generally occurs through protonation of the diazo carbon atom followed by nucleophilic substitution at this position, eq 1.[1] The nucleophile can be an external reagent or a



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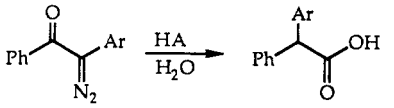
nucleophilic center present in the diazo compound, and the intramolecular cyclizations afforded by the latter variant provide an important route for the synthesis of four-membered and larger rings.[1b] Although 1,2-shifts do occur in the reactions of diazoalkanes without adjacent carbonyl groups, such rearrangements are rare in the case of α-diazocarbonyl compounds. A notable exception is the formation of some α-phenyl-α-*p*-tolylacetic acid in the acid-catalyzed hydrolysis of benzoyl-*p*-tolyldiazomethane, eq 2, Ar = *p*-$CH_3C_6H_4$.[2] This reaction, however, shows an



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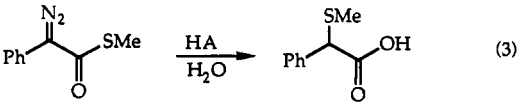
inverse hydronium-ion isotope effect, $k_{H^+}/k_{D^+} < 1$, and specific rather than general acid catalysis, and it was therefore assigned a mechanism in which proton transfer from the catalyst to the substrate occurs on carbonyl-oxygen rather than diazocarbon.

We have found that the predominant product formed in the acid-catalyzed hydrolysis of *S*-methyl phenyldiazothioacetate, **1**, is α-(methylthio)-α-phenylacetic acid, **2**, eq 3. 1,2-Migration of the methylthio group is thus the major reaction pathway in this case. This hydrolysis, however, gives a normal hydronium-ion isotope effect and shows general acid catalysis; this indicates that protonation of the substrate here occurs on carbon, but 1,2-migration nevertheless takes place. This is all the more remarkable



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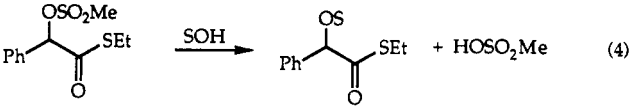
because, in the closely related solvolysis of the methanesulfonate ester of *S*-methyl thiomandelate, **3**, nucleophilic substitution by the solvent occurs without 1,2-migration of the ethylthio group, eq 4.[3]



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Experimental Section

Materials. *S*-Methyl phenyldiazothioacetate was prepared from *S*-methyl phenylthioacetate by diazo group transfer,[4] and α-(methylthio)-α-phenylacetic acid was obtained by treating [α-(methylthio)benzyl]lithium with carbon dioxide.[5] The methanesulfonate ester of *S*-ethyl thiomandelate was synthesized from *S*-ethyl thiomandelate, which in turn was made by treating the acetonide of mandelic acid with ethanethiolate.[3] Methyl phenyldiazoacetate was obtained by lead tetraacetate oxidation of the hydrazone of methyl phenylglyoxylate.[6] All other materials were best available commercial grades.

Kinetics. Rates of acid-catalyzed decomposition of methyl phenyldiazoacetate and *S*-methyl phenyldiazothioacetate were measured spectrophotometrically by monitoring the disappearance of the absorption bands of these compounds near λ = 300 nm. Measurements were made at substrate concentrations of ca. 10^{-4} M using a Cary Model 2200 spectrometer whose cell compartment was thermostated at 25.0 ± 0.02 °C. The rate data fit the first-order rate law well, and observed first-order rate constants were obtained by least-squares fitting to an exponential function.

Product Studies. Reaction products were determined by HPLC and GC–MS analysis of solutions that had been allowed to react for at least 10 half-lives; substrate concentrations were the same as in the kinetic runs. HPLC analysis was performed using a Varian Vista 5000 instrument interfaced with a Varian Polychrom 9060 diode array detector operating with a Waters

† Permanent address: Instituto de Química, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil.

(1) For recent reviews, see: (a) Regitz, M.; Maas, G. *Diazo Compounds, Properties and Synthesis*; Academic Press: New York, 1986; Chapter 3. (b) Smith, A. B., III; Dieter, R. K. *Tetrahedron* **1981**, *37*, 2407–2439.

(2) Jugelt, W.; Berseck, L. *Tetrahedron* **1970**, *26*, 5557–5579.

(3) Creary, X.; Geiger, C. C. *J. Am. Chem. Soc.* **1982**, *104*, 4151–4162.

(4) Jones, J., Jr.; Kresge, A. J. *J. Org. Chem.* **1992**, *57*, 6467–6469.

(5) Cabiddu, S.; Floris, C.; Melis, S.; Sotgiu, F. *Phosphorus Sulfur* **1984**, *19*, 61–64. Cabiddu, S.; Floris, C.; Melis, S.; Piras, P. P.; Sotgiu, F. *J. Organomet. Chem.* **1982**, *236*, 149–156.

(6) Ciganek, E. *J. Org. Chem.* **1970**, *35*, 862–864.

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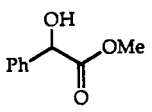
Novapack C18 column. GC–MS analysis was performed using an HP 5890 gas chromatograph linked to a VG 70–250S mass spectrometer.

Results

Product Studies. HPLC analysis of a solution in which *S*-methyl phenyldiazothioacetate had been allowed to react with 1.0 M aqueous $HClO_4$ showed one principal product plus a trace of another substance. The principal product was identified as α-(methylthio)-α-phenylacetic acid by spiking—adding an authentic sample to the solution being analyzed and observing an increase in signal intensity—and also by comparing its mass spectrum with that of an authentic sample.

The minor product was obtained in a larger relative amount by extracting another sample of spent reaction mixture with ether, removing most of the α-(methylthio)-α-phenylacetic acid by washing the ether extract with aqueous $NaHCO_3$ solution, evaporating off the ether, and subjecting the residue to HPLC and GC–MS analysis. The HPLC analysis showed two substances, one of which was again identified as residual α-(methylthio)-α-phenylacetic acid by spiking. The other substance had an HPLC retention time similar to that of methyl mandelate, **4**, as



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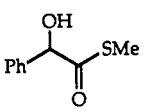

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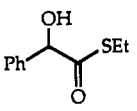

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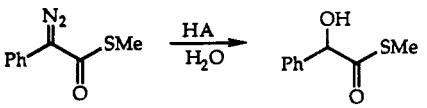
expected for *S*-methyl thiomandelate, **5**, which is the product that would be formed by normal acid-catalyzed hydrolysis of *S*-methyl phenyldiazothioacetate proceeding without 1,2-migration of the methylthio group, eq 5. This



(5)

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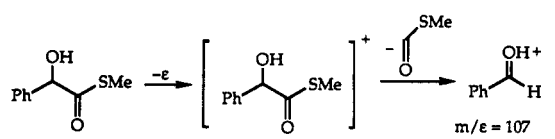
assignment of structure **5** to the minor product was confirmed by its mass spectrum whose principal peak occurred at $m/e = 107$; this mass fragment is characteristic of mandelic acid and its esters, which show little or no parent peaks in their mass spectra but rather break apart according to eq 6.[7]



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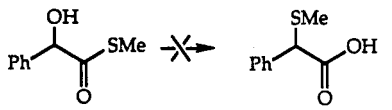
A control experiment was performed to determine whether *S*-methyl thiomandelate, **5**, could have been the principal product formed but had isomerized to the principal product found, α-(methylthio)-α-phenylacetic acid, eq 7, under the conditions of the diazo compound hydrolysis or the product analysis. Since *S*-methyl thiomandelate was not available at the time, this test was conducted using *S*-ethyl thiomandelate, **6**, which can be expected to behave in the same manner. This substance



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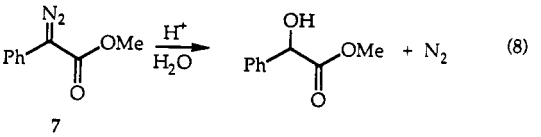
was allowed to remain dissolved in 0.1 M $HClO_4$ for 15 min, which corresponds to 20 diazo compound hydrolysis lifetimes; this solution was then extracted with ether and the extract was subjected to GC–MS analysis. The GC trace showed the presence of only one substance, whose mass spectrum was identical to that of an authentic sample of *S*-ethyl thiomandelate; the rearrangement of eq 7 thus did not occur, and α-(methylthio)-α-phenylacetic acid is indeed the principal reaction product.

In view of the fact that our work shows that hydrolysis of *S*-methyl phenyldiazothioacetate proceeds with rearrangement, eq 3, whereas solvolysis of the methanesulfonate ester of *S*-ethyl thiomandelate is reported to occur without rearrangement, eq 4, we also performed a product study of the methanesulfonate solvolysis reaction. A solution of the methanesulfonate (10^{-4} M) in THF/H_2O (1:1) containing 0.05 M $HClO_4$ was heated under reflux for 24 h and was then subjected to GC–MS analysis. Only one product could be detected, and its mass spectrum showed it to be *S*-ethyl thiomandelate. This corroborates the published report that solvolysis of this methanesulfonate occurs without rearrangement.

A product study was also performed for the acid-catalyzed hydrolysis of methyl phenyldiazoacetate, **7** the oxygen analog of *S*-methyl phenyldiazothioacetate. GC–MS analysis of a solution in which **7** had been allowed to react with 0.1 M aqueous perchloric acid showed only one product, whose mass spectrum was identical with that of an authentic sample of methyl mandelate. Hydrolysis of this diazo compound in our wholly aqueous solvent thus occurs without rearrangement, eq 8, just as reported for this substrate reacting in an aqueous dioxane medium.[8]



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Kinetics. Rates of hydrolysis of *S*-methyl phenyldiazothioacetate were determined in aqueous perchloric acid solution of H_2O and D_2O at constant ionic strength (0.10 M). Observed first-order rate constants, summarized in Table I, proved to be accurately proportional to acid concentration, and linear least-squares analysis gave the catalytic coefficients $k_{H^+} = (1.83 \pm 0.02) \times 10^{-1}\ M^{-1}\ s^{-1}$ and $k_{D^+} = (5.94 \pm 0.09) \times 10^{-2}\ M^{-1}\ s^{-1}$; these provide the isotope effect $k_{H^+}/k_{D^+} = 3.08 \pm 0.05$.

Rates of hydrolysis of *S*-methyl phenyldiazothioacetate were also determined in aqueous carboxylic acid buffer solutions; the data are summarized in Table II. Series of buffer solutions of constant buffer ratio and constant ionic strength (0.10 M) but varying buffer concentration were used. This served to hold hydronium ion concentrations constant along a series of buffer solutions when weaker acids were employed, but significant deviations from constancy occurred with the stronger acids. Buffer failure

(7) Anggard, E.; Sedvall, G. *Anal. Chem.* **1969**, *41*, 1250–1256. Sharp, T. R. *Org. Mass Spectrosc.* **1980**, *15*, 381–382.

(8) Bui-Nguyen, M.-H.; Dahn, H.; McGarrity, J. F. *Helv. Chim. Acta* **1980**, *63*, 63–75.

Table I. Rate Data for the Hydrolysis of *S*-Methyl Phenyldiazothioacetate in Aqueous Perchloric Acid Solutions at 25° C[a]

[acid]/10^{-2} M	$k_{obs}/10^{-2}$ s^{-1}
H_2O:	
10.0	1.78, 1.86, 1.77, 1.82, 1.84, 1.83
8.00	1.40, 1.45, 1.41, 1.52, 1.52, 1.48
5.00	0.854, 0.844, 0.845, 0.932, 0.927, 0.932
3.00	0.524, 0.517, 0.525, 0.527, 0.566, 0.578
1.00	0.191, 0.180, 0.187
$k_{obs}/s^{-1} = -(0.89 \pm 1.58) \times 10^{-4} + ((1.83 \pm 0.02) \times 10^{-1})[HClO_4]$	
D_2O:	
10.0	0.605, 0.601, 0.579
8.00	0.474, 0.481, 0.493
5.00	0.301, 0.300, 0.300
3.00	0.179, 0.181, 0.183
$k_{obs}/s^{-1} = (3.67 \pm 6.09) \times 10^{-5} + ((5.94 \pm 0.09) \times 10^{-2})[DClO_4]$	
$k_{H^+}/k_{D^+} = 3.08 \pm 0.05$	

[a] Ionic strength = 0.10 M ($NaClO_4$).

corrections[9] were therefore made in these cases by adjusting observed rate constants to the hydrogen ion concentration of the most concentrated buffer using the known hydronium-ion catalytic coefficient; hydronium ion concentrations needed for this purpose were obtained by calculation using literature values of thermodynamic acidity constants and activity coefficients recommended by Bates.[10]

Rate constants adjusted in this way, as well as observed rate constants in cases where adjustments were not made, increased with increasing buffer concentration, showing that the reaction is buffer catalyzed. Comparison of results obtained with the same buffer at different buffer ratios indicated this catalysis to be of the acid type; the rate law for a general-acid-catalyzed process, given in eq 9, was

$$k_{obs} \text{ (or } k_{adj}) = k_{H^+}[H^+] + k_{HA}[HA] \qquad (9)$$

therefore being obeyed. Least-squares fitting of the data to this expression then gave general acid catalytic coefficients, k_{HA}, for the various buffer acids as well as contributions to catalysis by the hydronium ion, $k_{H^+}[H^+]$, for each buffer series. The results are listed in Table II.

These general acid catalytic coefficients give a linear Bronsted plot, shown in Figure 1, whose slope is $\alpha = 0.70 \pm 0.03$. The hydronium ion catalytic coefficient determined in perchloric acid solutions falls below this plot by a considerable margin (30×), as is commonly the case for reactions involving proton transfer to carbon.[11]

The hydronium ion rate contributions obtained in the buffer solutions, $k^{H_3O^+}[H^+]$, decreased with decreasing hydronium ion concentrations of the solutions in which they were determined, as expected. Least-squares analysis of the relationship between these contributions and $[H^+]$ then gave $k_{H^+} = (2.13 \pm 0.11) \times 10^{-1}$ M^{-1} s^{-1}, which is consistent with the value measured directly in perchloric acid solutions, $k_{H^+} = (1.83 \pm 0.02) \times 10^{-1}$ M^{-1} s^{-1}. This analysis also revealed an "uncatalyzed" reaction as the zero $[H^+]$ intercept, whose rate constant is $k = (7.90 \pm 2.05) \times 10^{-5}$ s^{-1}. Such an "uncatalyzed" reaction of diazo compounds has been observed before,[12] but its mechanism

(9) Keeffe, J. R.; Kresge, A. J. In *Techniques of Chemistry, Vol. VI, Investigation of Rates and Mechanisms of Reactions*, 4th ed.; Bernasconi, C. F., Ed.; Wiley-Interscience: New York, 1986; Part I, Chapter XI.

(10) Bates, R. G. *Determination of pH. Theory and Practise*; Wiley-Interscience: New York, 1973; p 49.

(11) Kresge, A. J. *Chem. Soc. Rev.* **1973**, *2*, 475–503.

(12) (a) Engberts, J. B. F. N.; Bosch, N. F. Zwanenburg, B. *Rec. Trav. Chim.* **1966**, *85*, 1068–1071. (b) Engbersen, J. F. J.; Engberts, J. B. F. N. *Tetrahedron* **1974**, *30*, 1215–1218.

Table II. Rate Data for the Hydrolysis of *S*-Methyl Phenylthioacetate in Aqueous Carboxylic Acid Buffer Solutions at 25 °C[a]

[HA]/10^{-2} M	$k_{obs}/10^{-4}$ s^{-1}
HA = CH_2CNCO_2H; [HA]/[NaA] = 1.00; $[H^+] = 4.53 \times 10^{-3}$ M	
6.00	20.6, 21.1, 20.6
4.00	16.1, 16.1
2.00	12.9, 12.8, 12.8
1.00	9.12, 8.78
$k_{adj}/s^{-1} = (1.11 \pm 0.03) \times 10^{-3} + ((1.71 \pm 0.09) \times 10^{-2})$[HA]	
HA = CH_2ClCO_2H; [HA]/[NaA] = 0.98; $[H^+] = 1.93 \times 10^{-3}$ M	
5.88	12.4, 12.4, 12.7
3.96	9.59, 9.27
1.96	6.51, 6.51, 6.52
0.08	4.59, 4.40
$k_{adj}/s^{-1} = (4.14 \pm 0.11) \times 10^{-4} + ((1.46 \pm 0.03) \times 10^{-2})$ [HA]	
HA = CH_2ClCO_2H; [HA]/[NaA] = 1.46; $[H^+] = 2.92 \times 10^{-3}$ M	
14.6	25.1, 25.2, 25.8
11.7	20.6, 21.5, 20.2
8.76	17.3, 16.4, 16.4
5.84	13.6, 13.2, 12.8
2.92	9.43, 9.50
$k_{adj}/s^{-1} = (6.30 \pm 0.39) \times 10^{-4} + ((1.30 \pm 0.04) \times 10^{-2})$ [HA]	
HA = $CH_2OCH_3CO_2H$; [HA]/[NaA] = 3.95; $[H^+] = 1.62 \times 10^{-3}$ M	
39.5	17.1, 17.2
31.6	15.1, 15.2
23.7	12.1, 12.4
15.8	9.27, 9.31
7.90	6.52, 6.63
$k_{adj}/s^{-1} = (4.24 \pm 0.20) \times 10^{-4} + ((3.36 \pm 0.08) \times 10^{-3})$ [HA]	
HA = HCO_2H; [HA]/[NaA] = 0.93; $[H^+] = 2.59 \times 10^{-4}$ M	
6.50	3.47, 3.51, 3.54
4.70	3.07, 2.95, 3.07
2.79	2.44, 2.34, 2.48
0.93	1.90, 1.99, 1.90
$k_{adj}/s^{-1} = (1.67 \pm 0.04) \times 10^{-4} + ((2.84 \pm 0.08) \times 10^{-3})$ [HA]	
HA = HCO_2H; [HA]/[NaA] = 1.89; $[H^+] = 5.16 \times 10^{-4}$ M	
5.68	3.55, 3.59, 3.56
3.78	3.09, 3.05
1.89	2.49, 2.42, 2.54
0.95	2.16, 2.30
$k_{adj}/s^{-1} = (2.06 \pm 0.04) \times 10^{-4} + ((2.68 \pm 0.10) \times 10^{-3})$ [HA]	
HA = HCO_2H; [HA]/[NaA] = 2.78; $[H^+] = 7.41 \times 10^{-4}$ M	
5.60	3.86, 3.78, 3.88
3.60	3.29, 3.31
1.95	2.82, 2.83, 2.85
0.83	2.46, 2.46
$k_{adj}/s^{-1} = (2.50 \pm 0.02) \times 10^{-4} + ((2.41 \pm 0.06) \times 10^{-3})$ [HA]	
HA = HCO_2H; [HA]/[NaA] = 3.73; $[H^+] = 9.65 \times 10^{-4}$ M	
5.60	4.15, 4.18, 4.17
3.73	3.84, 3.72
1.87	3.09, 2.97, 3.14
0.93	2.76, 2.90
k_{adj}/s^{-1} $(2.98 \pm 0.08) \times 10^{-4} + ((2.18 \pm 0.18) \times 10^{-3})$ [HA]	
HA = CH_3CO_2H; [HA]/[NaA] = 0.500; $[H^+] = 1.36 \times 10^{-5}$ M	
4.86	1.10, 1.10
3.89	1.06, 1.07
2.92	1.00, 1.01
1.94	0.930, 0.938
0.97	0.917, 0.916
$k_{obs}/s^{-1} = (8.54 \pm 0.9) \times 10^{-5} + ((5.12 \pm 0.29) \times 10^{-4})$ [HA]	
HA = CH_3CO_2H; [HA]/[NaA] = 2.00; $[H^+] = 5.43 \times 10^{-5}$ M	
21.4	2.17, 2.16
17.1	1.86, 1.86
12.8	1.62, 1.62
8.56	1.38, 1.39
4.28	1.10, 1.14
$k_{obs}/s^{-1} = (8.62 \pm 0.15) \times 10^{-5} + ((5.99 \pm 0.11) \times 10^{-4})$ [HA]	

[a] Ionic strength = 0.10 M ($NaClO_4$).

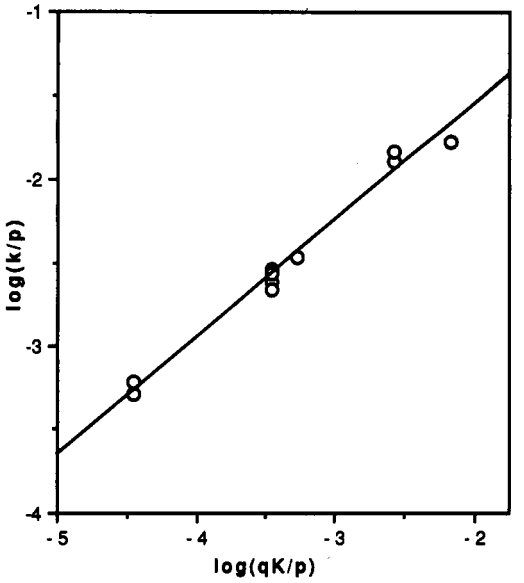


Figure 1. Bronsted plot for the hydrolysis of *S*-methyl phenyldiazothioacetate catalyzed by carboxylic acids in aqueous solution at 25 °C.

Table III. Rate Data for the Hydrolysis of Methyl Phenyldiazoacetate in Aqueous Perchloric Acid Solutions at 25° C[a]

[acid]/10^{-2} M	$k_{obs}/10^{-2}$ s^{-1}
H_2O:	
10.0	1.37, 1.35, 1.38, 1.44, 1.44, 1.43
8.00	1.09, 1.08, 1.10, 1.15, 1.12, 1.10
6.00	0.861, 0.812, 0.889
5.00	0.660, 0.650, 0.663
4.00	0.605, 0.574
3.00	0.386, 0.388
$k_{obs}/s^{-1} = -(2.18 \pm 2.30) \times 10^{-4} + ((1.42 \pm 0.03) \times 10^{-1})$ [$HClO_4$]	
D_2O:	
10.0	0.495, 0.495, 0.507, 0.529
8.00	0.399, 0.392, 0.420, 0.410
5.00	0.239
3.00	0.139, 0.139, 0.150
$k_{obs}/s^{-1} = -(1.50 \pm 0.94) \times 10^{-4} + ((5.23 \pm 0.12) \times 10^{-2})$[$DClO_4$]	
$k_{H^+}/k_{D^+} = 2.72 \pm 0.09$	

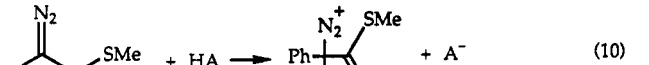
[a] Ionic strength = 0.10 M ($NaClO_4$).

is unknown. It cannot, at least in the present case, be due to proton transfer from a water molecule, for our Bronsted correlation predicts the rate constant $k = 8 \times 10^{-12}$ s^{-1} for such a process; this is many orders of magnitude less than the observed value.

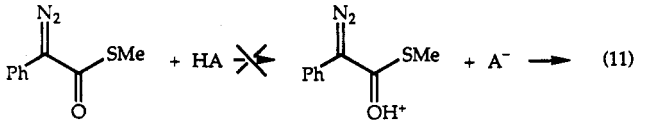
Rates of hydrolysis of the oxygen analog of *S*-methyl phenyldiazothioacetate, methyl phenyldiazoacetate, **7**, were also measured in aqueous perchloric acid solutions of H_2O and D_2O at constant ionic strength (0.10 M). The data are summarized in Table III. Observed first-order rate constants determined in both solvents proved to be accurately proportional to acid concentration, and linear least-squares analysis gave the catalytic coefficients $k_{H^+} = (1.42 \pm 0.03) \times 10^{-1}$ M^{-1} s^{-1} and $k_{D^+} = (5.23 \pm 0.12) \times 10^{-2}$ M^{-1} s^{-1}; these provide the isotope effect $k_{H^+}/k_{D^+} = 2.72 \pm 0.09$. The presently determined value of k_{H^+} is greater, by a factor of 17, than the hydronium ion catalytic coefficient determined for the same substance in a 60:40 dioxane/H_2O solvent;[8] this difference is consistent with decreases in reaction rate that have been observed before for acid-catalyzed hydrolysis of diazo compounds when the solvent is changed from a wholly aqueous medium to water–organic solvent mixtures.[1a,12b]

Discussion

The present work shows that the hydrolysis of *S*-methyl phenyldiazothioacetate is a general-acid-catalyzed reaction with a substantial, near-maximum,[13] hydronium ion isotope effect. This is classic evidence for rate-determining proton transfer to carbon,[9] and it implies that the site of protonation by the acid catalyst in this reaction is diazo carbon, eq 10, rather than carbonyl oxygen, eq 11.



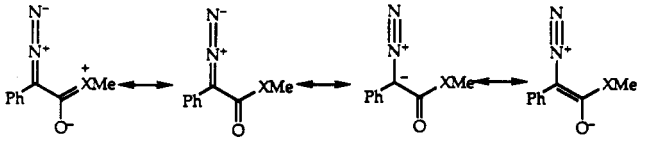
(10)



(11)

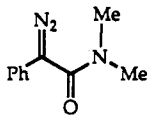
The major substance formed in this process is the rearranged product, α-(methylthio)-α-phenylacetic acid, **2**, eq 3, accompanied by only a trace of the normal, unrearranged product, *S*-methyl thiomandelate, **5**, eq 5. The 1,2-migration of the methylthio group needed to account for this product composition could occur either during or after the rate-determining proton transfer step. Migration during the rate-determining step should result in a rate acceleration, and the fact that the rate of reaction of the *S*-methyl thiol ester is quite similar to that of its oxygen analog, methyl phenyldiazoacetate, where rearrangement does not take place (k_{H^+}/M^{-1} $s^{-1} = 0.18$ and 0.14, respectively), suggests that acceleration by neighboring-group participation does not occur.

It can be argued, however, that the rate of reaction of the oxygen analog should be faster than that of the thiol ester, in the absence of participation, and that the observed similarity of rates really represents acceleration by neighboring group participation. This follows from a consideration of the principal resonance forms of the diazo compound substrates **8**–**11**. The rate of reaction of these



substances can be expected to increase with increasing electron density at the position of proton attack, the diazo carbon atom, which will be controlled by the relative importance of resonance form **10**. The importance of this form will in turn be determined in part by form **11**, which takes electron density away from the diazo carbon and puts it on the carbonyl oxygen atom; thus, the less important is form **11**, the greater is the electron density on the diazo carbon, and the faster will be the rate of reaction. Form **11** is opposed by form **8**, which also puts electron density on carbonyl oxygen; the greater the contribution of form **8**, therefore, the smaller the contribution of form **11** and the faster the reaction. This argument is supported by the fact that *N,N*-dimethylphenyldiazoacetamide, **12**, is considerably more reactive

(13) Kresge, A. J.; Sagatys, D. S.; Chen, H. L. *J. Am. Chem. Soc.* **1977**, *99*, 7228–7233.



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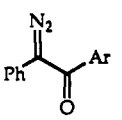

13

toward acid-catalyzed hydrolysis (310 times) than the oxygen ester, methyl phenyldiazoacetate,[8] in keeping with the greater conjugative electron-donating ability of nitrogen over oxygen; it also receives support from the fact that electron-donating substituents in the Ar group of aroylphenyldiazomethanes, 13, accelerate hydrolysis of these substrates.[2]

Resonance form 8 can be expected to be more important in the case of oxygen esters than in the case of thiol esters because mismatch of orbital size makes sulfur a less effective conjugative electron donor. Methyl phenyldiazoacetate should consequently be more reactive than *S*-methyl phenyldiazothioacetate in the absence of neighboring-group participation, and the close similarity of the two reaction rates may therefore be taken as evidence of rate acceleration and therefore rate-determining participation in the case of the thiol ester.

Neighboring-group participation during the rate-determining step also serves to rationalize the difference between the present reaction and solvolysis of the methanesulfonate ester of *S*-ethyl thiomandelate, eq 4, where rearrangement does not take place.[3] This solvolysis reaction is believed to occur through formation of an α-keto cation, aided by the good nucleofugicity of the methanesulfonate leaving group. The $-N_2^+$ group formed by carbon protonation of a diazo compound will be a still better leaving group,[14] and generation of such a group in the case of *S*-methyl phenyldiazothioacetate by rate-determining protonation without participation should lead to rapid formation of an α-keto cation similar to that formed by solvolysis of the methanesulfonate, which, as in the solvolysis, would not undergo 1,2-migration. An only partly charged $-N_2^{\delta+}$ group formed by partial proton transfer in the proton transfer transition state, however, will be a poorer leaving group, and assistance of its departure by neighboring sulfur would lead to rearranged product.

A mechanism involving neighboring-group participation during the rate-determining step, however, requires a rather contorted transition state in which proton transfer to carbon, migration, and leaving-group departure all occur at the same time. Such a process is likely to be difficult, and despite the arguments made above, a stepwise mechanism in which migration occurs after rate-determining proton transfer might be favored. The timing of events that must take place in this reaction would therefore seem to be still an open question.

Acknowledgment. We are grateful to Conselho Nacional de Desenvolvimento Cientifico e Technológico for a fellowship to J.J. and to the Natural Sciences and Engineering Research Council of Canada and the United States National Institutes of Health for additional financial support of this work.

(14) March, J. *Advanced Organic Chemistry*; Wiley-Interscience: New York, 1992; pp 352–357.