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Flash Photolytic Generation and Reactivity of Phenyl(methylthio)ketene in Aqueous Solution

J. Jones, Jr.,† and A. J. Kresge*

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

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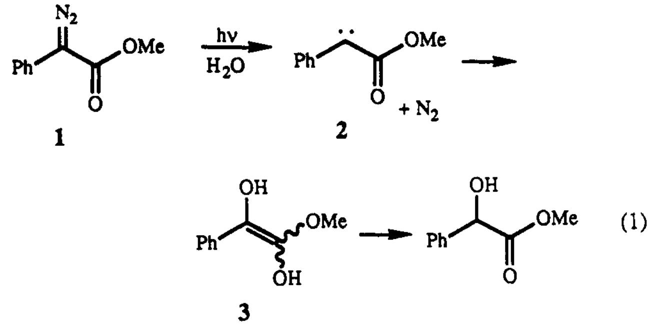
Methyl phenyldiazothioacetate is found to undergo Wolff rearrangement to phenyl(methylthio)ketene upon flash photolysis in aqueous solution and not to add water forming an ester enol as is the case with its oxygen analog, methyl phenyldiazoacetate. Hydration of phenyl(methylthio)ketene to α-(methylthio)phenylacetic acid occurs by both uncatalyzed and hydroxide ion catalyzed processes, whose rate constants, when compared to those for phenylketene, show the methylthio group to be rate-retarding. This is different from the effect of a hydroxyl group in the same position, which previous work had shown to be rate accelerating; possible reasons for this difference are advanced.

It was recently reported[1] that the acylcarbene, 2, generated by flash photolysis of methyl phenyldiazoacetate, 1, in aqueous solution, undergoes conjugate addition of water to give the enol of methyl mandelate, 3, eq 1, whose chemistry can then be studied in this medium. In an attempt to extend this work to enols of thiol esters, we have subjected methyl phenyldiazothioacetate, 4, to flash photolytic investigation. We found, however, that the acylcarbene formed in this case, 5, does not add water but rather undergoes Wolff rearrangement to phenyl(methylthio)ketene 6, eq 2. The evidence upon which this conclusion is based is presented here, together with some information on the chemistry of this ketene.



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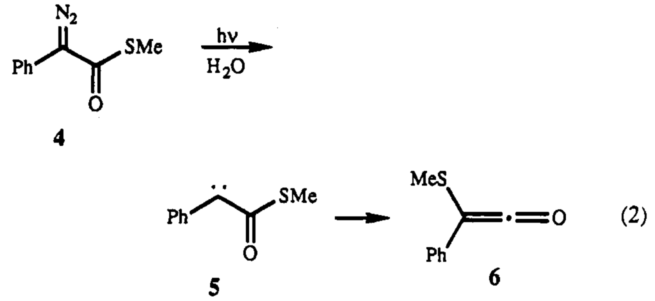

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Experimental Section

Materials. Methyl phenyldiazothioacetate, 4, was prepared by diazo group transfer from *p*-toluenesulfonyl azide to methyl phenylthioacetate, itself obtained by treating phenylacetyl chloride with methanethiol. A solution of 1.0 g of methyl phenylthioacetate and 2.4 g of *p*-toluenesulfonyl azide in 20 mL of dry diethyl ether was added to a solution of 1.8 g of 1,8-diazobicyclo[5.4.0]undec-7-ene (DBU) and 0.74 g of 4-(*N*,*N*-dimethylamino)pyridine in 70 mL of dry ether at 0 °C. When the addition was complete, the reaction mixture was shaken at room temperature for 12 h; an additional 0.89 g of DBU was then added, and shaking was continued for 2 days more. The brown solid which had formed was then separated by filtration and washed with another portion of diethyl ether. The combined ether solutions were washed with dilute aqueous HCl and with brine and were dried over anhydrous $MgSO_4$, and the ether was removed by evaporation to leave a red oil. This oil was subjected to flash chromatography using ethyl acetate–hexane (1:7) and the solvent. The product was collected as a yellow-colored fraction, and evaporation of the solvent gave a yellow oil with the following spectral properties: ^{1}H NMR ($CDCl_3$) δ/ppm = 2.43 (3 H, s), 7.2–7.5 (5 H, m); IR ω/cm^{-1} = 3057, 2931, 2362, 2074, 1661, 1651, 1321, 1222, 1089, 1053, 906, 814, 751; MS m/e = 192 (1), 164 (28), 136 (13), 121 (100), 105 (10), 91 (11), 77 (24); HRMS m/e = 192.036270 (found), 192.035734 (calcd).

α-(Methylthio)-α-phenylacetic acid was prepared by treating α-(methylthio)benzyllithium with carbon dioxide.[2]

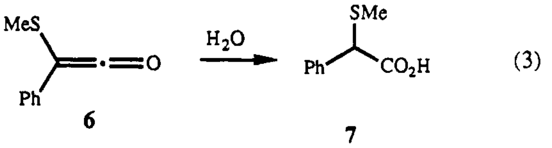
All other materials were best available commercial grades.

Flash Photolysis. Flash photolysis was performed using a conventional flash-lamp system that has already been described.[3] Irradiation of aqueous solutions of methyl phenyldiazothioacetate in this apparatus produced a transient species with λ_{max} = 260 nm; this transient was formed within the duration of the flash (50 μs) and decayed with a lifetime of ca. 10 ms. The decay followed the first-order rate law well, and observed first-order rate constants were obtained by least-squares fitting to an exponential function. Substrate concentrations were ca. 10^{-4} M, and the temperature of the reacting solutions was maintained at 25.0 ± 0.05 °C.

Results and Discussion

Reaction Pathway. The composition of spent reaction mixtures obtained after flash photolysis of methyl phenyldiazothioacetate, 4, in dilute aqueous solution (10^{-3} M) was examined by HPLC analysis. Determinations were made under three conditions of acidity and basicity: in 1×10^{-4} M $HClO_4$, in 2×10^{-3} M NaOH, and in water with nothing else added. In all three cases, only one product was found, and spiking with an authentic sample showed this to be α-(methylthio)phenylacetic acid, 7.

This is the product expected from hydration of phenyl(methylthio)ketene, 6, eq 3, formed by Wolff rear-



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

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Table I. Rate Data for the Hydration of Phenyl(methylthio)ketene in Aqueous Perchloric Acid Solutions at 25 °C[a]

$[\mathrm{HClO_4}]/10^{-2}$ M	$k_{\mathrm{obs}}/10^2\ \mathrm{s}^{-1}$
1.00	1.34, 1.40, 1.30, 1.23, 1.33
0.800	1.27, 1.31, 1.38, 1.31
0.600	1.32, 1.40, 1.49
0.400	1.27, 1.39, 1.34, 1.25
0.200	1.41, 1.36, 1.26, 1.30, 1.31
0.100	1.26, 1.36, 1.29

$k_{\mathrm{obs}}/\mathrm{s}^{-1} = (1.32 \pm 0.02) \times 10^2 + (0.99 \pm 3.93)[\mathrm{HClO_4}]$
$k = (1.33 \pm 0.01) \times 10^2\ \mathrm{s}^{-1}$ (simple average of k_{obs} values)

[a] Ionic strength = 0.10 M ($\mathrm{NaClO_4}$).

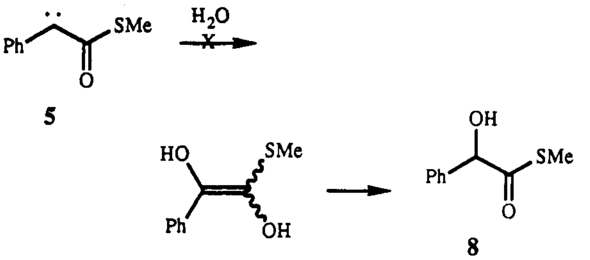
Table II. Rate Data for the Hydration of Phenyl(methylthio)ketene in Aqueous Sodium Hydroxide Solutions at 25 °C[a]

[NaOH]/10^{-2} M	$k_{\mathrm{obs}}/10^2\ \mathrm{s}^{-1}$
1.00	3.90, 4.25, 4.50
0.600	3.70, 3.28, 3.10
0.200	1.87, 1.87, 1.94, 2.00
0.100	1.45, 1.49, 1.37
0.0600	1.48, 1.43, 1.43

$k_{\mathrm{obs}}/\mathrm{s}^{-1} = (1.27 \pm 0.08) \times 10^2 + (3.09 \pm 0.16) \times 10^4[\mathrm{NaOH}]$

[a] Ionic strength = 0.10 M ($\mathrm{NaClO_4}$).

rangement of the carbene, 5, generated by photolysis of methyl phenyldiazothioacetate according to eq 2. A different product would have been formed if this carbene had added water to give an enol, as illustrated in eq 4, for



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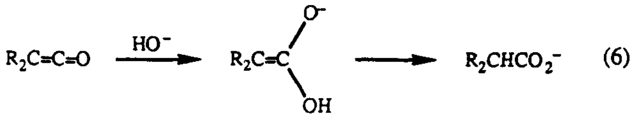
(4)

subsequent ketonization of that enol would have produced methyl thiomandelate, 8.[4] This product study demonstrates, therefore, that Wolff rearrangement and not acylcarbene hydration occurred during flash photolysis of methyl phenyldiazothioacetate and that the sulfur-substituted carbene, 5, reacts in a manner different from its oxygen analog, 2. This propensity of an S–Me group to migrate under conditions where an O–Me group does not is consistent with the greater migratory aptitude of sulfur over oxygen noted in photochemical Wolff rearrangements before.[6]

Ketene Chemistry. Rates of decay of the ketene transient formed by flash photolysis of methylphenyldiazothioacetate were measured in dilute perchloric acid and sodium hydroxide solutions. The data, summarized in Tables I and II, show that the hydration of this ketene is not catalyzed by the hydronium ion but is catalyzed by hydroxide ion. This behavior is typical of phenyl-substituted ketenes such as the present one. Acid catalysis of ketenes is in general quite weak,[7] and the presence of a phenyl substituent, as is the case here, suppresses that catalysis to the point where it often cannot be observed.[7a,8] Hydroxide-ion catalysis of ketene hydration, on the other hand, is generally quite prominent[7b,8] and is accelerated rather than retarded by phenyl substituents.[7b,8] This difference is a consequence of the fact that the two kinds of catalysis occur by different reaction mechanisms. Acid catalysis takes place by rate-determining protonation of the ketene carbon–carbon double bond, followed by rapid hydration of the acyl cation thus formed, eq 5; phenyl

$$\mathrm{R_2C{=}C{=}O} \xrightarrow[\mathrm{rd}]{\mathrm{HA,\ -A^-}} \mathrm{R_2CH\overset{+}{C}{=}O} \xrightarrow[\mathrm{fast}]{\mathrm{H_2O,\ -H^+}} \mathrm{R_2CHCO_2H} \tag{5}$$

groups stabilize the initial-state double bond, lowering the free energy of this state and retarding the reaction rate.[7a] Hydroxide-ion catalysis, on the other hand, occurs through rate-determining nucleophilic attack of this ion on the carbon atom of the ketene carbonyl group, followed by ketonization of the enolate ion thus formed, eq 6. Phe-

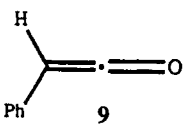


$$\mathrm{R_2C{=}C{=}O} \xrightarrow{\mathrm{HO^-}} \mathrm{R_2C{=}C(O^-)(OH)} \longrightarrow \mathrm{R_2CHCO_2^-} \tag{6}$$

nyl-group stabilization of the carbon–carbon double bond persists in this rate-determining step, and rate-retardation therefore does not take place. But the phenyl group also stabilizes the negative charge being generated on the substrate as the enolate ion is formed in this step, and that provides an additional lowering of the free energy of the transition state which accelerates the reaction.[7b,8,9]

The rates of decay of phenyl(methylthio)ketene measured here in sodium hydroxide solutions (Table II) show a linear dependence upon base concentration, and least-squares analysis gives the hydroxide-ion catalytic coefficient $k_{\mathrm{HO^-}} = (3.09 \pm 0.16) \times 10^4\ \mathrm{M^{-1}\ s^{-1}}$ plus an "uncatalyzed" intercept $k_o = (1.27 \pm 0.08) \times 10^2\ \mathrm{s}^{-1}$. The latter agrees well with the average value of the uncatalyzed rate constants measured in perchloric acid solution, $k_o = (1.33 \pm 0.01) \times 10^2\ \mathrm{s}^{-1}$, and the weighted average of these two results gives $k_o = (1.33 \pm 0.01) \times 10^2\ \mathrm{s}^{-1}$ as the best value of the rate constant for the uncatalyzed hydration of the present ketene.

Comparison of these rate constants with those for the hydration of phenylketene,[8] 9, shows that the methylthio



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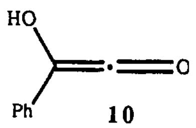

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group in phenyl(methylthio)ketene, 6, slows the reaction, in the case of the hydroxide-ion catalyzed process, by a factor of 39 and in the case of the uncatalyzed process, by a factor of 36. The close quantitative correspondence of the phenyl group substituent effect in these two cases implies that the two reactions are occurring by the same mechanism, and since the hydroxide ion operates by nucleophilic attack on carbonyl carbon, the uncatalyzed reaction must involve nucleophilic attack as well, this time

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(4) Methyl thiomandelate, obtained by thermal acid-catalyzed hydrolysis of methyl phenyldiazothioacetate, has an HPLC retention time distinctly different from that of α-(methylthio)phenylacetic acid.[5]

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by a water molecule. This is significant, inasmuch as the uncatalyzed reaction could, at least in principle, have been a process in which water acts as a proton donor (cf. eq 5) and not as a nucleophile.

It is interesting that, whereas the methylthio group in the present system slows ketene hydration, the hydroxyl group in the analogous phenylhydroxyketene, **10**, accelerates it—by a factor of 140 in the case of the uncatalyzed reaction, the only process for which a rate constant for **10** is available.[10] It can be argued that this acceleration is the expected result, for the electron-withdrawing inductive effect of oxygen should stabilize the negative charge of the enolate ion being formed by nucleophilic attack of water on the ketene. It may seem strange, therefore, that a methylthio group is rate-retarding, for the electronic effect of sulfur should be similar to that of oxygen, at least in direction if not in magnitude. Recent calculations of the effects of substituents on ketene stability, however, show the hydroxyl group to be appreciably destabilizing but the thiol group to be slightly stabilizing;[11] this difference leads to a differential initial state effect that makes the oxygen-substituted ketene the more reactive. It is known, also, that steric effects in the transition state play an important role in ketene reactions and the larger size of the methylthio group would be expected to have an adverse effect on reactivity.

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Laser Flash Photolysis Studies on 4-Oxocyclohexa-2,5-dienylidenes[1]

B. R. Arnold and J. C. Scaiano*,[2]

Steacie Institute for Molecular Sciences, National Research Council of Canada, Ottawa, Ontario, Canada K1A 0R6

G. F. Bucher and W. W. Sander*

Institut für Organische Chemie der Technischen Universität, Braunschweig, Federal Republic of Germany

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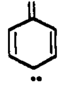
Reactions of 4-oxocyclohexa-2,5-dienylidene (**1**) and two derivatives have been investigated using laser flash photolysis techniques. Photolysis of 4-diazocyclohexa-2,5-dien-1-one (**4**) in 1,1,2-trichlorotrifluoroethane allows the indirect detection of the corresponding carbene **1**. This carbene reacts with triplet oxygen at close to the diffusion-controlled rate, forming the carbonyl *O*-oxide (λ_{max} = 470 nm). Reaction of triplet **1** with moderate concentrations of cyclohexane leads to formation of phenoxyl radical (λ_{max} = 395 nm). At high concentrations or in neat cyclohexane the predominant path appears to be carbene insertion into the C–H bond. Other reactions examined include O–H insertion in methanol and the indirect formation of ylides from acetone, acetonitrile, and pyridine. The reactivity pattern that emerges indicates that carbene **1** and its derivatives, **2** and **3**, have triplet ground states and that the singlet–triplet energy gap is moderately large. Ylide formation is only observed when the reactants are present in low concentrations and involve a two-step reaction from the triplet carbene; no ylides are observed in neat acetone or acetonitrile suggesting that for the singlet carbene insertion into C–H bonds is favored over direct ylide formation.

Introduction

Quinone diazides are among the most stable diazo compounds known. Their remarkable stability is due to the fact that they may be partially described as internal diazonium phenoxides, thus lowering their energy by resonance. This raises the question whether the carbenes formed by photolysis of quinone diazides display unexpected stability as well. To date, anthronylidene has been the only carbene derived from a 1,4-quinone diazide that has been studied by means of laser flash photolysis,[3] although the solution chemistry of several derivatives of 4-oxocyclohexadienylidene has been fairly well developed.[4] We undertook a study of the solution chemistry of the 4-oxocyclohexa-2,5-dienylidene (**1**), 3,5-dimethyl-4-oxocyclohexa-2,5-dienylidene (**2**), and 3-methyl-4-oxobenzocyclohexadienylidene (**3**) in order to establish how **1** and its derivatives would fit into the pattern of carbene reactivity.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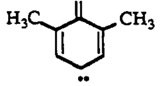

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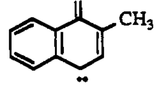

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Carbene **1** and its derivatives have been studied in solution by product studies. In most cases **1** adds to olefins

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(1) Issued as NRCC-33323.

(2) Present address: Department of Chemistry, University of Ottawa, Ottawa, Canada K1N 6N5.

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