

Δ^3 -1,3,4-Oxadiazolines: Photochemical Precursors to Diazoalkanes and *sec*-Alkanediazonium Ions in Acidic Solution¹

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Received July 24, 1996

Diazoalkanes and their conjugate acids, diazonium ions, are important reactive intermediates which have been implicated in the carcinogenicity and mutagenicity of *N*-alkyl-*N*-nitroso compounds.² Alkanediazoates have been studied extensively and have been shown to decompose via diazonium ion intermediates.³ Nitrous acid deaminations of aliphatic amines are known to involve the same diazonium ion intermediates.^{4,5} It has been postulated that *N*-alkyl-*N*-nitroso compounds may, under certain conditions, lead to the formation of diazoalkanes in biological systems,^{2,6} and their studies serve as models from which inferences about the biological implications have been made. Despite the considerable interest surrounding these reactive intermediates, there is little quantitative information on their reactivities. The only known bimolecular rate constant for protonation of an unstabilized diazoalkane by acidic species, such as hydronium ions, is that for protonation of diazomethane by hydronium ion at 25 °C, estimated as $k_{\text{H}^+} \approx 4 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$.⁷ The laser flash photolysis (LFP, 308 nm, with either UV or IR detection of transients) of alkoxy substituted Δ^3 -1,3,4-oxadiazoline precursors (**1**) has allowed us to determine rate constants for protonation of diazoalkanes in both aqueous and nonaqueous solutions.

The mechanism for the photochemical decomposition of alkoxy substituted Δ^3 -1,3,4-oxadiazolines **1** involves initial α -scission of the excited state to form biradicals, **2**, which subsequently undergo efficient β -scission selectively, to give primarily diazoalkanes, **3**, and an ester or carbonate (if $\text{R}^1 = \text{alkoxy}$).^{8,9}

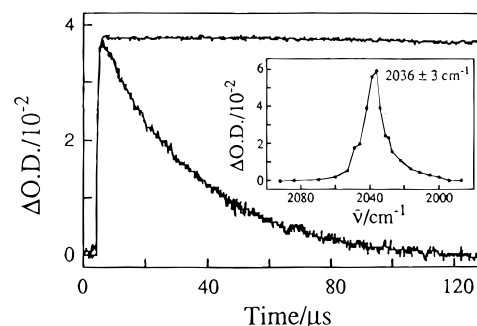
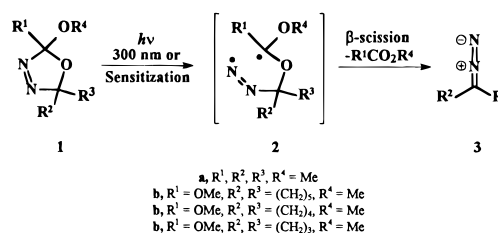


Figure 1. Time-resolved IR absorption traces and spectrum (inset) observed following 308-nm laser flash photolysis of **1a** in acetonitrile and in acetonitrile containing 3.0 mM TFA. Decay of absorption of **3a** monitored at 2037 cm^{-1} .



The formation of the two products upon 308 nm LFP of **1a** in acetonitrile at 25 °C, is readily confirmed with use of time-resolved infrared (TRIR) detection.¹⁰ Absorptions assigned to the diazo band of 2-diazopropane, centered at $2036 \pm 3 \text{ cm}^{-1}$, and to the carbonyl band of methyl acetate, centered at 1744 cm^{-1} (not shown), were formed instantaneously (within the response time of the instrument) from **1a**, Figure 1. Both absorptions were persistent under the experimental conditions. Under identical conditions, 308 nm LFP (UV–vis detection) of **1a** resulted in an instantaneous bleaching of its absorption at 322 nm and was accompanied by the instantaneous appearance of a strong persistent band, centered at 250 nm, assigned to **3a**.¹¹ Both the UV and the IR absorptions assigned to **3a** decayed with first-order kinetics ($\tau = 30 \mu\text{s}$) when trifluoroacetic acid (TFA, 3.0 mM) was present (Figure 1).

Rate constants for protonation of **3a** by carboxylic acids with $\text{p}K_{\text{A}}$'s ranging from 10 to 23 in acetonitrile,¹² at 25 °C, $\mu = 0 \text{ M}$, are listed in Table 1. They were obtained as the slopes of linear plots of observed rate constants (determined from LFP TRIR measurements) *vs* acid concentration.¹⁴ The linear least-squares analysis of $\log k_{\text{HA}}$ *vs* $\log K_{\text{A}}$ of the acids (data adjusted for statistics) by the Brønsted procedure gave $\alpha \approx 0.25$.¹⁵

The reaction between **3a** and hydronium ion was also studied by monitoring decay of the UV absorption of **3a** in aqueous perchloric acid solutions at 25 °C, $\mu = 1.0 \text{ M}$ (NaClO_4), and the rate constants found were $k_{\text{H}^+} = (2.46 \pm 0.07) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ in H_2O and $k_{\text{D}^+} = (1.32 \pm 0.04) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ in D_2O

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(12) The $\text{p}K_{\text{A}}$ values of the various acids in acetonitrile were obtained from *The IUPAC Chemical Data Series* No. 35, **1990**, compiled by K. Iztusu.

(13) Based on the proclivity of N_2 loss from *sec*-alkanediazonium ions⁵ we assume that the protonation reaction is irreversible in all cases ($k_{\text{obs}} = k_1[\text{HA}]$).

(14) Kinetic measurements were made by LFP largely for convenience. The long lifetime of diazopropane and the magnitude of the rate constants for its protonation should allow for these measurements to be made with conventional spectroscopic techniques.

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Table 1. Observed Proton Transfer Rate Constants (k_{HA}) for the Reaction of **3a** with Carboxylic Acids in Acetonitrile at 25 °C^a

acid	pK _A	k_{HA} , M ⁻¹ ·s ⁻¹
trichloroacetic	10.57	8.2×10^6
trifluoroacetic	12.65	6.8×10^6 (TRIR) 6.9×10^6 (UV)
dichloroacetic	13.20	2.8×10^6
oxalic	14.50	2.9×10^6
malonic	15.3	4.3×10^5
2,3-dibromopropionic	17.1	6.7×10^5
cyanoacetic	18.04	5.1×10^5
acetic	22.30	8.5×10^3 ^b

^a Measured by TRIR at 2037 cm⁻¹. ^b From quadratic fit of k_{obs} vs [acid].

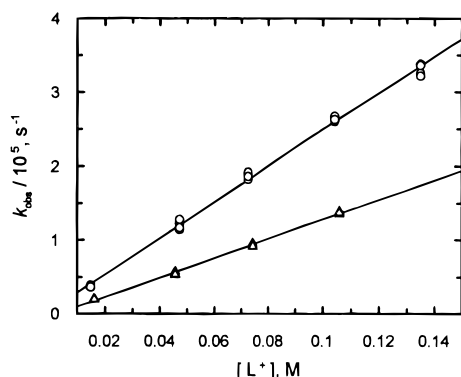


Figure 2. Plots of the change in k_{obs} for the decay of **3a**, as a function of H⁺ concentration (O), and as a function of D⁺ concentration (Δ), in aqueous perchloric acid solutions, at 25 °C, ionic strength 1.0 M (NaClO₄).

(Figure 2). The primary kinetic isotope effect for the reaction of hydronium ion with **3a** is $k_{\text{H}}/k_{\text{D}} = 1.86$. A Brønsted correlation for the protonation of **3a** with carboxylic acids in aqueous solutions showed a slope (~ 0.22) similar to that found in acetonitrile solutions.

Rate constants for protonation of diazocyclohexane (**3b**), diazocyclopentane (**3c**), and diazocyclobutane (**3d**) by TFA in acetonitrile at 25 °C were determined from the decays of their UV absorptions upon 308 nm LFP of **1b–d** in acetonitrile. The linear plots of k_{obsd} vs [HA] gave bimolecular rate constants (k_{HA}) equal to $(9.17 \pm 0.12) \times 10^6$, $(1.19 \pm 0.03) \times 10^7$, and $(4.28 \pm 0.10) \times 10^7$ M⁻¹ s⁻¹ for the reaction of TFA with **3b–d**, respectively.

It is unlikely that the magnitudes of rate constants of proton transfer are governed by diazonium ion stabilities, given that the observed Brønsted coefficient is consistent with an early, reactant-like, transition state.¹⁸ It also seems that torsional effects are not dominant since larger eclipsing interactions for the smaller rings are expected for hybridization changes at the diazocarbon in the transition state, which would give a trend opposite to that observed experimentally.¹⁹ Thus, we conclude that the relative reactivities, **3d** > **3c** > **3b**, of the cyclic diazo compounds largely reflect differences in their ground-state stabilities. They relate to the ring strain which is relieved at

(15) Alternatively, least-squares fitting of the data to a quadratic expression gave coefficients which yielded values of the Marcus theory parameters¹⁶ for the work required to bring the reactants into a reaction complex, $w^{\ddagger} \approx 9$ kcal mol⁻¹, and for the intrinsic reaction barrier, $\Delta G^{\ddagger} \approx 7$ kcal mol⁻¹.¹⁷ However, the resulting curve was statistically indistinguishable from a straight line, which best describes the reactivity of **3a** toward the carboxylic acids that were studied.

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the transition state by a change in hybridization, from sp² to sp³.

Our results are consistent with those of McGarity and Smyth⁷ in that the bimolecular rate constants for proton transfer to the diazo carbon by strong acids are large, although still 2–3 orders of magnitude below the limit for diffusion control. A Brønsted coefficient of ~ 0.25 for the protonation of **3a** suggests an early transition state and may indicate that the reaction is exothermic.²⁰ Another implication is that the pK_A's of carboxylic acids and of 2-propyl diazonium ions are significantly different.^{18,21}

It has been suggested that the carbon atom of diazomethane is a good hydrogen-bond acceptor.^{7,22} Stabilization of carbon bases by hydrogen bonding is expected to be most favorable when negative charge is localized at carbon. Examples of such bases are cyanide²³ and acetylide²⁴ ions and C-2 of the ylide thiamin.²⁵ However, Washabaugh and Jencks have shown that hydrogen bonding is not important in proton transfer reactions of C-2 thiazolium ions,²⁶ and rate constants for protonation at carbon can reach the diffusion controlled limit even when a lone pair on carbon is delocalized, at least formally, as in phenyl ynoate ions.²⁷ Thus, the effects of hydrogen bonding in formally neutral diazoalkanes, on rates of proton transfer, remain unclear. Whatever the reasons, protonations of dialkyldiazo compounds are intrinsically fast, as indicated by our estimate of the intrinsic barrier to protonation of 2-diazopropane.¹⁵

Phenyldiazomethane is *ca.* 70-fold less reactive than **3a** toward H₃O⁺, and α -diazocarbonyl compounds are slower yet by several orders of magnitude.²⁸ Such structural effects on rate constants for protonation at the diazo carbon atom presumably include effects from changes in the structure of the ground states (conjugation, H-bonding as well as other solvation) and in the structure of corresponding transition states.

Photochemical generation of diazoalkanes (**3**) from oxadiazolines (**1**) in a variety of media containing a proton source represents an alternative and convenient method for determining rate constants for diazoalkane protonation reactions. Fast protonation of dialkyldiazo compounds leads to the efficient and relatively indiscriminate formation of cation-counterion pairs which can then collapse to form alkylation products.²⁹ Further investigations of the effects of structure on the properties of diazo compounds, using oxadiazolines (**1**) as convenient photochemical precursors, are in progress.

Acknowledgment. J.P.P. and J.W. thank the Natural Sciences and Engineering Research Council of Canada for continued support through an operating grant. We also thank an anonymous referee for his/her thoughtful comments.

JA962550W

(19) It has been shown that the relative reactivity of cycloalkyl systems, toward nucleophilic addition, could result from a complex interplay of numerous factors. As an example, BH₄⁻ additions to cycloalkanones show the reactivity order $k_{\text{butyl}} > k_{\text{hexyl}} > k_{\text{pentyl}}$; see: (a) Brown, H. C.; Wheeler, O. H.; Ichikawa, K. *Tetrahedron* **1957**, *1*, 214. (b) Brown, H. C.; Ichikawa, K. *Tetrahedron* **1957**, *1*, 221.

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(29) Short-lived diazonium ions which alkylate via carbocations are well known. See: refs 3a and 5.