Photogeneration and reactivity of acyl nitroso compounds

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Abstract: Acyl nitroso compounds have been generated by photolysis of several different classes of precursors including 9,10-dimethylanthracene adducts, nitrodiazo compounds, and 1,2,4-oxadiazole-4-oxides. Consideration of the nitronate-like resonance structure of nitrodiazo compounds led to an examination of the photochemistry of nitronates with α -leaving groups. Photolysis of such nitronates has been shown to generate an acyl nitroso species along with a carbene intermediate. Nanosecond time-resolved infrared (TRIR) spectroscopy has been used to detect photogenerated acyl nitroso compounds directly and to examine their reaction kinetics with amines and thiols. The mechanism of acyl nitroso aminolysis by primary amines involves general base catalysis, while the mechanism of aminolysis by secondary amines is strictly bimolecular. Thiols do not seem to be reactive with acyl nitroso compounds on the microsecond time scale, but thiolates are quite reactive. The reaction between benzoyl nitroside and an organic-soluble thiolate, tetrabutylammonium dodecanethiolate, proceeds via a proposed tetrahedral intermediate, which is observable by TRIR spectroscopy.

Key words: acyl nitroso, nitrodiazo, nitronate photochemistry, 1,2,4-oxadiazole-4-oxides, time-resolved IR spectroscopy.

Résumé : On a généré des composés acylnitroso par photolyse des plusieurs classes différentes de précurseurs, y compris des adduits du 9,10-diméthylanthracène, des composés nitrodiazo et des 4-oxydes de 1,2,4-oxadiazoles. Une considération de la structure des composés nitrodiazo qui est similaire à la structure de résonance des nitronates a conduit à un examen de la photochimie des nitronates possédant un groupe partant en position α . On a montré que la photolyse de tels nitronates conduit à la formation d'espèces acylnitroso aux côtés d'un intermédiaire carbène. On a fait appel à la spectroscopie infrarouge résolue en fonction du temps (IR-RT) pour détecter directement les composés acylnitroso photogénérés et pour déterminer la cinétique de leurs réactions avec des amines et des thiols. Le mécanisme de l'aminolyse d'un acylnitroso par les amines primaires implique une catalyse basique générale alors que le mécanisme de l'aminolyse d'un acylnitroso par les amines secondaires est strictement bimoléculaire. Les thiols ne semblent pas être réactifs vis-à-vis des composés acylnitroso à l'échelle de temps de la microseconde, mais les thiolates sont très réactifs. La réaction entre le nitroside de benzoyle et le thiolate organique soluble, décanethiolate de tétrabutylammonium, se fait par le biais d'une intermédiaire tétraédrique que l'on peut observer par spectroscopie IR-RT.

Mots-clés : acylnitroso, nitrodiazo, photochimie du nitronate, 4-oxydes de 1,2,4-oxadiazoles, spectroscopie infrarouge résolue en fonction du temps (IR-RT).

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Introduction

Acyl nitroso (*C*-nitrosocarbonyl) compounds (**1**) are transient electrophiles that were originally proposed as intermediates in the pyrolysis of alkyl nitrites in the presence of aldehydes¹ as well as in the oxidation of hydroxamic acids.^{2–4} Seminal work strongly suggesting the intermediacy of acyl nitroso compounds in the oxidation of hydroxamic acids was reported in a series of papers by Kirby⁵ and Kirby and Sweeney.^{6,7} Building on previous studies of the dienophilic character of nitrosyl cyanide, it was reasoned that the electron-withdrawing character of the carbonyl functionality ought to render acyl nitroso species reactive in [4 + 2] cycloadditions as well. Indeed, the mild periodate oxidation of aceto- and benzohydroxamic acid in the presence of a variety of conjugated dienes such as 9,10-dimethylanthracene (DMA) yields the Diels–Alder product **2** in high yield (Scheme 1). Further studies with these Diels–Alder adducts revealed that they can undergo a retro-Diels–Alder reaction at elevated temperatures and that the generated acyl nitroso intermediate could be trapped by a different diene.⁷

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Scheme 1. The oxidative generation of acyl nitroso compounds (1) and subsequent reaction with DMA to form Diels–Alder adducts (2).



Scheme 2. The reaction of acyl nitroso compounds (1) with nucleophiles to generate HNO.



Scheme 3. The generation of acyl nitroso compounds (1) from nitrodiazo precursors (3).



Reactions of acyl nitroso species with nucleophiles had been suggested by initial observations but were more carefully examined by Corrie et al.⁸ Periodate oxidation of benzohydroxamic acid in aqueous media yields predominantly benzoic acid, while tetraalkyl-ammonium periodate oxidation in dichloromethane yields *O*-benzoylbenzohydroxamic acid. Atkinson et al.⁹ studied the reaction of acyl nitroso compounds with amines to give amides in reasonable yields. Clearly, **1** is able to acylate nucleophiles such as water, hydroxamic acids, and amines, presumably with concomitant generation of nitroxyl (HNO) (Scheme 2). The detection of nitrous oxide (N₂O), the product of HNO dimerization and subsequent dehydration, in the reaction of **1** with amines is consistent with HNO formation.⁹

Acyl nitroso species have also been proposed as intermediates in the decomposition of nitrodiazo compounds (**3**). Although nitrocarbene intermediates can be trapped following rhodium-catalyzed decomposition,^{10–14} thermolysis or photolysis leads only to acyl nitroso-derived products (Scheme 3).^{15,16} Calculations predict that singlet nitrocarbene has little to no barrier to rearrangement to nitrosoformaldehyde.¹⁷

Quadrelli et al. have developed 1,2,4-oxadiazole-4-oxide derivatives (4) as efficient photochemical¹⁸ and thermal¹⁹ precursors to acyl nitroso compounds (Scheme 4), and Quadrelli and Caramella²⁰ have made use of these precursors in a wide variety of synthetic applications. We have recently utilized 3,5-diphenyl-1,2,4-oxadiazole-4-oxide (4, R = Ph) in the first direct observation of an acyl nitroso species in solution by nanosecond time-resolved infrared (TRIR) spectroscopy.²¹ In this study, the strongest diagnostic signal for benzoyl nitroside (1, R = Ph) appeared at 1735 cm⁻¹; it was produced faster than the time resolution of our spectrometer ($k_{obs} > 2.0 \times 10^7 \text{ s}^{-1}$) and was stable for at least 1 ms in the absence of nucleophiles.

Scheme 4. The generation of acyl nitroso compounds (1) from 1,2,4-oxadiazole-4-oxide derivatives (4).

Fig. 1. TRIR difference spectra averaged over the time frames indicated following laser photolysis (266 nm, 5 ns, 3 mJ) of a 5 mmol L^{-1} solution of **2** (R = Ph) in dichloromethane.



In this manuscript, we are pleased to extend our original TRIR studies of acyl nitroso compounds generated from 4 and also to report on the photochemistry of DMA adducts (2), nitrodiazo compounds (3), and related nitronate derivatives.

Results and discussion

Photogeneration of acyl nitroso compounds from DMA adducts

Following our initial TRIR studies of benzoyl nitroside generated from a 1,2,4-oxadiazole-4-oxide,²¹ we have performed analogous studies on its DMA adduct (**2**, **R** = Ph). Laser photolysis (266 nm, 5 ns, 3 mJ) of a 5 mmol L⁻¹ solution of **2** (**R** = Ph) in dichloromethane produces the TRIR difference spectrum shown in Fig. 1. Interestingly, in addition to the diagnostic acyl nitroso band at 1735 cm⁻¹, another prominent band is observed at 1820 cm⁻¹. The 1820 cm⁻¹ band is formed faster than the time resolution of our spectrometer ($k_{obs} > 2.0 \times 10^7 \text{ s}^{-1}$) and decays on the microsecond time scale with concomitant additional growth of the 1735 cm⁻¹ acyl nitroso band.

IR absorbances above 1800 cm⁻¹ are relatively rare for organic species and are typically observed only for highly strained carbonyls, carbonyls substituted with strongly electronwithdrawing groups, and acyl radicals. Acyl radicals have been extensively studied in hydrocarbon solvent by TRIR spectroscopy.^{22,23} Benzoyl radical is reported to absorb at 1828 cm⁻¹, consistent with our 1820 cm⁻¹ signal in dichloromethane. We envision two potential pathways consistent with the TRIR data of Fig. 1: (*i*) simple secondary photoly-





Analogous TRIR experiments on the acetyl nitroside/ DMA adduct (**2**, R = Me) reveal only the characteristic acyl nitroso band, in this case observed at 1780 cm⁻¹ (consistent with B3LYP/6-31G* calculations), with no evidence for the acetyl radical (Supplementary data). Since acetyl nitroside is not expected to absorb at 266 nm, whereas benzoyl nitroside should, these experiments suggest that the secondary photolysis pathway (Scheme 5, path 1) is operative.

Photogeneration of acyl nitroso compounds from nitrodiazo compounds

We have also examined the photogeneration of acyl nitroso compounds from nitrodiazo precursors by TRIR spectroscopy. Ethyl nitrodiazoacetate (3, $R = CO_2Et$) and nitrodiazomethyl tert-butyl ketone (3, R = C(O)-t-Bu) both provide the characteristic acyl nitroso TRIR signal at 1788 and 1756 cm⁻¹, respectively, consistent with B3LYP/6-31G* calculations (Supplementary data). Each of these bands was produced faster than the time resolution of our spectrometer ($k_{\rm obs}$ > 2.0 \times 10 7 s $^{-1}$) and was stable for at least 1 ms in dichloromethane. In the spectral region between 2200 and 2000 cm⁻¹, we also observe diazo depletion bands with no TRIR evidence for the formation of ketene,^{25,26} which could potentially be formed via Wolff rearrangement from either of these precursors (Supplementary data). Consistent with the lack of Wolff rearrangement, nearly quantitative yields of N₂O (formed via acyl nitrosoproduced HNO) are observed following the photolysis of nitrodiazoacetate ethvl in 75:25 acetonitrile/water (Scheme 6).

Given the above results and previous observations that photogenerated nitrocarbenes are not trappable,^{15,16} we have begun to explore an alternative photochemical pathway to acyl nitroso compounds from nitrodiazo precursors that arose from consideration of their nitronate-like resonance structure (**3-N**). Alkyl nitronates (**6**) have been shown to undergo a photoinduced rearrangment to hydroxamic acids (Scheme 7a).^{27–31} An analogous reaction from a nitrodiazo compound leads to the *N*-oxirane intermediate **7**, which could undergo further rearrangement, via two potential pathways, to the acyl nitroso product (Scheme 7*b*).

Photogeneration of acyl nitroso compounds from nitronates with α -leaving groups

To test the reaction scheme shown in Scheme 7*b* we have examined the photochemistry of nitronates with α -leaving groups. Our initial studies have focused on phenylcyanonitromethane nitronate (8); results similar to those reported below have also been observed in preliminary experiments with the 4-chloro and 4-methoxy analogues.

Nitronate **8** is stable in sodium hydroxide or methanol solutions. As shown in Scheme 8, photolysis (Rayonet, 254 nm) of **8** in methanol cleanly provides two products, methyl benzoate (**10**) and methoxyphenylacetonitrile (**12**). HPLC and GC–MS analysis reveal a $29\% \pm 5\%$ yield of **10** and a $63\% \pm 7\%$ yield of **12** (values are means \pm SD). The production of methyl benzoate was confirmed by comparison with an authentic sample; the GC–MS data for nitrile **12** match well with its reported mass spectrum.³² N₂O quantification following photolysis of nitronate **8** in methanol indicates that HNO is formed in a $26\% \pm 5\%$ yield, consistent with the yield of methyl benzoate.

To explain the formation of nitrile 12, we propose that *N*-oxirane intermediate 9 partitions between the anticipated loss of cyanide ion and the loss of nitrite ion to form phenylcyano carbene (11), which is trapped by methanol to form nitrile 12, as has been previously observed.^{33,34} Although we have not yet conducted experiments that indicate whether carbene 11 is formed thermally or photochemically (analogous to epoxide photochemistry^{34–36}) from *N*-oxirane 9, this hypothesis is consistent with earlier studies of nitronate photochemistry where carbene intermediates were proposed.³⁰

Further experimental evidence for the formation of carbene **11** is provided by additional trapping experiments. GC–MS analysis following photolysis of nitronate **8** in acetonitrile containing either cyclohexene or 2,3-dimethyl-2butene reveals carbene–alkene adducts (both C–H and C=C insertion products).³⁶ Moreover, the addition of increasing concentrations of alkene to a methanol-containing acetonitrile solution of nitronate **8** results in a decrease of the carbene–methanol adduct **12** accompanied by a concomitant increase in carbene–alkene derived products. Finally, photolysis of nitronate **8** in THF results in products (**14** and **15**, Scheme 8) consistent with the rearrangement of carbenederived ylide **13**. Analogous THF–ylide rearrangement products have been observed in the study of 2-naphthyl(carbomethoxy)carbene.³⁷

Reactivity of acyl nitroso compounds with amines

We have examined the reactivity of three acyl nitroso compounds (1, R = Ph, Me, and 4-Cl-Ph) with a variety of amines in dichloromethane. Acyl nitroso compounds (1, R = Ph and 4-Cl-Ph) were generated from 1,2,4-oxadiazole-4-oxides (4), and acyl nitroso 1 (R = Me) was generated from





Scheme 7. (*a*) The photochemistry of alkyl nitronates. (*b*) The analogous photochemistry of nitrodiazo precursors to produce acyl nitroso compounds.



its DMA adduct (2). The decay kinetics of the characteristic acyl nitroso TRIR signals were monitored as a function of varying concentrations of added amine to derive reaction rate constants.

For the secondary amines, diethylamine (DEA) and piperidine (PIP), plots of observed decay rates (k_{obs}) versus amine concentration are linear and fit well to the pseudo-first-order rate equation $k_{obs} = k_o + k_{amine}$ [amine] (Fig. 2 and Supplementary data). Derived second-order rate constants are shown in Table 1. (Note that the reaction of benzoyl nitroside (1, R = Ph) with DEA has been refined slightly from that originally reported ($k_{DEA} = 1.3 \times 10^5 \pm 0.5 \times 10^5 \text{ L}$ mol⁻¹ s⁻¹).²¹) The twofold faster rate constant for the reaction of 1 (R = Ph) with PIP versus DEA is consistent with the decreased steric bulk of the ring-constrained PIP.

For the primary amines, *n*-butylamine (NBA) and benzylamine (BA), in contrast to the above secondary amines, plots of k_{obs} versus amine concentration are not linear, but rather fit to the rate equation $k_{obs} = k_o + k_{amine}[amine]^2$ (Fig. 3 and Supplementary data), indicating that the reaction of acyl nitroso species with primary amines is a third-order reaction, requiring two molecules of the primary amine. Relative rate constants derived for NBA and BA (Table 1) are again consistent with expected reactivity. No reactivity was observed with *tert*-butylamine (TBA), even at concentrations approaching 2 mol L⁻¹, owing to the steric bulk of this poorly nucleophilic amine.

The dependence of the reaction order of the aminolysis of acyl nitroso species on amine structure (i.e., primary vs. secondary) is consistent with previous reports of the aminolysis of esters by primary and secondary amines in organic solvent.^{38–40} Our results indicate that the mechanism of acyl nitroso aminolysis by primary amines involves general base catalysis, while the mechanism of aminolysis by secondary amines is strictly bimolecular.

For a given amine, the rate of aminolysis is also dependent on the structure of the acyl nitroso compound. Consistent with expected electronic effects, 1 (R = 4-Cl-Ph) reacts 2 to 3 times more rapidly than 1 (R = Ph) with DEA and NBA, respectively. Also, aliphatic acyl nitroso (1, R = Me) reacts 2.5 to 10 times more rapidly than aromatic acyl nitroso (1, R = Ph) with NBA and PIP, respectively.

Reactivity of acyl nitroso compounds with thiols

We have also examined the kinetics and mechanism of the reaction of 1 (R = Ph) with thiols. Initial experiments surprisingly revealed no observed increase in the acyl nitroso decay rate upon the addition of up to 100 mmol L⁻¹ N-acetylcysteine methyl ester (NAC). However, in the presence of 3.4 mmol L⁻¹ NAC and 48 mmol L⁻¹ DEA, the decay of 1 was observable and faster than that in the presence of 48 mmol L⁻¹ DEA alone. We postulate that although the thiol itself is not reactive (on the microsecond time scale), the in situ generated diethylammonium thiolate is. We examined thiolate reactivity directly using organic-soluble tetrabutylammonium dodecanethiolate (TBA-D). The dependence of the acyl nitroso decay rate fit well to the pseudo-first-order rate equation $k_{obs} = k_o + k_{TBA-D}[TBA-D]$ and a value of $k_{\text{TBA-D}} = 4.2 \ (\pm 0.6) \times 10^7 \ \text{L mol}^{-1} \ \text{s}^{-1}$ was determined (Supplementary data).

For all amines examined, acyl nitroso decay is accompanied by concomitant growth of the corresponding amide product (~1660 cm⁻¹). In the case of the reaction of TBA-D with **1** (R = Ph), however, the acyl nitroso (1735 cm⁻¹) decays over the microsecond time scale to a strongly absorbing intermediate that is observed at 1615 cm⁻¹ (Fig. 4). This intermediate subsequently decays on the millisecond time scale to the product thiobenzoate (**17**), observed at 1706 cm⁻¹, consistent with the reported carbonyl stretching frequency of ethylthiobenzoate.⁴¹ We have tentatively assigned this 1615 cm⁻¹ band to tetrahedral intermediate **16** (Scheme 9), which is calculated (Supplementary data) to have a very intense N=O stretch at 1597 cm⁻¹, reasonably consistent with the observed TRIR band.

The rate of decay of the intermediate 1615 cm^{-1} band and the rate of growth of the 1706 cm⁻¹ product band are both independent of the concentration of TBA-D, consistent with a unimolecular reaction of **16**. A similar tetrahedral intermediate has been proposed in the alkaline hydrolysis of thiobenzoates.⁴²



Table 1. Rate constants for the reaction of acyl nitroso compounds with amines.

| | $k \times 10^{-5} (\text{L mol}^{-1} \text{ s}^{-1})$ | | $k \times 10^{-4} (L^{-1} \text{ mol}^{-2} \text{ s}^{-1})$ | | |
|---------------------|---|---------|---|----------|--------|
| Acyl nitroso 1, R = | DEA | PIP | NBA | BA | TBA |
| Ph | 1.2±0.1 | 2.0±0.1 | 2.8±0.1 | 0.36±0.9 | No rxn |
| Me | ND | 22±1 | 7.1±0.1 | ND | No rxn |
| 4-Cl-Ph | 2.3±0.1 | ND | 10.1±0.1 | ND | No rxn |

| Note: DEA | , diethylamine; | PIP, piperidine | ; NBA, <i>n</i> -but | ylamine; BA, | benzylamine; | TBA, te | <i>ert</i> -butylamine | э; |
|---------------|-----------------|-----------------|----------------------|--------------|--------------|---------|------------------------|----|
| ND, not deter | mined; no rxn, | no reaction obs | erved on the | microsecond | time scale. | | | |

Fig. 2. Plots of observed rate of decay of 1 (R = Ph) in dichloromethane monitored at 1735 cm⁻¹ as a function of diethylamine (squares) or piperidine (circles) concentration. The dotted lines are the least-squares fit to a linear function.



Conclusions

Acyl nitroso compounds have been generated by photolysis of several different classes of precursors including DMA adducts (2), nitrodiazo compounds (3), and 1,2,4-oxadiazole-4-oxides (4). Consideration of the nitronate-like resonance structure of nitrodiazo compounds led to an examination of the photochemistry of nitronates with α -leaving groups (e.g., 8). Photolysis of nitronate 8 has been shown to generate an acyl nitroso species along with a carbene intermediate. **Fig. 3.** Plots of observed rate of decay of 1 (R = Ph) in dichloromethane monitored at 1735 cm⁻¹ as a function of benzylamine (squares) or *n*-butylamine (circles) concentration. The dotted lines are the least-squares fit to a polynomial function.



Nanosecond TRIR spectroscopy has been used to detect photogenerated acyl nitroso compounds directly and to examine their reaction kinetics with amines and thiols. The mechanism of acyl nitroso aminolysis by primary amines involves general base catalysis, while the mechanism of aminolysis by secondary amines is strictly bimolecular. Thiols do not seem to be reactive with acyl nitroso compounds on the microsecond time scale, but thiolates are quite reactive. The reaction between benzoyl nitroside (1, R = Ph) and the organic-soluble thiolate TBA-D proceeds via a proposed tet-



Fig. 4. (*a*) TRIR difference spectra averaged over the time frames indicated and (*b* and *c*) kinetic traces observed following laser photolysis (355 nm, 5 ns, 4 mJ) of a 1 mmol L^{-1} solution of **4** (R = Ph) containing 10 mmol L^{-1} TBA-D in dichloromethane.

Scheme 9. The postulated mechanism for the thiolysis of benzoyl nitroside illustrating the intermediacy of 16.



rahedral intermediate, which is observable by TRIR spectro-scopy.

Experimental section

General methods

Unless otherwise noted, materials were obtained from the Sigma-Aldrich Chemical Company, Fisher Scientific, or Cambridge Isotope Laboratories. All solvents were purified with a PureSolv MD 5 solvent purification system. All amines were redistilled prior to use and stored over potassium hydroxide.

¹H NMR spectra were recorded on a Bruker Avance 400 MHz FT NMR operating at 400 MHz; ¹³C NMR spectra were recorded on a Bruker Avance 300 MHz FT NMR operating at 75 MHz. All ¹H resonances are reported in parts per million, and are referenced to solvent (¹H NMR (chloroformd) δ : 7.26, (methanol- d_4) δ : 3.3). Melting points were recorded on a Mel-Temp apparatus and are uncorrected. High resolution mass spectra were obtained on a VG70SE double focusing magnetic sector mass spectrometer operating in fast atom bombardment ionization mode. Reported masses were referenced to a doubly potassiated PEGMME mass calibrant. Ultraviolet-visible (UV-vis) absorption spectra were obtained using a Hewlett Packard 8453 diode array spectrometer. Infrared (IR) absorption spectra were obtained using a Bruker IFS 55 Fourier transform infrared spectrometer. All density functional theory (DFT) calculations were performed using Spartan '04 (Wavefunction, Inc.) for Macintosh or Spartan '08 (Wavefunction, Inc.) for Windows using the B3LYP/6-31G* method and basis set.

Time-resolved IR methods

TRIR experiments were conducted following the method of Iwata and Hamaguchi⁴³ as described previously.²⁵ Briefly, the broadband output of a MoSi₂ IR source (JASCO) is crossed with excitation pulses from a Continuum Minilite II Nd:YAG laser (266 nm or 355 nm) operating at 15 Hz. Changes in IR intensity are monitored using an AC-coupled mercury/cadmium/tellurium (MCT) photovoltaic IR detector (Kolmar Technologies, KMPV11-J1/ AC), amplified, digitized with a Tektronix TDS520A oscilloscope, and collected on a Macintosh with IGOR for data processing. The experiment is conducted in dispersive mode with a JASCO TRIR 1000 spectrometer.

N₂O quantification via GC headspace analysis

GC headspace analysis was performed on a Varian CP-3800 instrument equipped with a Restek ShinCarbon ST 80/ 100 molecular sieve-packed column and an electron capture detector.

Photolysis of Angeli's salt (a classic HNO donor under physiologically relevant conditions⁴⁴) has been shown to produce HNO/NO-, which subsequently yields N2O.45 To quantify the amount of N₂O produced following photolysis of Angeli's salt, a 1 mmol L⁻¹ solution in 0.01 mol L⁻¹ NaOH was prepared and 1 mL of this solution was placed in series of 1 cm quartz cuvettes. The cuvettes were sealed with rubber septa and sparged with argon for 20 min. Samples were then photolyzed (Rayonet, 254 nm) until completion as indicated by the disappearance of the characteristic Angeli's salt UV absorbance at 254 nm. Samples were allowed to equilibrate at 37 °C for 1 h and then 100 µL of headspace was analyzed for N₂O. N₂O yields are taken as an average of five injections. The theoretical yield of Angeli's salt-derived N₂O was calculated for the NaOH solution using Henry's law and was found to be quantitative versus authentic samples. N₂O yields were determined analogously for ethyl nitrodiazoacetate (3, $R = CO_2Et$) in 75:25 acetonitrile/water and phenylcyano-nitromethane nitronate (8) in methanol and compared with that found for Angeli's salt (assumed to be 100%) in 75:25 acetonitrile/water and methanol, respectively.

GC-MS methods

GC–MS analysis was performed on a Shimadzu GC17A/ QP5050A instrument equipped with electron ionization. Nitronate samples were prepared in methanol, THF, or acetonitrile, sparged with argon, photolyzed (Rayonet, 254 nm), concentrated under vacuum, reconstituted in 1 mL of methanol, and then analyzed by GC–MS. Carbene trapping by alkenes (cyclohexene and 2,3-dimethyl-2-butene) was analyzed analogously in acetonitrile solutions. Competitive carbene trapping by methanol versus alkene (cyclohexene or 2,3-dimethyl-2-butene) was also performed in acetonitrile with 10 mmol L⁻¹ methanol and 0–50 mmol L⁻¹ alkene. Yields are reported as an average of four individual experiments.

HPLC methods

HPLC data were collected on a Waters Delta 600 system equipped with a Model 6000A pump and a Model 2487 dual wavelength UV detector monitoring at 230 nm equipped with a Waters C-18 symmetry column. All HPLC eluents contained 0.1% trifluoroacetic acid. Nitronate samples were prepared in methanol, sparged with argon, and then photolyzed (Rayonet, 254 nm). HPLC analysis was then performed with a flow rate of 1 mL min⁻¹ with 35:65 acetonitrile/water. Yields are reported as an average of four individual experiments.

General procedure for the synthesis of DMA cycloadducts (2)

The synthesis of DMA cycloadducts (2) was carried out in accordance with a literature procedure, using tetrabutylammonium periodate instead of tetraethyl-ammonium periodate.⁷ Benzoyl nitroside/DMA cycloadduct (2, R = Ph): mp 126–128 °C (lit. value⁷ mp 127–128 °C). Acetyl nitroside/DMA cycloadduct (2, R = Me): mp 133–136 °C (lit. value⁷ mp 133–136 °C).

General procedure for the synthesis of nitrodiazocarbonyl compounds (3)

Ethylnitrodiazoacetate and nitrodiazomethyl *tert*-butyl ketone were synthesized by the method reported by Charette et al.⁴⁶ Ethylnitrodiazoacetate (**3**, R = CO₂Et): IR (film, cm⁻¹) ν_{max} : 2148, 1750, 1693. ¹H NMR (CDCl₃) δ : 4.42 (2H, q), 1.38 (3H, t). Nitrodiazomethyl *tert*-butyl ketone (**3**, R = C(O)-*t*-Bu): IR (film, cm⁻¹) ν_{max} : 2142, 2180, 1690, 1650. ¹H NMR (CDCl₃) δ : 1.35 (s, 9 H).

General procedure for the synthesis of 1,2,4-oxadiazole-4-oxides (4)

The synthesis of 1,2,4-oxadiazole-4-oxides was performed using a slight modification of a literature procedure.⁴⁷ The synthesis of 3,5-diphenyl-1,2,4-oxadiazole-4-oxide is shown below as a general procedure.

3,5-Diphenyl-1,2,4-oxadiazole-4-oxide (4, R = Ph)

Benzohydroximoyl chloride was prepared from benzaldehyde oxime in accordance with literature procedures and used directly for the next step.⁴⁸ Dehydrohalogenation was performed in ethanol using triethanolamine to yield benzonitrile oxide. The nitrile oxide dimerization was accomplished in situ with triethanolamine, yielding a mixture of three dimeric species. The desired dimer was initially purified by silica gel column chromatography (10%–30% ethyl acetate / hexanes). The column-purified product was further purified by recrystallization from methanol/water, yielding white needles; mp 132–133 °C (lit. value⁴⁹ mp 134 °C).

3,5-Bis(4-chlorophenyl)-1,2,4-oxadiazole-4-oxide (4, R = 4-Cl-Ph)

Prepared from 4-chlorobenzaldehyde oxime using the general procedure; mp 189–190 $^{\circ}$ C (lit. value⁴⁹ mp 189–190 $^{\circ}$ C).

General procedure for the synthesis of arylcyanonitromethane potassium nitronates

Arylcyanonitromethane potassium nitronate derivatives

were prepared via modification of a literature procedure.⁵⁰ Synthesis of phenylcyanonitromethane potassium nitronate is shown below as a general procedure.

Phenylcyanonitromethane potassium nitronate (8)

Benzyl cyanide (2.93 g, 0.025 mol) was added to a solution of potassium tert-butoxide (9.25 g, 0.0825 mol) in 90 mL of THF at -50 °C in a dry ice/acetone bath. Isoamyl nitrate (7.3 g, 0.55 mol) was added dropwise, maintaining the temperature at -45 to -50 °C. The cooling bath was removed and the reaction mixture allowed to warm to room temperature. The precipitate that formed was filtered and washed with THF and then ether. The residue was recrystallized from ethanol/hexanes (2.25 g, 45%). IR (mineral oil, cm⁻¹) v_{max}: 2201, 1495, 1455, 1417, 1366, 1339, 1310, 1284, 1264, 1190, 1167, 1034, 1005, 989, 762. ¹H NMR (methanol-d₄) & 7.15 (1H, t), 7.32 (2H, d), 7.90 (2H, d). ¹³C NMR (D₂O) δ: 129.40, 128.52, 127.68, 125.87, 117.88, 102.10. HR-FAB-MS m/z: 238.9629 [M + 2K]+. Calcd. for C₈H₅K₂N₂O₂: 238.9625.

4-Chloro-phenylcyanonitromethane potassium nitronate

Prepared from 4-chlorobenzyl cyanide using the general procedure. IR (mineral oil, cm⁻¹) ν_{max} : 2200, 1497, 1397, 1303, 1279, 1248, 1115, 1098, 996, 824. ¹H NMR (methanol- d_4) δ : 7.32 (2H, d), 7.90 (2H, d). ¹³C NMR (D_2O) δ : 132.14, 128.31, 128.05, 126.89, 117.48, 101.49. HR-FAB-MS m/z: 272.9232 [M + 2K, ³⁵Cl]⁺, 274.9210 $[M + 2K, {}^{37}C1]^+$. Calcd. for C₈H₄ClK₂N₂O₂: 272.9235.

4-Methoxy-phenylcyanonitromethane potassium nitronate

Prepared from 4-methoxybenzyl cyanide using the general procedure. IR (mineral oil, cm⁻¹) v_{max}: 2205, 1600, 1514, 1412, 1351, 1310, 1290, 1241, 1189, 1151, 1028, 991, 828. ¹H NMR (methanol- d_4) δ : 3.79 (3H, s), 6.90 (2H, d), 7.80 (2H, d). ¹³C NMR (D₂O) δ: 158.07, 127.60, 122.14, 117.60, 113.87, 101.80, 55.28. HR-FAB-MS m/z: 268.9726 [M + 2K]⁺. Calcd. for C₉H₇K₂N₂O₃: 268.9731.

Synthesis of tetrabutylammonium dodecanethiolate (TBA-D)

The synthesis was carried out in accordance with the published procedure.51,52

Supplementary data

Supplementary data (additional TRIR data, kinetic analyses, and computational results) for this article are available on the journal Web site (canjchem.nrc.ca).

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