it thoroughly with the acidic media in the cell. The increase in the optical density of the solution at 299 nm with time was then followed. The rate of rearrangement was determined from the slope of a plot of ln $(A_\infty - A_t)/(A_\infty - A_0)$ vs time. The kinetics were cleanly pseudo first order over 10 half-lives unless otherwise stated.

Preparation of 4-Methyl-4-vinylcyclohex-2-enone (4). To a stirred slurry of 4.290 g (12.0 mmol) of triphenylmethylphosphonium bromide in 100 mL of dry THF was added 9.6 mL (12 mmol) of 1.25 M methyllithium in ether under a nitrogen atmosphere at room temperature. After 30 min of stirring, to the resulting methylene triphenylphosphorane (red solution) was added 2.76 g (20 mmol) of 4-methyl-4-formylcyclohex-2-enone (3), which was prepared by the method of Danishefsky and Kitahara,[10] in 10 mL of dry THF at 0 °C (immediate exothermic reaction). After 30 min, the reaction mixture was poured into 200 mL of ether and washed with 150-mL portions of water. The aqueous washings were extracted twice with 100-mL portions of ether. After being dried ($MgSO_4$), the combined organic layers were concentrated under reduced pressure. Chromatography of the residue on 25 g of silica gel with 1:99 ether/petroleum ether eluted first 0.175 g (7%) of undesired byproduct triene as a colorless oil (which decomposed on storage): NMR ($CDCl_3$) δ 1.10 (s, 3 H), 1.45–2.47 (m, 4 H), 4.70–6.25 (m, 7 H). Further elution with 10:90 ether/petroleum ether afforded 0.780 g (29%) of vinyl enone 4 as a colorless oil: R_f 0.35 (silica gel, 10:90 ether/petroleum ether); IR (CCl_4) 1720, 1685, 1635 cm^{-1}; NMR ($CDCl_3$) δ 1.21 (s, 3 H), 1.77–2.57 (m, 4 H), 5.00 (dd, 1 H, J = 18, 2 Hz), 5.08 (dd, 1 H, J = 10, 2 Hz), 5.82 (dd, 1 H, J = 18, 10 z), 5.96 (d, 1 H, J = 10 Hz), 6.63 (d, 1 H, J = 10 Hz).

Preparation of 4-Methyl-4-vinylcyclohexa-2,5-dienone (1). A solution of 272 mg (2 mmol) of vinyl enone 4, 0.681 g (3 mmol) of DDQ, and 10 mL of dioxane was refluxed for 48 h. After cooling, the hydroquinone was filtered off under reduced pressure. The reaction with poured into water and extracted with CH_2Cl_2 twice. The combined organic layers were dried and concentrated under reduced pressure. Chromatography of the residue on 10 g of silica gel with 10:90 ether/petroleum ether eluted first 67 mg (25%) of starting material and 45 mg (17%) of 4-methyl-3-vinylphenol (9): R_f 0.19 (silica gel, 10:90 ether/petroleum ether); NMR ($CDCl_3$) δ 2.25 (s, 3 H), 5.12–5.77 (m, 2 H), 6.55–7.17 (m, 4 H). There were then eluted 93 mg (35%) of vinyl dienone 1. After microdistillation using a micropipette under vacuum, a slightly yellow liquid of vinyl dienone 1 was obtained: R_f 0.11 (silica gel, 10:90 ether/petroleum ether); UV λ_{max} 238 nm (H_2O); IR (neat) 1662, 1620 cm^{-1}; NMR ($CDCl_3$) δ 1.33 (s, 3 H), 4.95–6.04 (m, 3 H), 6.27 (d, 2 H, J = 10 Hz), 6.87 (d, 2 H, J = 10 Hz). Anal. Calcd for $C_9H_{10}O$: C, 80.56; H, 7.51. Found: C, 80.10; H, 7.77.

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Registry No. 1, 114300-63-9; 3, 54125-08-5; 4, 114300-64-0; 5, 114300-65-1; 6, 114300-66-2; 7, 114300-67-3; 8, 114300-68-4; 9, 66164-30-5; triphenylmethylphosphonium bromide, 1779-49-3.

Reaction of α-Bromoisobutyronitrile with Nitroalkane Anions

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The ability of a nitro group in the substrate to bring about electron-transfer free-radical chain nucleophilic substitutions ($S_{RN}1$) at a saturated carbon atom is well documented.[1] Among other nitro derivatives,[2] the 2-halo-2-nitropropanes are substrates of $S_{RN}1$ reactions.[3] We have found that 2-bromo-2-cyanopropane (1) alkylates the anion of nitromethane and of primary and secondary nitroalkanes (**2a–e**) at the carbon atom (reaction 1), and a mechanistic examination shows that this is an electron-transfer chain nucleophilic substitution.[4]

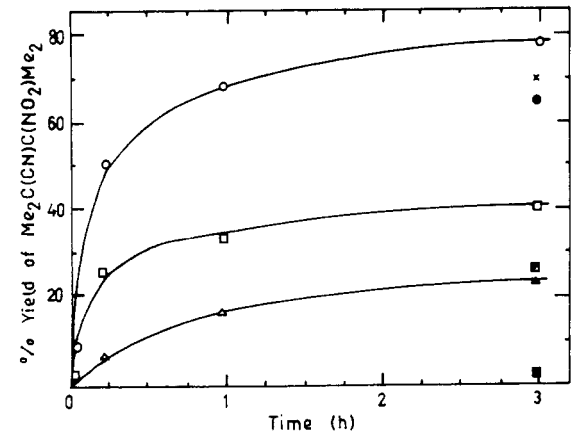
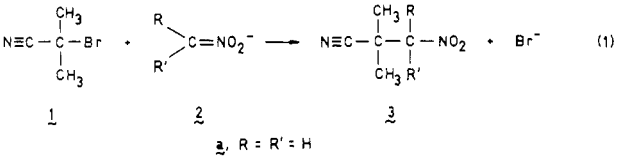


Figure 1. Formation of $Me_2C(CN)C(NO_2)Me_2$ by reaction of an equimolar mixture of $Me_2C(Br)CN$ and $Me_2C{=}NO_2K$ in HMPA at 20 °C under N_2 in ordinary laboratory light ($[Me_2C(Br)CN]_0$ = 0.3), as affected by inhibitors: ○, control reaction; ●, in the dark; ×, with 20 mol % of O_2 added; □, with 5 mol % of $(t\text{-Bu})_2NO^\bullet$; ◪, with 10 mol % of $(t\text{-Bu})_2NO^\bullet$; ■, with 25 mol % of $(t\text{-Bu})_2NO^\bullet$; △, with 10 mol % of $m\text{-}(O_2N)_2C_6H_4$.

Table I. Alkylation of Nitroalkane Anions ($RR'C{=}NO_2^-$) by α-Bromoisobutyronitrile[a]

R, R′	% yield of $Me_2C(CN)C(NO_2)RR'$[b]
H, H	45, *36*, 42,[c] 44,[d] 37,[e] 27,[f] 8,[g] 8,[h]
H, Me	72, *57*
H, *n*-Hex	67, *61*
Me, Me	82, *68*, 58,[i] 81,[j] 79[d]
$(CH_2)_5$	*76*

[a] Reactions conducted under N_2 with a $RR'C{=}NO_2^-K^+/Me_2C(Br)CN$ molar ratio of 0.9 in HMPA at 20 °C for 6 h in ordinary laboratory light, unless otherwise noted. [b] Crude yields estimated by ^1H NMR with internal standard; yields of pure isolated products in italics. [c] In DMSO with K^+/18-crown-6 as counterion. [d] With 2 equiv of H_2O added. [e] In the dark. [f] With 20 mol % of O_2. [g] With 10 mol % of $(t\text{-Bu})_2NO^\bullet$. [h] With 10 mol % of $m\text{-}(O_2N)_2C_6H_4$. [i] In DMSO. [j] With 1 equiv of H_2O.



1 2 3

a, R = R′ = H
b, R = H; R′ = Me
c, R = H; R′ = *n*-Hex
d, R = R′ = Me
e, R, R′ = $(CH_2)_5$

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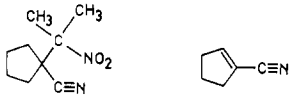
0022-3263/88/1953-2868$01.50/0

The yields of isolated C-alkylation products (**3a–e**) range from 36% with $H_2C{=}NO_2^-$ to ca. 70% with $Me_2C{=}NO_2^-$ and cyclohexanenitronate anion, using the potassium nitronates in HMPA (Table I). Under these conditions, 1-bromocyclopentanecarbonitrile and $Me_2C{=}NO_2^-$ give the *C*-alkylate **4** and the elimination product **5** in 16 and 56% yield, respectively.



4 **5**

The reactions of **1** with $H_2C{=}NO_2^-$ and $Me_2C{=}NO_2^-$ have attributes of the $S_{RN}1$ mechanism (reactions 2–5): the formation of **3a** and **3d** is restrained by small proportions (5–10 mol %) of di-*tert*-butyl nitroxide and *m*-dinitrobenzene (Table I, Figure 1). O_2, 20 mol %, has a humble effect on these systems.[5] The reactions proceed in the dark, indicating a spontaneous thermal initiation of the chain process (reaction 2).[6] The relatively small effects of the inhibitors observed appear to reflect the occurrence of short chains.[7] With this difficultly reduced substrate this possibly results from a low efficiency of the electron transfer propagating step of the chain process. In this instance, a dissociative electron transfer (reaction 6),[8] which will gain the dissociation energy of the unstable $Me_2C(Br)CN^{\bullet-}$, may take place.

$$Me_2C(Br)CN + RR'C{=}NO_2^- \rightarrow Me_2C(Br)CN^{\bullet-} + RR'C{=}NO_2^{\bullet} \quad (2)$$

$$Me_2C(Br)CN^{\bullet-} \rightarrow Me_2\dot{C}CN + Br^- \quad (3)$$

$$Me_2\dot{C}CN + RR'C{=}NO_2^- \rightarrow Me_2C(CN)CRR'NO_2^{\bullet-} \quad (4)$$

$$Me_2C(CN)CRR'NO_2^{\bullet-} + Me_2C(Br)CN \rightarrow Me_2C(CN)CRR'NO_2 + Me_2C(Br)CN^{\bullet-} \quad (5)$$

$$Me_2C(CN)CRR'NO_2^{\bullet-} + Me_2C(Br)CN \rightarrow Me_2C(CN)CRR'NO_2 + Me_2\dot{C}CN + Br^- \quad (6)$$

We examined the possibility that **3** did not arise from a free-radical chain substitution in **1** but in $RR'C(Br)NO_2$ by $Me_2\bar{C}CN$, formed in small amounts by nucleophilic displacement at the bromine atom of **1** by the nitronate anions (reactions 7, 8).[9] A similar sequence has been

$$Me_2C(Br)CN + RR'C{=}NO_2^- \rightarrow Me_2\bar{C}CN + RR'C(Br)NO_2 \quad (7)$$

$$Me_2\bar{C}CN + RR'C(Br)NO_2 \rightarrow \mathbf{3} \quad (8)$$

proposed for the radical chain C-alkylation and C-sulfonylation of secondary nitroalkane anions by tertiary α-bromonitroalkanes[1a] and *p*-toluenesulfonyl bromide,[10] respectively. If this is the case for **1**, the yield of β-nitronitrile should be significantly affected by the presence of 2 equiv of H_2O, which should quench the supposed, strongly basic $Me_2\bar{C}CN$ intermediate. This effect is not observed (see Table I). Reaction of potassium 2-cyano-2-propanide with 2-bromo-2-nitropropane in HMPA gave only traces of **3d** (<0.1%) while 2,3-dimethyl-2,3-dinitrobutane [$Me_2C(NO_2)C(NO_2)Me_2$, **6**] was formed in 12% yield, apparently by the reversal of reaction 7 followed by the $S_{RN}1$ coupling of $Me_2C{=}NO_2^-$ and $Me_2C(Br)NO_2$.[11] Contrariwise, 1% of **6** and 82% of **3d** were produced in the reaction between **1** and $Me_2C{=}NO_2K$ in HMPA. These results support the view that **1** is an actual substrate of the free-radical chain nucleophilic substitution.

Experimental Section

Melting points were determined on an electrically heated Gallenkamp block and are uncorrected. ^1H NMR spectra were obtained at 90 MHz. GC analyses were performed on a SE-30 capillary column along with flame-ionization detection and electronic integration.

α-Bromoisobutyronitrile (**1**),[12] 2-bromo-2-nitropropane,[11a] and 1-nitroheptane[13] were prepared according to the literature. 1-Bromocyclopentanecarbonitrile was prepared in 50% yield from cyclopentanecarbonitrile[14] by reaction with PBr_5:[15] bp 88–89 °C (18 Torr); IR (neat) 2230 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.7–2.2 (br, 4 H), 2.2–2.6 (br, 4 H); by GC it was ca. 98% pure. Commercial samples of nitromethane, nitroethane, 2-nitropropane, and nitrocyclohexane were fractionally distilled under reduced pressure. HMPA and DMSO were distilled from CaH_2 under reduced pressure and were stored over molecular sieves in the dark.

CAUTION! The cancer suspect agents 2-nitropropane and HMPA should be handled with care.

General Procedures. To a stirred solution of potassium *tert*-butoxide in HMPA was added at room temperature (20 °C) under N_2 a solution of 0.9 equiv of nitroalkane in HMPA by a hypodermic syringe through a rubber septum. N_2 was then bubbled through the mixture of potassium nitronate and HMPA for about 30 min followed by addition of 1 equiv of α-bromo nitrile [density 1.36 (**1**), 1.45 (1-bromocyclopentanecarbonitrile]. For the experiments in Table I and Figure 1 carried out with an additive, this was added just before the substrate in solution [for H_2O, $(t\text{-Bu})_2NO^{\bullet}$, and $m\text{-}(O_2N)_2C_6H_4$]; O_2 was bubbled through the stirred mixture contained in an almost-full flask by a hypodermic syringe. For the experiments in the dark, the flask was wrapped with aluminum foil. After 6 h, the reaction mixture was poured into water and ether; in the case of the acidic β-nitro nitriles **3a–c**, this was followed by acidification with acetic acid or dilute perchloric acid to pH 3, and when $(t\text{-Bu})_2NO^{\bullet}$ was employed, a few milligrams of ascorbic acid was added with stirring to destroy the nitroxide. The water layer was extracted once more with ether, followed by several washings with water to eliminate HMPA, drying (Na_2SO_4), and removal of the solvent in vacuum (water pump) at ca. 30 °C. The ^1H NMR yields reported in Table I were estimated with a weighed, small proportion of DMF as an internal standard added to the crude product. The product was eventually recovered from the NMR tube thoroughly with ether for purification and complete identification as described in the following.

α-(Nitromethyl)isobutyronitrile (3a). $H_2C{=}NO_2K$ (from 132 mg of $MeNO_2$ and 261 mg of Me_3COK) and 250 μL of **1**

(5) Kornblum, N.; Cheng, L.; Davies, T. M.; Earl, G. W.; Holy, N. L.; Kerber, R. C.; Kestner, M. M.; Manthey, J. W.; Musser, M. T.; Pinnick, H. W.; Snow, D. H.; Stuchal, F. W.; Swiger, R. T. *J. Org. Chem.* **1987**, *52*, 196.

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(9) Reaction 7 should be endothermic as judged from pK_a values; see: Bordwell, F. G.; Bartmess, J. E.; McCollum, G. J.; Van Der Puy, M.; Vanier, N. R.; Matthews, W. S. *J. Org. Chem.* **1977**, *42*, 321. Bordwell, F. G.; Bartmess, J. E.; Hautala, J. A. *J. Org. Chem.* **1978**, *43*, 3113 and references therein.

(10) Zielstra, J. J.; Engberts, J. B. F. N. *Recl. Trav. Chim. Pays-Bas* **1974**, *93*, 11.

(11) The reductive dimerization of $Me_2C(Br)NO_2$ by malonate anions has been accounted for in a similar fashion: (a) van Tamelen, E. E.; Van Zyl, G. *J. Am. Chem. Soc.* **1949**, *71*, 835. (b) Russell, G. A.; Norris, R. K.; Panek, E. J. *J. Am. Chem. Soc.* **1971**, *93*, 5839. (c) For a two electron reduction interpretation of the formation of $Me_2C{=}NO_2^-$ from $Me_2C(X)NO_2$, see: Russell, G. A.; Jawdosiuk, M.; Makosza, M. *J. Am. Chem. Soc.* **1979**, *101*, 2355.

(12) Stevens, C. L. *J. Am. Chem. Soc.* **1948**, *70*, 165.

(13) Kornblum, N.; Taub, B.; Ungnade, H. E. *J. Am. Chem. Soc.* **1954**, *76*, 3209.

(14) Rogers, M. T.; Roberts, J. D. *J. Am. Chem. Soc.* **1946**, *68*, 843.

(15) Stevens, C. L.; Coffield, T. H. *J. Am. Chem. Soc.* **1951**, *73*, 103.

reacted in 7 mL of HMPA. Titration for bromide ion of the aqueous workup phase showed a 98% yield of the ion. Flash chromatography of the crude product using silica gel and benzene afforded 99 mg (36%) of TLC-pure **3a**: mp 39–40 °C (from petroleum ether/CH_2Cl_2; lit.[16] mp 42 °C); IR (KBr) 2245 (w), 1557 (s), 1379 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.52 (s, 6 H), 4.44 (s, 2 H).

The reaction in DMSO with the soluble K^+/18-crown-6 salt of the nitroalkane yielded 42% (by NMR) of **3a** and the theoretical amount of Br^-; **3a** was further identified by TLC.

α,α-Dimethyl-β-nitrobutyronitrile (3b). Reaction of $MeCH{=}NO_2K$ (from 83 mg of $EtNO_2$ and 129 mg of Me_3COK) with 125 μL of **1** in 3.5 mL of HMPA gave after recrystallization from petroleum ether/CH_2Cl_2 90 mg (57%) of **3b**: white crystals; mp 54.5–57 °C; IR (Nujol) 2240 (m), 1564 (s), 1365 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 and 1.43 (2 s, 6 H), 1.71 (d, J = 7 Hz, 3 H), 4.49 (q, J = 7 Hz, 1 H). Anal. Calcd for $C_6H_{10}N_2O_2$: C, 50.68; H, 7.10; N, 19.71. Found: C, 50.49; H, 7.15; N, 19.94.

α,α-Dimethyl-β-nitrononanonitrile (3c). Reaction between $CH_3(CH_2)_5CH{=}NO_2K$ (from 308 mg of 1-nitroheptane and 246 mg of Me_3COK) and 250 μL of **1** in 7 mL of HMPA yielded after Kugelrohr distillation at 195 °C (19 Torr) 276 mg (61%) of **3c**: colorless liquid; IR (neat) 2240 (w), 1558 (s), 1379 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.7–1.0 (br, 3 H), 1.0–2.6 (br absorption with 2 s at 1.43 and 1.47, 16 H), 4.33 (dd, J = 3 and 7 Hz, 1 H). Anal. Calcd for $C_{11}H_{20}N_2O_2$: C, 62.22; N, 9.51; N, 13.20. Found: C, 61.98; N, 9.54; N, 12.99.

α,α-Dimethyl-β-nitroisovaleronitrile (3d). $Me_2C{=}NO_2K$ (from 192 mg of Me_2CHNO_2 and 255 mg of Me_3COK) and 250 μL of **1** reacted in 7 mL of HMPA. Titration of the aqueous workup phase indicated a 96% yield of Br^-. By GC, **6** was detected in the crude β-nitro nitrile by comparison of the retention time with that of an authentic sample, prepared from $Me_2C(Br)NO_2$ and $Me_2C{=}NO_2K$ in DMSO;[11b] from the NMR yield of **3d** (82%) and the chromatographic peak areas for **3d** and **6**, assuming an equal detector response for both compounds, the yield of dimer amounted to 1%. On recrystallization from petroleum ether/CH_2Cl_2, 228 mg (68%) of **3d** was obtained, mp 191–192 °C (lit.[17] mp 195–196 °C), identified further by IR and ^1H NMR spectra.

The reaction in DMSO yielded 58 and 3% (by NMR) of **3d** and **6** respectively (further identified by GC) and 97% of Br^-. For the reaction in Figure 1, the formation of **3d** was followed by working up aliquots and analyzing by NMR.

α-(1-Nitrocyclohexyl)isobutyronitrile (3e). Reaction of potassium cyclohexanenitronate (from 140 mg of nitrocyclohexane and 131 mg of Me_3COK) with 125 μL of **1** in 3.5 mL of HMPA gave after recrystallization from petroleum ether/CH_2Cl_2 161 mg (76%) of **3e**, mp 105–106 °C (lit.[17] mp 108–109 °C), identified further by IR and ^1H NMR spectra.

Reaction of 1-Bromocyclopentanecarbonitrile with 2-Nitropropane Anion. $Me_2C{=}NO_2K$ (from 155 mg of Me_2CHNO_2 and 206 mg of Me_3COK) and 225 μL of the α-bromo nitrile reacted for 8 h in 6 mL of HMPA. By Kugelrohr distillation were collected two fractions at 105–150 °C (180 Torr; 140 mg) and 200 °C (9 Torr; 51 mg). The latter fraction was 1-(2-nitro-2-propyl)cyclopentanecarbonitrile (**4**, 16%), mp 43.5–44 °C (from petroleum ether; lit.[17] mp 44–45 °C), further identified by IR and ^1H NMR spectra. GC–MS of the first collected fraction showed that it was a mixture of 1-cyclopentenecarbonitrile (**5**, major component), **4**, Me_2CHNO_2, and unreacted α-bromo nitrile. **5**: mass spectrum (70 eV; relative intensity), m/e 93 (24, M^+), 66 (100, M^+ – HCN). In agreement with the presence of **5**, the IR spectrum of the mixture showed peaks at 3060, 2210, and 1612 cm^{-1}, the UV spectrum (EtOH) a maximum at 221 nm [**5**: lit.[18] λ_{max} (EtOH) 216 nm], and the ^1H NMR spectrum a multiplet at δ 6.6. By NMR analysis of the mixture the yield of **5** was 56%; isolation of the product was not attempted.

Reaction of 2-Bromo-2-nitropropane with Isobutyronitrile Anion. NH_2K was prepared under N_2 from 123 mg (3.15 mmol) of potassium and ca. 7 mL of liquid ammonia directly distilled from sodium into the reaction flask. The excess ammonia was then evaporated by a stream of N_2, 10 mL of HMPA was added, and N_2 was bubbled through the mixture for 10 min. This was followed by the addition of 275 μL (3.07 mmol) of freshly distilled Me_2CHCN and, after 30 min, of 325 μL (3.15 mmol) of $Me_2C(Br)NO_2$. After 5 h, the reaction mixture was worked up in the usual manner. The NMR spectrum of the crude product indicated the presence of **6** (12% yield), further identified by GC, which also showed the presence of traces of **3d** (<0.1%).

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Reaction of Secondary Acetylenic Bromides with Sodium Nitrite: Synthesis of 3,5-Alkyl(aryl)-4-nitroisoxazoles

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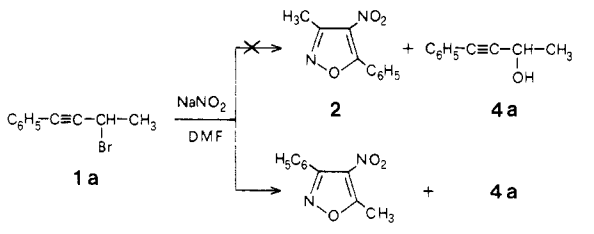
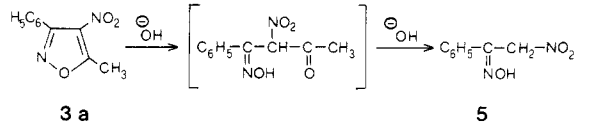
A few years ago, Mechkov and co-workers[1] reported a repetition, with minor modifications, of one of our previous experiments on the synthesis of 3-nitroisoxazoles[2] from primary acetylenic bromides and sodium nitrite in DMF. In addition, they reported that reaction of the secondary acetylenic bromide 3-bromo-1-phenyl-1-butyne (**1a**) under the same conditions gave 3-methyl-5-phenyl-4-nitroisoxazole (**2**). This structure seemed not to agree with our previous experiments, and upon reinvestigation we have found that the product is the isomeric 5-methyl-3-phenyl-4-nitroisoxazole (**3a**).



Our assignment of structure is based on the following: (1) the compound we prepared had the same IR and ^1H NMR spectra and melting point as those reported by Mechkov;[1] (2) our compound showed no melting point depression when mixed with an authentic sample of **3a** prepared in a different way;[3] (3) our compound gave a mass spectrum consistent with our structure; (4) the compound was hydrolyzed by sodium hydroxide to ω-nitroacetophenone oxime (**5**).[4]



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