Carbon–Carbon Bond Scission in an Aliphatic S_{RN} Reaction[1]

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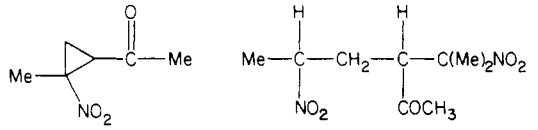
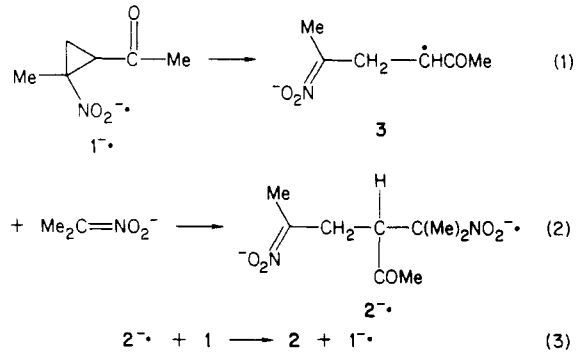
We have examined the photostimulated reactions of the nitrocyclopropane 1 with several nucleophiles. We have



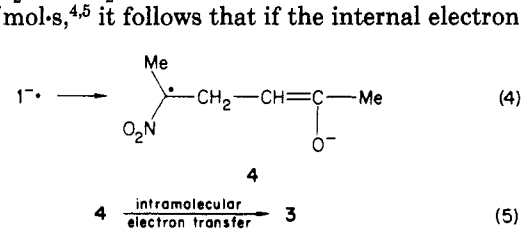
1 2

found that no reaction occurs with PhS^-, $PhSO_2^-$, or $(EtO_2C)_2CMe^-$ in Me_2SO or DMF (sunlamp irradiation, 40 °C). However, with $Me_2C{=}NO_2^-$, a clean reaction to form the ring-opened product 2 was observed in DMF. The reaction did not occur in the dark, and the photochemical reaction was completely inhibited by oxygen or by 10 mol % *t*-$Bu_2NO\cdot$ or *p*-dinitrobenzene (Table I).

If the reaction proceeds by the $S_{RN}1$ sequence,[2,3] the chain reaction will involve the propagation sequence of reactions 1–3. An alternative to the direct conversion of



$1^{-}\cdot$ to 3 (reaction 1) would be the two-step process of reactions 4 and 5. Since the trapping of primary alkyl radicals by $Me_2C{=}NO_2^-$ has a rate constant in the order of 10^5–10^6 L/mol·s,[4,5] it follows that if the internal electron



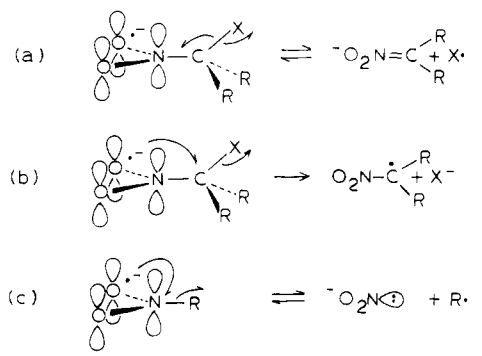
transfer (reaction 5) has a unimolecular rate constant of 10^7–10^8 s^{-1}, there will be no chance of trapping the intermediate 4.

If the conversion of $1^{-}\cdot$ occurs directly to 3, it represents a reversal of the trapping reaction of an alkyl radical by a nitronate anion (Scheme I, a). The usual decomposition

Table I. Reaction of 1 with $Me_2C{=}NO_2^-Li^+$ in DMF at 40 °C

conditions	yield by ^1H NMR, % 1	2
sunlamp, 14.5 h, N_2	27	58
dark, 14.5 h, N_2	92	0
sunlamp, 14.5 h, O_2	91	0
sunlamp, 14.5 h, 10 mol % *t*-$Bu_2NO\cdot$, N_2	93	0
sunlamp, 14.5 h, 10 mol % *p*-dinitrobenzene, N_2	90	0

Scheme I



of a nitroaliphatic radical anion involving the cleavage of a bond at the α-carbon atom occurs by process b of Scheme I (e.g., $1^{-}\cdot \rightarrow 4$).[2,3,6] It seems reasonable that both processes a and b should be allowed depending on the stability of X·, X^-, $R_2\dot{C}NO_2$ and $R_2C{=}NO_2^-$. Process c involving formation[7] or cleavage of a bond in the nodal plane of the NO_2 moiety is a recognized process for radical anions of α-nitro ketones and esters or of simple nitro compounds.[6,8,9] However, in the case of $1\cdot^-$, apparently process Ia becomes the preferred reaction pathway because of the relief in strain from opening of the cyclopropyl ring.

Ketone 1 underwent reduction to the cyclopropylcarbinol with $NaBH_4$ or with $Na_2S_2O_4$ in aqueous DMF at 110 °C without any evidence of the formation of ring-opened products. The lack of ring opening with $S_2O_4^{2-}$ was surprising since $S_2O_4^{2-}$ is known to yield $SO_2\cdot^-$ which readily reduces nitro compounds to radical anions.[10] It has even been suggested that the reduction of ketones by $S_2O_4^{2-}$ involves electron transfer to form the ketyl.[11] Cyclopropyl ketones are reduced by Li/NH_3 to yield ring-opened products,[12] but the ring opening may occur at the dianion rather than at the ketyl stage of reduction.[13] Since phenyl cyclopropyl ketone or nortricyclanone are reduced by $S_2O_4^-$ to the alcohols without any evidence of ring opening, it was concluded that reduction involved the nucleophilic addition of SO_2^{2-} or its equivalent to the carbonyl group.[14] Our results are most consistent with this interpretation or with the interpretation that $SO_2\cdot^-$

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adds as a nucleophile to the carbonyl group rather than undergoing electron transfer to either the carbonyl group or the nitro group of 1.

Experimental Section

2-Methyl-2-nitrocyclopropyl methyl ketone (1) was prepared in 71% yield by the reaction of 5-chloro-5-nitrohexan-2-one with NaH in DMF, bp 103 °C (25 torr).[15]

3-(2-Nitro-2-propyl)-5-nitro-2-hexanone (2) was isolated from the reaction of 4.6 mmol of 1 and 4.6 mmol of $Me_2C{=}NO_2Li$[16] in 10 mL of DMF after irradiation under N_2 for 22 h with a 275-W sunlamp ca. 16 cm from the reaction flask. Hydrolysis of the reaction mixture followed by ether extraction and Kugelrohr distillation, 85 °C (29 torr), gave 51% of 2: ^{1}H NMR ($CDCl_3$) δ 4.55 (m, 1), 2.82 (m, 2), 2.32 (s, 3), 1.90 (s, 3), 1.83 (s, 3), 1.50 (d, 3, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 204.59, 141.44, 132.27, 82.07, 35.26, 30.95, 22.89, 21.59, 18.59; IR (neat) 3000, 2980, 1690 (s), 1550 (s), 1460, 1400, 1360, 1300, 1195, 1145, 1105, 860 cm^{-1}; HRMS calcd for $C_9H_{15}O$ (P – HN_2O_4) 139.11229, found 139.11235; calcd for $C_8H_{12}NO_3$ (P – CH_3, HNO_2) 170.08172, found 170.08228.

1-(2-Methyl-2-nitrocyclopropyl)ethanol was prepared in 80% yield by reaction of 1 with $NaBH_4$ in Me_2CHOH at reflux for 1 h mp 89–90 °C; ^{1}H NMR ($CDCl_3$) δ 3.40 (m, 1), 1.83 (s, 3), 1.35 (d, 3); ^{13}C NMR ($CDCl_3$) δ 68.28, 64.38, 37.14, 23.10, 22.39, 14.87; IR (KBr) 3250 (br s), 2990, 1570 (s), 1450, 1390, 1370, 1350 (s), 1170, 1110, 1080 (s), 1060, 965, 880 (s), 860, 720; HRMS calcd for $C_5H_8NO_3$ (P – CH_3) 130.05042, found 130.05018.

The alcohol was also prepared by the reaction of 6 mmol of the ketone with 12 mmol of $Na_2S_2O_4$ and 24 mmol of $NaHCO_3$ in a mixture of 14 mL of DMF and 6 mL of H_2O at 110 °C for 2 h. Hydrolysis and CH_2Cl_2 extraction gave a crude product that was analyzed by ^{1}H NMR as 29% of recovered ketone and a 45% yield of 1-(2-methyl-2-nitrocyclopropyl)ethanol.

Registry No. 1, 96194-32-0; 2, 96194-33-1; $Me_2C{=}NO_2^-$, 20846-00-8; 1-(2-methyl-2-nitrocyclopropyl)ethanol, 96194-34-2.

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Synthesis of 2,2-Disubstituted *N*-Nitrosooxazolidines wiih Nitrosyl Chloride†

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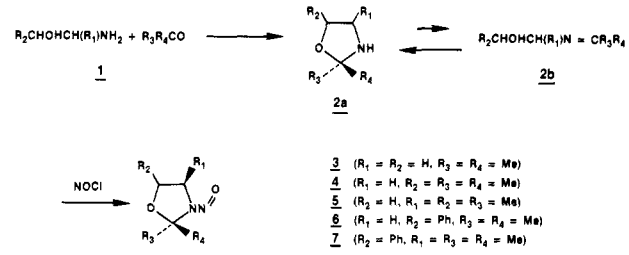
Recently, we reported a method in which α-nitrosaminoalkyl ethers serve as α-primary amino carbanion synthons.[1] β-Alkanolamines form *N*-nitrosooxazolidines, with a substituent on the C-2 position, in the presence of aldehydes and nitrous acid.[2,3] These compounds, which are cyclic congeners of α-nitrosaminoalkyl ethers, have acidic protons on the C-4 position and can serve as umpoled synthons of β-alkanolamines.[3,4] However, the single substitution on the C-2 position does involve some problems. One of these is the existence of 2-substituted nitrosooxazolidines as a mixture of *E* and *Z* rotamers,[3] which

Scheme I



leads to complications in the nuclear magnetic resonance analysis of the products. Moreover, no regioselectivity of alkylation is observed in the reaction, and multiple alkylation occurs to a large extent.[4] To overcome some of these problems oxazolidines with symmetrical 2,2-disubstitutions were prepared. That is, symmetrical ketones were used in lieu of aldehydes during the condensation reaction with the alkanolamine. The standard nitrous acid method used for the high yield syntheses of nitrosooxazolidines[2,3] with mono, or no, substitution at C-2 gives either low yields or no production of *N*-nitroso 2,2-disubstituted oxazolidines. Even when the compound is formed in low yields, there is always contamination with nitroso compounds derived from self-condensation of the parent amine and degradation products.[3]

We report here an efficient preparation of *N*-nitroso 2,2-disubstituted oxazolidines via in situ condensation of a primary alkanolamine (1) with a ketone in methylene chloride–anhydrous potassium carbonate, followed by nitrosation with nitrosyl chloride. The condensation takes place within 6 h at room temperature to give an oxazolidine (**2a**)-Schiff base (**2b**) equlibrium mixture, the ratio **2a**:**2b** depending on the structure. However, the oxazolidine is always the predominant form[5] —see Experimental Section. Nitrosyl chloride is added to the reaction mixture at 0 °C and after minimal workup the product is isolated and distilled.[6] Only a single nitroso compound is detected in the reaction, and the yields are fairly high (Scheme I). Here, the potassium carbonate serves a dual purpose—as a water scavenger in the condensation reaction and as an hydrochloric acid trap during nitrosation.

Condensation of ethanolamine and acetone, followed by nitrosation with nitrosyl chloride at 0 °C gave on workup and purification a 72% yield of *N*-nitroso-2,2-dimethyloxazolidine (**3**). *N*-Nitroso-2,2,3-trimethyloxazlidine (**4**) was obtained from 1-amino-2-propanol in 75% yield. This is a vast improvement over the 11% yield reported previosly[3] from nitrosation in aqueous media. Other yields were *N*-nitroso-2,2,4-trimethyloxazolidine (**5**, 58%), *N*-nitroso-2,2-dimethyl-5-phenyloxazolidine (**6**, 73%), and *N*-nitroso-2,2,4-trimethyl-5-phenyloxazolidine (**7**, 72%).

The lack of byproducts in these reactions indicates that the small amounts of Schiff bases present in the mixtures are also converted to the nitrosooxazolidine. It is well-documented that imines react with nitrosyl chloride to form the corresponding α-chloronitrosamine, where the chloro derivative undergoes rapid nucleophilic displacement by methanol and acetic acid giving α-methoxy- and

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