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Synthesis of Nitrocyclopropanes by Cyclization of γ-Chloro-γ-nitro Carboxylic Esters and Derivatives[1]

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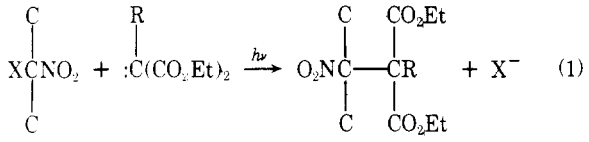
Michael addition of the anions of 1-chloro-1-nitro alkanes to α,β-unsaturated esters, nitriles, or ketones yields γ-chloro-γ-nitro esters, nitriles, or ketones, which in the presence of base undergo cyclization to form the 2-alkyl-2-nitrocyclopropanecarboxylic ester, cyclopropanenitrile, or cyclopropyl methyl ketone, in which the nitro group and the ester, nitrile, or ketone functions are in a trans arrangement. The reaction appears to proceed via $S_{RN}i$ substitution.

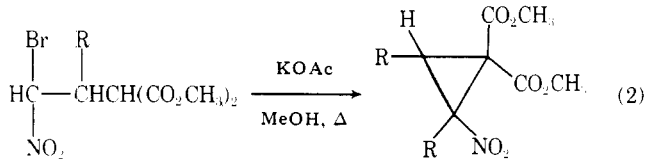
A number of 2-substituted-2-nitropropanes react with carbanions such as ethyl malonate anions to form a new carbon–carbon bond by a radical chain process[2,3] which has been labeled $S_{RN}1$ (eq 1).[4] The $S_{RN}1$ process should be capable of



(1)

X = Cl, NO_2, $ArSO_2$

leading to cyclized products with the proper substrates. We were thus intrigued by the reports of Kohler[5] and Perekalin[6] that nitrocyclopropanes could be formed as shown in eq 2 and 3.[7] Shechter has also shown that nitrocyclopropanes can be



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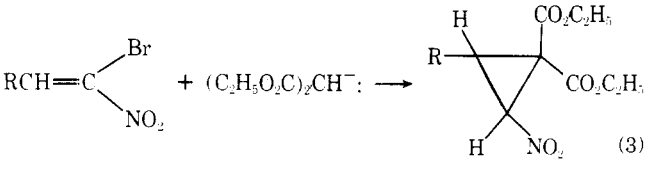
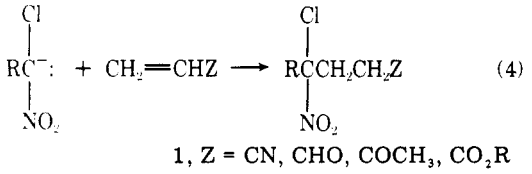


(3)

formed by the addition of sulfoxonium ylides to 1-nitro alkenes.[8]

We have synthesized a series of 4-chloro-4-nitro esters, nitriles, ketones, and aldehydes (1) by the Michael addition of 1-chloro-1-nitroethane and -propane to the appropriate Michael acceptors (reaction 4).[9] The Michael reaction with methyl methacrylate gave low yields, and methyl 4-chloro-2-methyl-4-nitrovalerate was prepared by the Michael addition of nitroethane to methyl methacrylate followed by chlorination in basic solution. Yields of isolated products are shown in Table I.



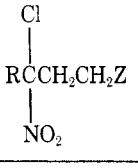
(4)

1, Z = CN, CHO, $COCH_3$, CO_2R

The Michael adducts of Table I are versatile intermediates in organic synthesis. The aldehydes can be reduced to the corresponding alcohols by sodium borohydride, while the esters can be hydrolyzed to the free acids which can be converted to the corresponding alkyl bromides by the Hunsdiecker reaction.

Compounds **1a,b,c,f,g,h** were converted to nitrocyclopropanes in the presence of strong bases. The esters were cyclized

Table I. Michael Adducts



	R	Z	yield, %	boiling point °C (torr)
1a	CH_3	CN	74	111 (3)
1b	C_2H_5	CN	68	103 (0.8)
1c	CH_3	$COCH_3$	74	84 (0.8)
1d	CH_3	CHO	70	65 (0.2)
1e	C_2H_5	CHO	73	75 (0.5)
1f	CH_3	CO_2Et	52	85 (1)
1g	C_2H_5	CO_2Et	60	85 (1)
1h[a]	CH_3	CO_2Me	79	89 (2.5)

[a] $CH_3C(Cl)(NO_2)CH_2CH(CH_3)CO_2CH_3$.

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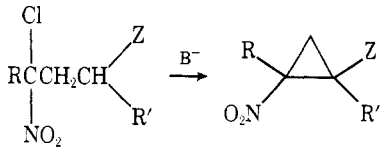
Table II. Nitrocyclopropanes Isolated in the Reaction



nitrocyclopropane	R	R′	Z	cyclization condition	yield %	boiling point, °C (torr)
2a	CH_3	H	CN	NaOH (aq)/CH_3CN/R_4N^+ Cl^-	71	69 (1)
2b	C_2H_5	H	CN	NaOH (aq)/CH_3CN/R_4N Cl^-	74	79 (2)
2c	CH_3	H	$COCH_3$	NaH/DMF	70	103 (25)
2f	CH_3	H	$CO_2C_2H_5$	NaH/DMF	53[a]	112 (25)
2g	C_2H_5	H	$CO_2C_2H_5$	NaH/DMF	64	125 (30)
2h	CH_3	CH_3	CO_2CH_3	NaH/DMF	48	115 (35)

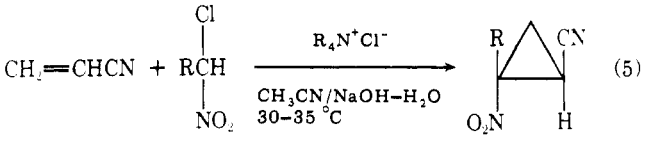
[a] An additional 12% of ethyl methylenecyclopropanecarboxylate (**5**) was isolated.

Table III. ^1H NMR Spectra (60 MHz, CCl_4/Me_4Si) of Nitrocyclopropanes

	chemical shifts, δ			coupling constants, Hz		
	H_X	H_Y	H_Z	J_{XY}	J_{XZ}	J_{YZ}
2a	1.55 (t)	2.2 (d of d)	2.70 (d of d)	6.5	6.5	11.0
2b	1.53 (t)	2.0–2.5 (m)[a]	2.71 (d of d)	6.5	7.0	10.5
2c	1.65 (s, d of d)[b]	2.0 (d of d)	3.08 (d of d)	8.0	5.0	10.0
2f	1.53 (d of d)	2.1 (d of d)	2.84 (d of d)	5.0	7.5	10.0
2g	1.56 (d of d)	1.9–2.5 (m)[a]	2.86 (d of d)	6.0	7.0	10.0
2h	1.69 (s, d)[b]	2.0 (d)		6.0		

[a] Multiplet of intensity 3 produced by overlap of H_Y and methylene group of the ethyl substituent. [b] Multiplet of intensity 4 from overlap of methyl group and H_X.

by treatment with sodium hydride in DMF. The nitriles gave low yields (20%) of cyclopropanes when treated with sodium amide in liquid ammonia, but over 70% of cyclized product in a two-phase system of acetonitrile and 40% aqueous sodium hydroxide in the presence of catalytic amounts of triethylbenzylammonium chloride. In fact, with acrylonitrile the Michael addition and subsequent cyclization could be performed in one step using phase-transfer catalysis (eq 5).[10] In

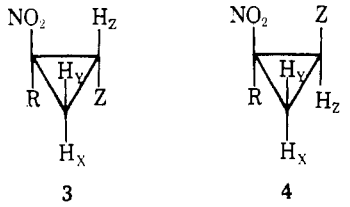


(5)

2a, R = CH_3; 56% yield
b, R = C_2H_5; 60% yield

the case of the ketone **1c**, essentially the same yields of cyclized products (~70%) were obtained with sodium hydride in THF or Me_2SO or by the phase-transfer process. The isolated nitrocyclopropanes are summarized in Table II.

Only a single stereoisomer (**3**) was isolated in the cyclization reaction as judged by GLC and ^1H NMR spectra.[11] On the basis of the NMR spectra, the stereochemistry has been assigned as a trans arrangement of the nitro group and the functional group Z. The two diastereomers **3** and **4** would be expected to have considerably different values of J_{YZ}. In cyclopropane systems the coupling constant between cis protons are typically in the range of 7 to 11 Hz, whereas trans protons have J = 3–8 Hz.[12] For cyclopropanes **2a–h** the values of J_{YZ} were all between 10 and 11 Hz with $J_{YX} \cong J_{XZ} \cong 6.5$ Hz. The proton H_Z absorbed at lower field (δ 2.7–3.1), whereas H_Y absorbed at intermediate field (δ ≅ 2) and H_X absorbed at high field (δ 1.5–1.6). The observed chemical shifts and coupling constants are listed in Table III. In the case of **2a–g**, H_Z is epimerizable and perhaps only the thermodynamically more stable isomer of **2** is observed. However, for **2h** only a single isomer was observed.

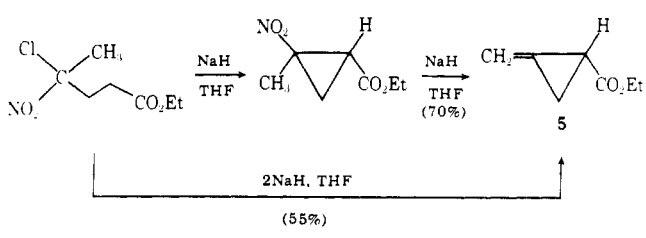


3 **4**

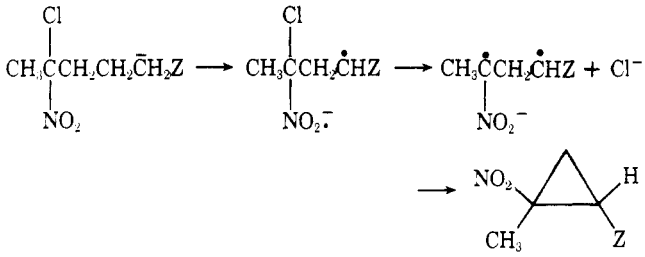
In the presence of excess base, the 1-methyl-1-nitrocyclopropanes can eliminate nitrous acid to form the methylenecyclopropanes (Scheme I).

We observed no light effect on the yield of the nitrocyclopropanes. This and the high stereoselectivity of the reaction make it appear as if the cyclization reaction is occurring by S_Ni substitution. However, it is difficult to completely exclude the analogous $S_{ET}i$ process (Scheme II).

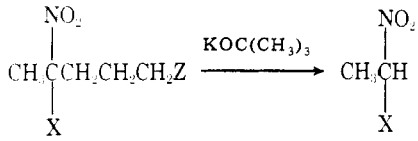
Scheme I



Scheme II



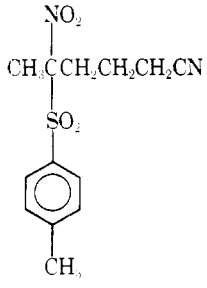
Previous work in bimolecular reactions of 2-substituted-2-nitroalkanes has indicated that 2,2-dinitropropane or 2-nitro-2-(*p*-tolylsulfonyl)propane radical anions decompose by the loss of nitrite and sulfinate anions, respectively.[2,3] We thus synthesized by Michael addition compounds **6a–c** with



6a, X = *p*-$CH_3C_6H_4SO_2$; Z = CN
b, X = *p*-$CH_3C_6H_4SO_2$; Z = $COCH_3$
c, X = NO_2; Z = CN

the expection that conversion to the nitrocyclopropane would be a strong indication of the occurrence of the $S_{ET}i$ or $S_{RN}1$ processes. However, all attempts at cyclization in basic solution for **6** have led to reverse Michael reactions without detectable amounts of nitrocyclopropane formation.

5-Nitro-5-(*p*-tolylsulfonyl)capronitrile (**7**) was synthesized to avoid the problem of the reverse Michael reaction. However,



7

irradiation of **7** in the presence of base failed to form any detectable amounts of a cyclobutane and gave products still containing the sulfonyl group. The lack of formation of cyclobutane derivatives in these reactions, but the easy formation of cyclopropanes, again seems most consistent with a S_Ni reaction rather than a $S_{ET}i$ or $S_{RN}1$ process.

Experimental Section

4-Chloro-4-nitrocapronitrile (1b). To a stirred mixture of acetonitrile (10 mL), 40% aqueous sodium hydroxide solution (10 mL), and triethylbenzylammonium chloride (1 g) cooled in an ice bath was added a solution of 24.7 g (0.2 mol) of 1-chloro-1-nitropropane and 13.4 g (0.25 mol) of acrylonitrile in 20 mL of acetonitrile dropwise over a 1-h period at a rate that maintained a temperature of 15–20 °C. The mixture was subsequently stirred for 1 h at 20 °C, diluted with water, and extracted with methylene chloride. The product was purified by vacuum distillation through a short Vigreux column to yield 24 g (68%) of **1b**: bp 100–103 °C (0.8 torr); n^{25}_D 1.4669; ^{1}H NMR (CCl_4) δ 0.9–1.2 (3 H), 2.18–3.04 (6 H); IR (neat) 1562 and 1324 (NO_2), 2247 (CN) cm^{-1}.

Anal. Calcd for $C_6H_9ClN_2O_2$: C, 40.81; H, 5.09; N, 15.84. Found: C, 40.9; H, 5.2; N, 15.3.

4-Chloro-4-nitrovaleronitrile (1a). From 21.9 g (0.2 mol) of 1-chloro-1-nitroethane and 13.4 g (0.25 mol) of acrylonitrile, according to the preceding procedure, was obtained 24 g (74%) of **1a**: bp 111 °C (3 torr); n^{25}_D 1.4656; NMR δ 2.14 (s, 3 H), 2.4–2.9 (m, 4 H); IR 1562 and 1328 (NO_2), 2252 (CN) cm^{-1}.

Anal. Calcd for $C_5H_7ClN_2O_2$: C, 36.94; H, 4.31; N, 17.2. Found: C, 37.1; H, 4.5; N, 16.7.

5-Chloro-5-nitrohexan-2-one (1c). A solution of 1-chloro-1-nitroethane (27.5 g, 0.25 mol) and methyl vinyl ketone (19 g, 0.27 mol) in 100 mL of acetonitrile was cooled to 0 °C, and 4 mL of Triton B (40% in methanol) was added in small portions at such a rate that the temperature was maintained at 15–20 °C. The reaction was strongly exothermic, and effective cooling was necessary. After about 1 h, the addition was completed and the mixture was left for 2 h at 15–20 °C before treatment with diluted hydrochloric acid and ice. The product was extracted with methylene chloride and vacuum distilled to yield 33 g (74%) of **1c**: bp 84 °C (0.8 torr); n^{25}_D 1.4587; ^{1}H NMR δ 2.1–2.2 (m, 6 H), 2.6 (s, 4 H).

Anal. Calcd for $C_6H_{10}ClNO_3$: C, 40.13; H, 5.56; N, 7.78. Found: C, 40.1; H, 5.5; N, 7.7.

4-Chloro-4-nitropentanal (1d). 1-Chloro-1-nitroethane (22 g, 0.2 mol) and acrolein (15 mL, ~0.21 mol) were dissolved in 50 mL of acetonitrile, and the solution was cooled to 0 °C. To this solution was added 40% Triton B in methanol (2.5 mL) in small portions during 1 h. The addition of each portion resulted in an exothermic reaction. The mixture was efficiently cooled so that the temperature was maintained between 3 and 8 °C throughout the reaction. The green solution was then poured onto ice and acidified to pH 4, and the product was extracted with methylene chloride. Vacuum distillation gave 23 g (70%) of **1d**: bp 65 °C (0.2 torr); ^{1}H NMR δ 2.1 (s, 3 H), 2.4–2.9 (m, 4 H), 9.6 (s, 1 H); IR (neat) 1725 and 2725 (CHO), 1565 and 1325 (NO_2) cm^{-1}.

4-Chloro-4-nitrohexanal (1e). 1-Chloro-1-nitropropane (13.4 g, 0.08 mol) and acrolein (0.12 mol), according to the preceding procedure, yielded 13.2 g (73%) of **1e**, bp 75 °C (0.5 torr). In order to obtain high yields of the adducts, the conditions must be strictly maintained. Slight changes in temperature and time result in a dramatic decrease in the yield.

Ethyl 4-Chloro-4-nitrovalerate (1f). To a stirred mixture of 10.9 g of 1-chloro-1-nitroethane (0.1 mol) and 13 g of ethyl acrylate (0.13 mol) was added triethylamine (7 mL) at such a rate that the temperature remained between 50 and 60 °C (exothermic reaction). After the addition of triethylamine was completed (1 h), the mixture was left for 7 h and then treated with diluted hydrochloric acid and extracted with methylene chloride. The product was purified by vacuum distillation to yield 11 g of **1f** (52%): bp 85 °C (1 torr); n^{25}_D 1.4502; ^{1}H NMR δ 1.1–1.4 (t, 3 H), 2.1 (s, 3 H), 2.2–2.8 (m, 4 H), 3.9–4.3 (q, 2 H); IR 1739 (C=O), 1562 and 1333 (NO_2) cm^{-1}.

Anal. Calcd for $C_7H_{12}ClNO_4$: C, 40.12; H, 5.71; N, 6.68. Found: C, 40.3; H, 5.9; N, 6.5.

Ethyl 4-Chloro-4-nitrocaproate (1g). From 24.7 g (0.2 mol) of 1-chloro-1-nitropropane and 22 g (0.22 mol) of ethyl acrylate was obtained 27.5 g (60%) of **1g**: bp 85 °C (0.5 torr); n^{25}_D 1.4512; NMR δ 0.9–1.4 (m, 6 H), 2.1–2.9 (m, 6 H), 3.9–4.3 (q, 2 H); IR 1724 (C=O), 1562 and 1333 (NO_2) cm^{-1}

Anal. Calcd for $C_8H_{14}ClNO_4$: C, 42.97; H, 6.26; N, 6.26. Found: C, 42.8; H, 6.2; N, 6.2.

Methyl 4-Chloro-2-methyl-4-nitrovalerate (1h). Methyl 2-methyl-4-nitrovalerate (17.5 g, 0.1 mol, obtained by Michael addition of methyl methacrylate to nitroethane in the presence of sodium methoxide) was dissolved in 100 mL of 2 M methanolic sodium methoxide. The solution was cooled, 100 g of ice was added, and chlorine was passed into the solution at a temperature below 0 °C. After saturation with chlorine, the mixture was diluted with cold water and extracted with methylene chloride. The product was purified by vacuum distillation to yield 16.5 g (79%) of **1h**: bp 89 °C (2.5 torr); n^{25}_D 1.4491; NMR δ 1.17–1.35 (d, 3 H), 2.01 (s, 3 H), 2.15–3.05 (m, 3 H), 3.65 (s, 3 H).

Anal. Calcd for $C_7H_{12}ClNO_4$: C, 40.12; H, 5.71; N, 6.68. Found: C, 40.2; H, 5.8; N, 6.6.

4-Chloro-4-nitrohexanol. 4-Chloro-4-nitrohexanal (9 g, 0.05 mol) was dissolved in ethanol (25 mL) and cooled to 5 °C. A solution of sodium borohydride (0.51 g, 0.0135 mol) in 5 mL of ethanol was added dropwise with cooling of the reaction mixture in order to keep the temperature at 10 °C. The mixture was left for 1 h at room temperature and diluted with water. The product was extracted with benzene and vacuum distilled to yield 7.5 g (83%) of product, bp 92 °C (0.4 torr).

Anal. Calcd for $C_8H_{12}ClNO_3$: C, 39.66; H, 6.66; N, 7.71. Found: C, 39.4; H, 6.8; N, 7.7.

4-Chloro-4-nitropentanol. 4-Chloro-4-nitropentanal (13.5 g, 0.081 mol) and sodium borohydride (1.1 g, 0.04 mol), according to the preceding procedure, yielded 10.3 g (78%) of 4-chloro-4-nitropentanol: bp 93 °C (0.8 torr); n^{25}_D 1.4662.

Anal. Calcd for $C_5H_{10}ClNO_3$: C, 35.85; H, 5.96; N, 8:47. Found: C, 35.8; H, 6.1; N, 8.4.

1-Bromo-3-chloro-3-nitropentane. Ethyl 4-chloro-4-nitrocaproate (22.4 g, 0.1 mol) was refluxed in 120 mL of methanol containing 10 mL of water (6 g) and NaOH for 20 min. The resulting solution was evaporated and the residue dissolved in 100 mL of water. The solution was purified with charcoal and, after cooling, acidifed with 50% aqueous hydrochloric acid. The product was extracted with benzene to yield, after evaporation, 18.5 g of crude acid which was used without further purification. The acid was dissolved in dilute sodium hydroxide (4.1 g in 30 mL of water and 30 mL of methanol), and the resulting solution was poured with vigorous stirring into a solution of

silver nitrate (20 g, 0.12 mol) in 50 mL of water. The resulting thick suspension was left in the dark for 24 h before filtration. The precipitate was washed with methanol and then acetone and dried under vacuum over P_2O_5. The silver salt in 300 mL of carbon tetrachloride was refluxed for 0.5 h. After 100 mL of the carbon tetrachloride was removed by distillation, the residue was cooled to room temperature and 16 g of bromine in 30 mL of carbon tetrachloride was added immediately. After a few minutes, a strong exothermic reaction occurred with copious evolution of gas. When the reaction ceased, the mixture was refluxed for 10 min before cooling. The precipitate was filtered and washed three times with small portions of carbon tetrachloride. The combined filtrates were washed with a cold solution of sodium sulfite and water and dried, and the solvent was evaporated. Vacuum distillation of the residue gave 15 g (65%, calculated on the ester used) of product: bp 109 °C (33 torr); n^{25}_D 1.4916; NMR δ 0.95–1.25 (t, 3 h), 2.15–3.7 (m, 6 H).

Anal. Calcd for $C_5H_9BrClNO_2$: C, 26.04; H, 3.91; N, 6.05. Found: C, 26.2; H, 4.2; N, 6.0.

1-(Bromobutane)-3-chloro-3-nitrobutane. Ethyl 4-chloro-4-nitrovalerate, according to the preceding procedure, yielded 63% of material: bp 98 °C (25 torr); n^{25}_D 1.4946; NMR δ 2.15 (s, 3 H), 2.64–3.02 (m, 2 H), 3.2–3.6 (m, 2 H).

Anal. Calcd for $C_4H_7BrClNO_2$: C, 22.21; H, 3.24; N, 6.46. Found: C, 22.6; H, 3.4; N, 6.4.

2-Methyl-2-nitrocyclopropanenitrile (2a). To a stirred mixture of acetonitrile (5 mL), 50% aqueous NaOH (5 mL), and triethylbenzylammonium chloride (0.8 g) was added a solution of 1-chloro-1-nitroethane (8.2 g, 0.075 mol) and acrylonitrile (4.5 g, 0.085 mol) in acetonitrile (5 mL) dropwise at such a rate that the temperature was maintained at 30–35 °C. After the addition was completed (45 min), the reaction was held at 30–35 °C for 0.5 h, diluted with cold water, and extracted with methylene chloride. The product was purified by vacuum distillation to yield 5.4 g (56%) of **2a**: bp 69 °C (1 torr); n^{25}_D 1.4707; ^{1}H NMR (see Table III); IR (neat) 2247 (CN), 1545 and 1355 (NO_2) cm^{-1}.

Anal. Calcd for $C_5H_6N_2O_2$: C, 47.62; H, 4.8; N, 22.21. Found: C, 48.0; H, 4.5; N, 21.8.

The same product was obtained in 71% yield when 4-chloro-4-nitrovaleronitrile dissolved in acetonitrile was stirred with 50% aqueous sodium hydroxide and triethylbenzylammonium chloride.

2-Ethyl-2-nitrocyclopropanenitrile (2b). The same procedure employed for 2-methyl-2-nitrocyclopropanenitrile yielded 60 (direct synthesis from 1-chloro-1-nitropropane) and 74% (by cyclization of 4-chloro-4-nitrocapronitrile) of **2b**: bp 79 °C (2 torr); n^{25}_D 1.4678; NMR (see Table III).

Anal. Calcd for $C_6H_8N_2O_2$: C, 51.42; H, 5.75; N, 19.99. Found: C, 51.5; H, 5.8; N, 20.0.

2-Methyl-2-nitrocyclopropyl Methyl Ketone (2c). To a solution of 4-chloro-4-nitrohexan-2-one (5.4 g, 0.03 mol) in 35 mL of DME was added sodium hydride (0.75 g, 0.031 mol) in small portions at 40 °C over a 1-h period. During the addition an exothermic reaction occurred with evolution of hydrogen. Vacuum distillation yielded 3 g (70%) of **2c**: bp 103 °C (25 torr); n^{25}_D 1.4640; NMR (see Table III); IR (neat) 1709 (C=O), 1543 and 1351 (NO_2) cm^{-1}.

Anal. Calcd for $C_6H_9NO_3$: C, 50.35; H, 6.34; N, 9.79. Found: C, 50.4; H, 6.4; N, 9.7.

Ethyl 2-Methyl-2-nitrocyclopropanecarboxylate (2f). To a stirred deoxygenation solution of ethyl 4-chloro-4-nitrovalerate (7.2 g, 0.035 mol) in 50 mL of DMF was added in small portions sodium hydride (0.9 g, 0.037 mol). The temperature of the mixture increased to 50 °C with the evolution of hydrogen. After 1.5 h at 50 °C, the mixture was poured on ice and extracted with hexane. Vacuum distillation gave two fractions: bp 58–60 °C (25 torr), 0.6 g; bp 110–114 °C (25 torr), 3 g (53% of **2f**). Redistillation of the higher boiling fraction gave **2f**: bp 112 °C (25 torr); n^{25}_D 1.4522; NMR (see Table III); IR (neat) 1733 (C=O), 1550 and 1355 (NO_2) cm^{-1}.

Anal. Calcd for $C_7H_{11}NO_4$: C, 48.55; H, 6.40; N, 8.09. Found: C, 48.4; H, 6.33; N, 8.0.

Ethyl Methylenecyclopropanecarboxylate. From ethyl 4-chloro-4-nitrovalerate (4.2 g, 0.02 mol) and sodium hydride (0.92 g, 0.04 mol), following the preceding procedure, 1.4 g (55%) of ethyl methylenecyclopropanecarboxylate was obtained: bp 153 °C (58 °C at 25 torr); n^{25}_D 1.4454 (lit.[12] bp 152–154 °C, n^{25}_D 1.4447); NMR δ 1.1–1.4 (t, 3 H), 1.45–1.93 (m, 2 H), 2–2.33 (m, 1 H), 3.88–4.3 (q, 2 H), 5.35–5.53 (m, 2 H).

This product was also obtained in 70% yield by action of sodium hydride in DMF on ethyl 2-methyl-2-nitrocyclopropanecarboxylate.

Ethyl 2-Ethyl-2-nitrocyclopropanecarboxylate (2g). Ethyl 4-chloro-4-nitrocapronate (4.5 g, 0.02 mol) and sodium hydride (0.46 g, 0.02 mol) were stirred in 40 mL of DMF at 70 °C for 2 h. After being cooled the mixture was poured into cold water and extracted with hexane. Vacuum distillation gave 2.4 g (64%) of **2g**: bp 125 °C (30 torr); NMR (see Table III).

Anal. Calcd for $C_8H_{13}NO_4$: C, 51.33; H, 7.00; N, 7.48. Found: C, 51.5; H, 7.4; N, 7.8.

Methyl 1,2-Dimethyl-2-nitrocyclopropanecarboxylate (2h). Methyl 4-chloro-2-methyl-4-nitrovalerate (7.3 g, 0.035 mol) in 50 mL of DMF was mixed with sodium hydride (0.9 g, 0.037 mol), and the mixture was warmed. At about 40 °C an exothermic reaction occurred with a sudden rise in temperature to 55 °C with gas evolution. The reaction mixture was held at 40 °C for 6 h and then poured on water and extracted with hexane. Vacuum distillation gave 2.8 g (48%) of **2h**: bp 115 °C (35 torr); n^{25}_D 1.4503; IR (neat) 1725 (C=O), 1538 and 1351 (NO_2) cm^{-1}.

Anal. Calcd for $C_7H_{11}NO_4$: C, 48.55; H, 6.40; N, 8.09. Found: C, 48.6; H, 6.4; N, 8.0.

Synthesis and Reverse Michael Reaction of 4-Nitro-4-(*p*-tolylsulfonyl)butyronitrile (6a).[13] α-Nitroethyl *p*-tolyl sulfone[13] (4.33 g, 0.02 mol) and acrylonitrile (1.21 g, 0.022 mol) in 30 mL of ethanol were treated with 0.4 mL of triethylamine, and the solution was refluxed for 3.5 h. Acidification with acetic acid yielded 4.0 g (78%) of **6a**: mp 111–113 °C; ^{1}H NMR δ 1.96 (s, 3 H), 2.5 (s, 3 H), 2.5–2.9 (m, 4 H), 7.35–7.85 (m, 4 H).

Anal. Calcd for $C_{11}H_4N_2O_4S$: C, 51.05; H, 5.00; N, 9.92; S, 11.37. Found: C, 51.23; H, 5.08; N, 9.91; S, 11.26.

Reverse Michael Reaction for 6b. The keto sulfone[14] (1.0 g, 3.3 mol) and potassium *tert*-butoxide (0.45 g, 4 mol) in Me_2SO gave, after irradiation for 2 h followed by acidification and chloroform extraction, 1.1 g of an oil which by ^{1}H NMR was shown to contain 0.7 g (95%) of α-nitroethyl *p*-tolyl sulfone. The same result was obtained for a reaction conducted for 4.5 h at −50 °C.

4-(*p*-Tolylsulfonyl)-4-nitro-1-cyanopentane (7). The 4-(*p*-tolylsulfonyl)-4-nitro-1-pentanol was converted to the mesylate by methanesulfonyl chloride in methylene chloride/triethylamine. The mesylate in refluxing acetone reacted with sodium iodide over a 2-h period to yield the iodide of which 4 g (0.1 mol) was dissolved in a mixture of 150 mL of ethanol and 35 mL of chloroform. Sodium cyanide (5 g, 0.1 mol) in 50 mL of water was added, and the mixture was refluxed for 1 h. The solution was evaporated to 50 mL under vacuum and extracted with chloroform to give 2.2 g of product, which was eluted from silica gel with benzene to give **7**: mp 93.5–95 °C; ^{1}H NMR δ 1.3–1.7 (m, 4 H), 1.9 (s, 3 H), 2.35 (t, 2 H), 2.5 (s, 3 H), 7.3–7.8 (m, 4 H); IR 1160, 1340 (SO_2), 1350, 1560 (NO_2), 2240 (C≡N) cm^{-1}.

Anal. Calcd: C, 52.69; H, 5.44. Found: C, 52.8; H, 5.4.

Registry No.—**1a**, 69102-16-5; **1b**, 69102-17-6; **1c**, 69102-18-7; **1d**, 69102-19-8; **1e**, 69102-20-1; **1f**, 69102-21-2; **1g**, 69102-22-3; **1h**, 69102-23-4; **2a**, 69102-24-5; **2b**, 69102-25-6; **2c**, 69102-26-7; **2f**, 69102-27-8; **2g**, 69102-28-9; **2h**, 69102-29-0; **6a**, 69102-30-3; **6b**, 52260-66-9; **7**, 69102-31-4; 1-chloro-1-nitropropane, 600-25-9; acrylonitrile, 107-13-1; 1-chloro-1-nitroethane, 598-92-5; methyl vinyl ketone, 78-94-4; acrolein, 107-02-8; ethyl acrylate, 140-88-5; methyl 2-methyl-4-nitrovalerate, 16507-04-3; 4-chloro-4-nitrohexanol, 69102-32-5; 4-chloro-4-nitrohexanal, 69102-20-1; 4-chloro-4-nitropentanol, 69102-33-6; 4-chloro-4-nitropentanal, 69102-19-8; 1-bromo-3-chloro-3-nitropentane, 69102-34-7; 1-(bromobutane)-3-chloro-3-nitrobutane, 69102-35-8; ethyl methylenecyclopropancarboxylate, 18941-94-1; α-nitroethyl *p*-tolyl sulfone, 51351-86-1; 4-(*p*-tolylsulfonyl)-4-nitro-1-pentanol, 69102-36-9.

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Cationic Polar Cycloaddition of Cyclopropenes

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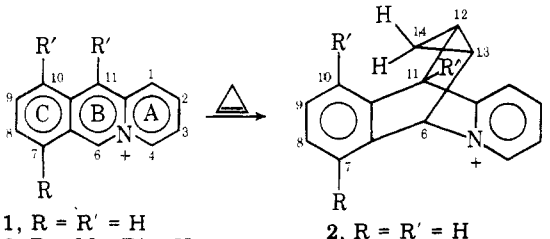
Cyclopropene undergoes polar 1,4-cycloaddition rapidly and stereoselectively at the 6 and 11 positions of the acridizinium cation. The cycloaddition of 1-methylcyclopropene to the acridizinium ion or its homologues is likewise stereoselective and shows a marked preference (80–90%) for that regioisomer which would be expected if the initial interaction were an electrophilic attack of the acridizinium cation on 1-methylcyclopropene.

Since the discovery[1] that the acridizinium (benzo[*b*]quinolizinium) ion (1) will undergo 1,4-cycloaddition with certain alkenes, this ion and its derivatives have been established as the most useful substrates for the study of cationic polar cycloaddition.[2,3] Characteristic of such polar cycloadditions is not only inverse electron demand[4,5] but also regioselectivity[3,4,6] that is in nearly all cases 100% complete as well as significant stereoselectivity.[5,7-9] Each of these phenomena has been attributed[3,6,9] to the existence of a high degree of positive charge at position 6 in the acridizinium nucleus in contrast to that of position 11, the other terminus for cycloaddition. The various orientation phenomena have been explained in terms of charge-transfer complexes at, or along the reaction pathway leading to, the transition state.[10]

A promising alkene for the extension of this study was cyclopropene since it had been shown[11] to react vigorously with tetraphenylcyclopentadienone, an electron-deficient (but nonionic) "diene". Highly reactive alkenes are of particular interest in polar cycloaddition since such reactivity is frequently associated with a 100% stereoselectivity believed to have its origin in coulombic repulsion.[7,9,12,13]

Cyclopropene was generated from allyl chloride and sodium amide by a modification of the method of Closs and Krantz.[14] Since it had been suggested[15] that the 2 N H_2SO_4 wash originally recommended lowered the yield of cycloalkene, and since the sensitivity of acridizinium ion to bases[16] made it necessary to trap out basic impurities (presumably allylamine), dilute acetic acid was substituted for dilute sulfuric acid. Cycloaddition of the acridizinium ion was complete (83% yield) after 1.75 h at room temperature[17] and NMR of the product (2) indicated that it consisted of only a single racemate.

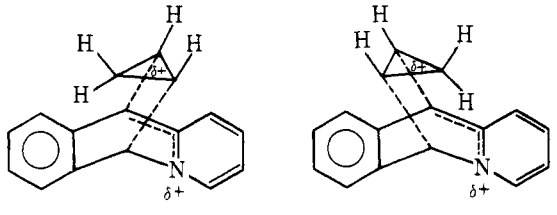


1, R = R′ = H
3, R = Me; R′ = H
5, R = R′ = Me

2, R = R′ = H
4, R = Me; R′ = H
6, R = R′ = Me

Stereoselectivity in cycloaddition reactions involving cyclopropene is not new. With cyclopentadiene,[18] substituted cyclopentadienones,[19] 6,6-dimethylfulvene,[20] and other diene derivatives[21] the orientation of the cyclopropane ring has been found to be endo, but with 1,3-diphenylisobenzofuran at variance with the Alder endo rule[22] the exo isomer appears to be the only product. A few cases have been reported in which mixtures of diastereomers are formed.[23,24]

The Alder rule had not been useful in rationalizing the stereoselectivity shown in cationic polar cycloaddition, for in the acridizinium system the terms exo and endo are meaningless. It is convenient to designate acridizinium adducts as syn or anti with reference to the phenylene ring. According to the coulombic repulsion generalization[9,13] the syn conformation should be preferred since that part of the positive charge that is delocalized into the cyclopropene ring at or near the transition state would produce less repulsion with the residual charge of the pyridinium ring (hence have less potential energy) when the orientation is syn (**7a**) than when it is anti (**7b**).



7a **7b**

For each of the nonaromatic protons in the adduct **2** the ^1H NMR gives a clear signal which can be identified by decoupling experiments. Of the C-14 methylene protons the farthest upfield (H_A) appears as a multiplet at δ 0.13, a chemical shift comparable to that shown by the methylene protons of norcarane (bicyclo[4.1.0]heptane) which have been reported to appear at δ 0.02[25] or 0.15.[26] The other C-14 proton (H_B) is responsible for a quartet at δ 0.96 suggesting a more strongly deshielded environment.[27]

Experience with the acridizinium adducts of norbornadiene showed that conclusive evidence concerning the stereochemistry of addition could be afforded by selective hydrogenation, which in effect removes those biases in chemical shift which are due to the diamagnetic anisotropy of the pyridinium ring.[8]

When a sample of the cyclopropene adduct (**2**) was selectively reduced the methylene signals (C-14 H_A and C-14 H_B) moved to *higher* field appearing at δ −0.88 (multiplet) and 0.45 (quartet). The reduction product has a C-14 proton with a resonance at too high a field (δ −0.88) to be explicable in terms of the cyclopropane ring current alone, but this observation is easily rationalized if the proton lies in the shielding zone above the phenylene ring. From this it follows that in the reduction product, and hence in the original adduct **2**, the configuration of the cyclopropane ring must be syn with re-

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