(d, J = 7.7 Hz, 1 H, Ar), 7.46 (d, J = 7.7 Hz, 1 H, Ar); ^{13}C NMR ($CDCl_3$) δ 19.6, 21.2, 28.9, 29.6, 38.5, 53.6, 120.0, 121.2, 124.6, 127.3, 146.7, 154.2, 189.9. One of the peaks of saturated carbons was not separated from another.

***N*,3-Dimethyl-1,2,3,4-tetrahydrocyclopent[*b*]indole:** 94%; TLC R_f 0.50 (hexane-ether, 10:1); ^{1}H NMR ($CDCl_3$) δ 1.30 (d, J = 7.0 Hz, 3 H, Me), 2.06-2.08 (m, 1 H, CH_2), 2.72-2.89 (m, 3 H, CH_2), 3.32 (m, 1 H, CH), 3.68 (s, 3 H, NMe), 7.03-7.14 (m, 2 H, Ar), 7.27 (d, J = 6.2 Hz, 1 H, Ar), 7.43 (d, J = 7.1 Hz, 1 H, Ar); ^{13}C NMR ($CDCl_3$) δ 20.4, 23.3, 30.5, 32.9, 38.2, 109.3, 116.9, 118.7, 119.0, 120.0, 124.2, 141.6, 149.9.

Acknowledgment. This work was supported by a Grant-in-Aid from the Ministry of Education, Science, and Culture, Japan.

Supplementary Material Available: ^{1}H and ^{13}C NMR spectral data and the differential NOE experiments after N-methylation (22 pages). Ordering information is given on any current masthead page.

Synthesis of 3-Nitrocyclopropenes

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Received September 17, 1990

Recently there has been considerable interest in strained-ring nitro compounds as high-energy density materials.[1] Our work in this area has focused on nitrocyclopropanes. While there are several methods for nitrocyclopropane formation,[2] the addition of a nitrocarbene to an alkene has only recently been described by us.[3] In this reaction pioneered by Doyle, rhodium(II) acetate catalyzes the cyclopropanation of alkenes[4] by nitrodiazo compounds.[5] Detailed studies have shown that the success of the reaction is dependent on both the alkene and the nitrodiazo precursor.

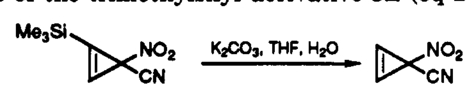
Here, we describe the extension of this method to the formation of nitrocyclopropenes **5** from nitrodiazo compounds **1-3** and alkynes (Scheme I). These results are presented in Table I along with the corresponding data for ethyl diazoacetate (**4**).[6]

It is apparent from these data that terminal acetylenes are the best substrates for this reaction and that diazo compounds **1** and **2** cyclopropanate a wider range of alkynes than **3**. Very hindered internal alkynes (diphenylacetylene, bis(trimethylsilyl)acetylene) are not cyclopropanated. These observations are consistent with results from the cyclopropanation of alkenes with diazo compounds **1-3**. The cyclopropene derived from styrene and diazo compound **3** could not be purified beyond 60%. It is curious that the nitrodiazo compounds cyclopropanate phenylacetylene and ethyl diazoacetate does not. We have reinvestigated this reaction with ethyl diazoacetate and find no evidence of cyclopropene. The phenyl-substituted nitrocyclopropenes must not be as susceptible to polymerization by the rhodium catalyst as ethyl phenylcyclopropenecarboxylate.[6]

The parent 3-nitrocyclopropene (**6**) and 3-cyano-3-nitrocyclopropene (**7**) can be obtained from the corresponding trimethylsilyl-substituted cyclopropenes **5d** and **5h**. In the case of nitrocyclopropene, deprotection with (TBA)F in wet diethyl ether affords a ca. 5% solution of nitrocyclopropene (eq 1). This material can be detected by NMR and by TLC. Our attempts to isolate **6** have been unsuccessful.

5d **6** (1)

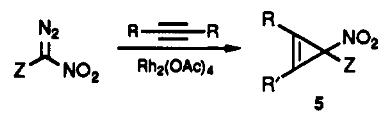
3-Cyano-3-nitrocyclopropene (**7**), on the other hand, is a relatively stable compound as a neat liquid at room temperature. It is prepared by potassium carbonate hydrolysis of the trimethylsilyl derivative **5h** (eq 2).



5h **7** (2)

There is one prior example of a nitrocyclopropene. 1,2-Diphenyl-3-nitrocyclopropene was prepared by Jones and Kobzina in 1965.[7] In 1988 Cheer, Greenberg, and

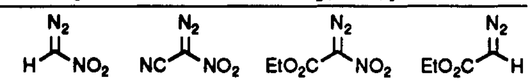
Scheme I



Z = H, EtO_2C, CN

	R	R'	Z
5a	Ph	H	H
5b	*n*-pentyl	H	H
5c	Me	Me	H
5d	TMS	H	H
5e	Ph	H	CN
5f	*n*-Bu	H	CN
5g	Et	Et	CN
5h	TMS	H	CN
5i	Ph	H	CO_2Et
5j	*n*-Bu	H	CO_2Et

Table I. Yields of Cyclopropenes from Alkynes and Diazo Compounds with Use of $Rh_2(OAc)_4$



	1	2	3	4[a]
PhCCH	60	65	*b*	0
n-BuCCH	33[c]	35	84	84
RCCR	35[d]	35[e]	0	68[d]
(TMS)CCH	30	28[f]	0	86
PhCCPh	0	0	0	

[a] Taken from ref 6. [b] Product was formed but could not be purified beyong 60% purity. [c] Reaction was carried out with 1-heptyne. [d] Reaction was carried out with 2-butyne. [e] Reaction carried out with 2-hexyne. [f] This compound was not purified but was converted directly to 3-cyano-3-nitrocyclopropene in 28% overall yield.

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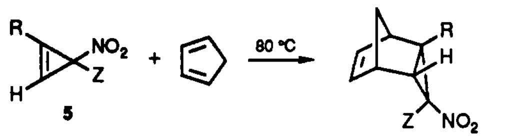
0022-3263/91/1956-2258$02.50/0 © 1991 American Chemical Society

co-workers reported the crystal structure of this compound.[8] Otherwise, these compounds are unprecedented in the literature.

With the exception 6, all of these compounds are stable to air at room temperature for several days. On heating or stirring with acid, they do decompose to give uncharacterizable polar materials. Nitrocyclopropenes derived from 1 solvolyze readily in hydroxylic solvents while those derived from 2 are stable to solvolysis. These compounds undergo a Diels–Alder reaction with cyclopentadiene to afford adducts 9 that may be fully characterized. For instance, a single compound was obtained from **5d** and cyclopentadiene. The stereochemistry of adduct **9a** was assigned as endo/anti by analogy to that for **9b** (see below). Similarly, heating nitrocyanocyclopropene (**7**) with cyclopentadiene afforded a single isomer **9b** (eq 3). In this case the stereochemistry of the adduct was determined by X-ray crystallography.[9] The details of the structural determination are included in the supplementary material. As further proof of structure, we have determined the crystal structure of 1-nitro-2-phenylcycloprop-2-enecarbonitrile (**5e**).[10]



(3)

9a: R = TMS, Z = H
b: R = H, Z = CN

In summary, we have demonstrated that the hitherto virtually unknown 3-nitrocyclopropenes are easily prepared in a one-step reaction between a nitrodiazo compound and an alkyne.

Experimental Section

General Methods. ^{1}H NMR spectra were obtained in $CDCl_3$ at 250 or 500 MHz with $CHCl_3$ as an internal standard. ^{13}C NMR spectra were obtained at 125 MHz with $CDCl_3$ as an internal standard. High-resolution mass spectra were obtained on a VG-ZAB-E mass spectrometer under ammonia chemical ionization conditions. Infrared spectra were obtained as thin films. All reagents were used as supplied. All of the products were isolated as colorless oils unless otherwise noted. Products were judged to be >95% pure by ^{1}H and ^{13}C NMR.

General Procedure for the Catalytic Cyclopropanation of Alkynes with Nitrodiazomethane. A solution of nitrodiazomethane[11] in CH_2Cl_2 was titrated manometrically with use of sulfuric acid. Aliquots of this solution were added with stirring to excess neat alkyne-containing rhodium(II) acetate (3 mol %) under ambient conditions such that nitrogen evolution was not too vigorous. After completion of addition, inorganic material and organic impurities were removed by diluting the reaction mixture with ether and then washing with saturated sodium carbonate solution. The organic layer was dried and concentrated on a rotary evaporator to afford 95% pure material. The yields listed below are for three steps and are based on starting *tert*-butyl nitrodiazoacetate.

3-Nitro-1-phenylcyclopropene (5a) was prepared in 60% yield from the cyclopropanation of phenylacetylene with nitrodiazomethane according to the general procedure: ^{1}H NMR δ 5.01 (s, 1 H), 7.04 (s, 1 H), 7.40–7.42 (m, 3 H), 7.52–7.56 (m, 2 H); ^{13}C NMR δ 59.1, 99.3, 117.2, 123.3, 129.1, 130.3, 131.5; IR 3160, 1550, 1380 cm^{-1}.

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3-Nitro-1-pentylcyclopropene (5b) was prepared in 33% yield by the cyclopropanation of 1-heptyne with nitrodiazomethane according to the general procedure: ^{1}H NMR δ 0.80 (m, 3 H), 0.85–1.28 (m, 4 H), 1.52 (m, 2 H), 2.46 (dt, J = 1.2, 7.5 Hz, 2 H), 4.64 (s, 1 H), 6.62 (d, J = 1.2 Hz, 1 H); ^{13}C NMR δ 13.8, 22.1, 24.2, 25.8, 31.1, 60.2, 99.5, 120.5; IR 3160, 1550, 1370 cm^{-1}.

1,2-Dimethyl-3-nitrocyclopropene (5c) was prepared in 35% yield by the cyclopropanation of 2-butyne with nitrodiazomethane according to the general procedure: ^{1}H NMR δ 1.99 (s, 6 H), 4.51 (s, 1 H); ^{13}C NMR δ 8.6, 63.7, 108.3; IR 1540, 1370 cm^{-1}.

3-Nitro-1-(trimethylsilyl)cyclopropene (5d) was prepared in 29% yield by the cyclopropanation of (trimethylsilyl)acetylene with nitrodiazomethane according to the general procedure: ^{1}H NMR δ 0.20 (s, 9 H), 4.65 (d, J = 1.3 Hz, 1 H), 7.36 (d, J = 1.3 Hz, 1 H); ^{13}C NMR δ −2.1, 58.5, 65.8, 116.6, 120.5; IR 3160, 1710, 1550, 1365 cm^{-1}.

Preparation of 3-Nitrocyclopropene (6). Nitrodiazomethane (from 800 mg of *tert*-butyl nitrodiazoacetate, 4.27 mmol) was added to 1.0 g of (trimethylsilyl)acetylene containing a few milligrams of rhodium(II) acetate catalyst. This crude cyclopropanation mixture were diluted with ether and stirred with saturated carbonate solution. The organic layer was concentrated to ca. 1.5 mL and cooled in an ice bath to 0 °C. A 1-mL portion of a 1 M commerical solution of (TBA)F in THF was added dropwise, and the reaction mixture turned brown. Water and ether were added. After the organic layer was washed a few times with water, it was dried and concentrated to ca. 5 mL. TLC and NMR analysis of this solution indicated the presence of nitrocyclopropene. On further concentration of this solution, the product decomposed: ^{1}H NMR δ 4.67 (s, 1 H), 7.16 (s, 2 H); ^{13}C NMR δ 60.2, 108.2 (J_{CH} = 234, 7.0 Hz).

Catalytic Cyclopropanation of Alkynes with Nitrocyanodiazomethane. A CH_2Cl_2 solution of nitrodiazoacetonitrile[5] was added via a Pasteur pipet to a stirred solution of alkyne containing 10–40 mg of catalyst at 0 °C. After the mixture was stirred for 30 min, 5 mL of ether and 30 mL of saturated sodium carbonate solution were added. This biphasic mixture was stirred vigorously for 1 h to remove all of the inorganic material as well as organic side products. The organic fraction was dried and concentrated to yield 95% pure nitrocyanocyclopropenes. These compounds are stable to silica gel, mild heating, and air.

1-Nitro-2-phenylcyclopropenecarbonitrile (5e) was prepared in 35% yield from the cyclopropanation of phenylacetylene with nitrocyanodiazomethane: ^{1}H NMR δ 7.14 (s, 1 H), 7.44–7.53 (m, 3 H), 7.54–7.62 (m, 2 H); ^{13}C NMR δ 56.8, 96.5, 113.7, 115.0, 119.6, 129.5, 130.7, 133.1; IR 3160, 2250, 1790, 1570, 1360 cm^{-1}. Anal. Calcd for $C_{10}H_6N_2O_2$: C, 64.51; H, 3.25. Found: C, 64.45; H, 3.26.

2-Butyl-1-nitrocyclopropenecarbonitrile (5f) was prepared in 35% yield from the cyclopropanation of 1-hexyne with nitrocyanodiazomethane: ^{1}H NMR δ 0.88 (t, J = 7.5 Hz, 3 H), 1.36 (tq, J = 7.4, 7.9 Hz, 2 H), 1.54–1.66 (tt, J = 7.2, 7.9 Hz, 2 H), 2.60 (dt, J = 1.3, 7.2 Hz, 2 H), 6.78 (t, J = 1.3 Hz, 1 H); ^{13}C NMR δ 13.3, 22.0, 23.0, 27.5, 57.6, 97.7, 114.2, 118.9; IR 3160, 2250, 1630, 1560, 1355 cm^{-1}; HRMS ($M^+ + NH_4$) 184.107, calcd for $C_{10}H_{14}N_3O_2$ 185.109.

2,3-Diethyl-1-nitrocyclopropenecarbonitrile (5g) was prepared in 35% yield from the cyclopropanation of 3-hexyne with nitrocyanodiazomethane: ^{1}H NMR δ 1.21 (t, J = 7.5 Hz, 6 H), 2.53 (q, J = 7.5 Hz, 4 H); ^{13}C NMR δ 10.6, 16.7, 60.1, 111.1, 114.5; IR 2240, 1670, 1565, 1360 cm^{-1}.

Preparation of 1-Nitrocycloprop-2-enecarbonitrile (7). Nitrocyanodiazomethane (1.1 g of a 50% solution in CH_2CL_2) was added to 3 mL of (trimethylsilyl)acetylene containing 30 mg of catalyst at 0 °C over 5 min. The reaction mixture was stirred for an additional 30 min. TLC analysis indicated formation of the cyclopropene, which was not isolated but was directly hydrolyzed with sodium carbonate to afford the product 7. Ether (5 mL) and saturated sodium carbonate (50 mL) were added, and this reaction mixture was stirred vigorously for 1.5 h. More ether was added, and the organic layer was separated, washed with water, dried with magnesium sulfate, and concentrated on a rotary evaporator at 30 °C to afford 150 mg (1.4 mmol, 28%) of 95% pure (NMR, TLC, IR) product: ^{1}H NMR δ 7.34 (s); ^{13}C NMR δ 67.8, 106.0 (J_{CH} = 255, 10 Hz), 113.8; IR 3140, 2250, 1630, 1560, 1350 cm^{-1}.

Ethyl 2-Butyl-1-nitrocyclopropenecarboxylate (5j). Ethyl nitrodiazoacetate[5] (700 mg, 4.4 mmol) was added to 3 mL of 1-hexyne containing 30 mg of catalyst at 20 °C. The mixture was stirred for 30 min, ether and saturated sodium carbonate were added, and this solution was stirred for 10–15 min. Separation of the organic layer followed by drying with magnesium sulfate and concentration afforded 800 mg (3.8 mmol, 87%) of 95% pure cyclopropenecarboxylate. While stable to air, this material was sensitive to acid, base, and silica gel: ^{1}H NMR δ 0.85 (t, J = 7.1 Hz, 3 H), 1.21 (t, J = 7.2 Hz, 3 H), 1.30 (m, 2 H), 1.49–1.59 (m, 2 H), 2.58 (dt, J = 1.0, 9 Hz, 2 H), 4.23 (q, J = 7.1 Hz, 2 H), 6.67 (s, 1 H); ^{13}C NMR δ 13.4, 13.9, 22.0, 23.1, 28.0, 62.2, 69.6, 98.3, 119.4, 166.1; IR 3160, 1740, 1550 cm^{-1}.

***anti*-3-Nitro-2-(trimethylsilyl)-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (9a).** (Trimethylsilyl)nitrocyclopropene (5d) (40 mg, 0.23 mmol) and cyclopentadiene (100 mg, 1.5 mmol) were heated in 0.5 mL of toluene under an inert atmosphere in a 10 mL round-bottom flask on an oil bath at 70 °C for 4 h. The entire reaction mixture was then chromatographed over a short silica gel column (0–20% ether/pentane) to afford 50 mg (0.21 mmol, 91%) of colorless oil: ^{1}H NMR δ 0.08 (s, 9 H), 1.48 (m, 2 H), 2.58 (m, 1 H), 3.05 (m, 2 H), 3.37 (m, 1 H), 5.76 (m, 1 H), 5.87 (m, 1 H); ^{13}C NMR δ −1.2, 21.2, 29.3, 43.5, 48.7, 62.4, 71.5, 131.2, 132.1; IR 1550, 1370 cm^{-1}; HRMS (M$^+$ + NH$_4$) 241.141, calcd for $C_{11}H_{21}N_2O_2$ 241.137.

***anti*-3-Nitro-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene-3-*syn*-carbonitrile (9b).** Nitrocyanocyclopropene (7) (60 mg, 0.54 mmol) and cyclopentadiene (150 mg, 2 mmol) were heated in 0.5 mL of toluene in a sealed flask for 2 h in an oil bath at 70 °C. Chromatography of the entire reaction mixture over silica gel (0–20% ether/hexane) afforded 70 mg (0.40 mmol, 74%) of white solid: ^{1}H NMR δ 1.81 (d, J = 7.6 Hz, 1 H), 2.06 (d, J = 7.6 Hz, 1 H), 3.08 (t, J = 2.1 Hz, 2 H), 3.36 (br, 2 H), 6.23 (t, J = 2.1 Hz, 2 H); ^{13}C NMR δ 38.0, 45.0, 66.8, 70.0, 112.7, 136.4; IR 2160, 1570, 1340 cm^{-1}; HRMS (M$^+$ + H) 177.068, calcd for $C_9H_{10}N_2O_2$ 177.066; mp 111–112 °C. Anal. Calcd for $C_9H_8N_2O_2$: C, 61.34; H, 4.58. Found: C, 61.20, H, 4.59.

Acknowledgment. We thank Dr. Patrick J. Carroll of this department for carrying out an X-ray crystallographic analysis of compound **9b**. P.E.O. acknowledges support by a fellowship from the Division of Organic Chemistry of the American Chemical Society sponsored by Dow Chemical Co. during 1989–1990. This research was sponsored by the Air Force Office of Scientific Research (AFSC) under Contract F49620-90-C-0046. The U.S. Government is authorized to reproduce and distribute reprints for governmental purposes notwithstanding any copyright notation hereon.

Supplementary Material Available: ^{1}H and ^{13}C NMR spectra for compounds **5a–d,f,g,j**, **7**, and **9a** and crystallographic data for **9b** (23 pages). Ordering information is given on any current masthead page.

Optimizations in the Preparation of the First Benzimidazolyl Salicylic Acid Derivative. An Efficient One-Pot Synthesis of 2-[(2′-Carbomethoxyphenoxy)methyl]benzimidazole†

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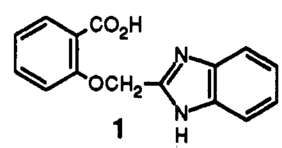
Received June 26, 1990

Introduction

Considerable interest has been directed toward modeling active sites of enzymes, especially those of the serine proteases.[1] Most of these studies involve reconstructing the *charge-relay* system on a small framework.[2] Quite recently, models with the syn lone pair of carboxylate oriented toward the imidazole have appeared.[3,4] Such models allow an evaluation of our hypothesis that the syn lone pairs of carboxylate are more basic than the anti.[5]

Our interest in *biomimetic*[6] chemistry focuses in part on the design and synthesis of biomodels with two or more functional groups with defined spatial arrangement between these groups. In particular, we desire chemical models that possess both syn- and anti-oriented carboxylates in addition to other functionalities. We have prepared the acid derivative, 1, of the title compound as an *intra*molecular model for hydrogen bonding between carboxyl and imidazole. The crystal structure exhibits a strong *inter*molecular syn-oriented hydrogen bond between the carboxyl and the benzimidazolyl instead of an *intra*molecular anti-oriented hydrogen bond.[7] We describe herein the preparation of 1 by optimized procedure, which has general applicability to the synthesis of functionalized benzimidazoles.[8] Benzimidazoles are commercially important as pharmaceuticals, veterinary anthelminitics, fungicides, and insecticides.[9] Furthermore, they are established inhibitors of cytochrome P-450 mediated enzyme activity of various species.[10]



1

Results and Discussion

Williamson's Route. Initially, we attempted to prepare 1 via the Williamson ether synthesis by coupling methyl salicylate and 2-(chloromethyl)benzimidazole. Bahadur and Pandey[11] had synthesized the para analogue of 1 by

† Presented in part at the 197th National Meeting of the American Chemical Society, Dallas, TX, Apr 9–14, 1989; Abstract ORG 168.

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