Welch et al. have reported stereoselective formation of 3-fluoro-β-lactams via ketene–imine condensation.[17] However, their stereochemistry is completely reversed to ours since they observed that the cis form was solely or predominantly formed.[18]

In conclusion, we have succeeded in anodic monofluorination of sulfur-containing heterocycles for the first time and developed a convenient preparation of monofluoro β-lactams.

Acknowledgment. This work was financially supported by a Grant-in-Aid for Scientific Research (No. 04650765) from the Ministry of Education, Science and Culture. We are grateful to Prof. Tomoya Kitazume of the Tokyo Institute of Technology for obtaining ^{19}F NMR spectra and to Dr. Kokoro Iio of Industrial Products Research Institute for obtaining the high-resolution mass spectra. We also thank Prof. Naomich Furukawa of Tsukuba University for his valuable suggestion.

Supplementary Material Available: ^1H NMR, IR, MS, and high-resolution MS data for all new compounds (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(18) For example, the reaction of monofluoroacetic acid chloride with ethylidene aniline in the presence of triethylamine provided cis 4c solely in 33%.

Intramolecular Mitsunobu Displacement with Carbon Nucleophiles: Preparation of α-Nitrocyclopropanes

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Summary: γ-Nitroalkanols are converted to α-nitrocyclopropanes with inversion of configuration in good to excellent yields using diethyl azodicarboxylate and Ph_3P.

Three-membered carbocycles are present in a wide range of terrestrial and marine natural products, inter alia, insecticides,[1] pheromones,[2] fatty acids,[3] terpenoids/steroids,[4] and antibiotics.[5] They are also intermediates in primary and secondary metabolism and show promise as mimetics of biolabile groups.[6] As a consequence of their inherent strain energy, functionalized members of this class have proven to be exceedingly versatile synthetic reagents.[7] Cyclopropanes are most often prepared by intra- and intermolecular addition of sulfur ylides, diazoalkanes, or carbenoids to unsaturated systems, and considerable attention has been devoted to the development of stereocontrolled modifications of these approaches.[7,8] In contrast, comparatively few chiral cyclopropanes have been made via nucleophilic displacement.[9]

We report herein that treatment of a wide variety of γ-nitroalkanols with a preformed complex of diethyl azodicarboxylate (DEAD) and triphenylphosphine affords α-nitrocyclopropanes[10] in good to excellent yields. The reaction proceeds rapidly at ambient tempertaure under essentially neutral conditions in benzene or THF. This represents a highly efficient intramolecular variant[11] of the Mitsunobu[12] displacement procedure in which a nitronate anion acts as a carbon nucleophile resulting in a new carbon–carbon bond. Competitive alkylation of the oxygens in the ambident nitronate anion is not observed.

Some representative annulations are summarized in Table I. Acyclic primary (entry 1) and secondary (entry 2) nitro alcohols react smoothly as do related carbocycles

(1) Elliott, M. *Synthetic Pyrethroids*; ACS Symposium Series 87; American Chemical Society: Washington, D.C., 1977.

(2) Sirenin: Corey, E. J.; Achiwa, K.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 4318.

(3) Hybridalactone: Higgs, M. D.; Mulheirn, L. J. *Tetrahedron* **1981**, *37*, 4259. Halicholactone/neohalicholactone: Niwa, H.; Wakamatsu, K.; Yamada, K. *Tetrahedron Lett.* **1989**, *30*, 4543.

(4) Halimedatrial: Paul, V. J.; Fenical, W. *Science* **1983**, *221*, 747. Marine sterols: Kerr, R. G.; Baker, B. J. *Nat. Prod. Rep.* **1991**, 465.

(5) Cyclopropylamino acids: Williams, R. M.; Fegley, G. J. *J. Am. Chem. Soc.* **1991**, *113*, 8796 and references cited therein. FR-900848: Yoshida, M.; Ezaki, M.; Hashimoto, M.; Yamashita, M.; Shigematsu, N.; Okuhara, M.; Kohsaka, M.; Horikoshi, K. *J. Antibiotics* **1990**, *43*, 748.

(6) Martin, S. F.; Austin, R. E.; Oalmann, C. J. *Tetrahedron Lett.* **1990**, *31*, 4731. Walsh, C. *Tetrahedron* **1982**, *38*, 871. Norbeck, D. W.; Sham, H. L.; Herrin, T.; Rosenbrook, W.; Plattner, J. J. *J. Chem. Soc., Chem. Commun.* **1992**, 128.

(7) Salaun, J. *Chem. Rev.* **1989**, *89*, 1247.

(8) Recent examples: Romo, D.; Romine, J. L.; Midura, W.; Meyers, A. I. *Tetrahedron* **1990**, *46*, 4951. Mori, A.; Arai, I.; Yamamoto, H.; Nakai, H.; Arai, Y. *Ibid.* **1986**, *42*, 6447. Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1989**, *54*, 3525. Lautens, M.; Delanghe, P. H. M. *Ibid.* **1992**, *57*, 798. Charette, A. B.; Cote, B.; Marcoux, J.-F. *J. Am. Chem. Soc.* **1991**, *113*, 8166. Fontani, P.; Carboni, B.; Vaultier, M.; Maas, G. *Synthesis* **1991**, *605*. Casey, C. P.; Vosejpka, L. J. S. *Organometallics* **1992**, *11*, 738. Maxwell, J. L.; O'Malley, S.; Brown, K. C.; Kodadek, T. *Ibid.* **1992**, *11*, 645. Rodriques, K. E. *Tetrahedron Lett.* **1991**, *32*, 1275. Lowenthal, R. E.; Masamune, S. *Ibid.* **1991**, *32*, 7373.

(9) Krohn, K.; Borner, G. *J. Org. Chem.* **1991**, *56*, 6038. Tanaka, K.; Matsuura, H.; Funaki, I.; Suzuki, H. *J. Chem. Soc., Chem. Commun.* **1991**, 1145.

(10) For alternative preparations of α-nitrocyclopropanes see: (a) O'Bannon, P. E.; Dailey, W. P. *Tetrahedron* **1990**, *46*, 7341. (b) Kai, Y.; Knochel, P.; Kwiatkowski, S.; Dunitz, J. D.; Oth, J. F. M.; Seebach, D.; Kalinowski, H.-O. *Helv. Chim. Acta* **1982**, *65*, 137.

(11) There is precedent for cyclopropanation under these conditions: Magnus, P.; Gallagher, T.; Schultz, J.; Or, Y.-S.; Ananthanarayan, T. P. *J. Am. Chem. Soc.* **1987**, *109*, 2706.

(12) Review: Mitsunobu, O. *Synthesis* **1981**, 1.

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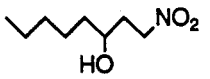
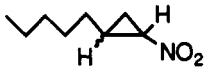
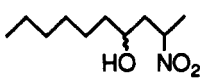
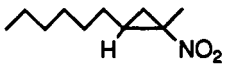
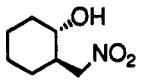
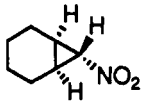
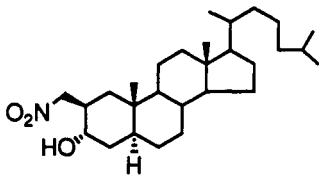
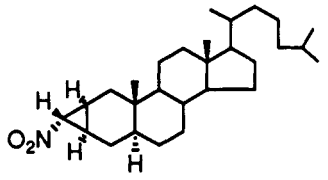
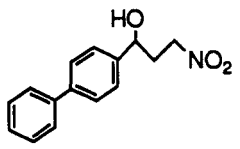
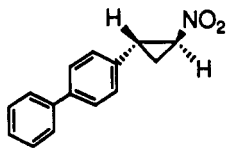
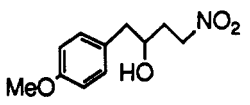
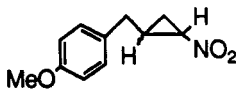
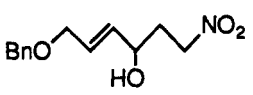
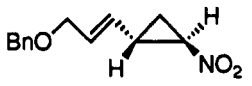
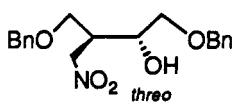
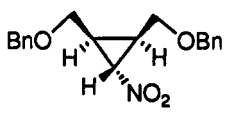
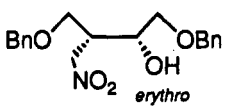
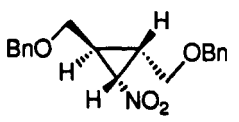
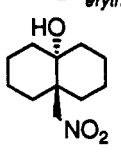
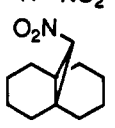
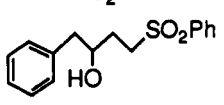
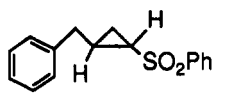
Table I. Synthesis of Cyclopropanes[a]

entry	nitro alcohol	product	trans/cis[b]	yield,[c] %
1			10:1	82
2			10:1[d]	87
3			*trans* only	92
4			*trans* only	76
5			*trans* only	75
6			7:1	92
7			*trans* only	64
8			*trans* only	94
9			N.A.[e]	98
10			–	0
11			–	0

[a] Except as noted, all compounds are racemic and only relative stereochemistry is implied. [b] Stereochemistry of nitro determined by ^1H and/or ^{13}C NMR. [c] Based on isolated, chromatographically homogeneous material. [d] Stereochemistry not determined; ratio based on integration of ^1H NMR. [e] N.A. = not applicable.

(entry 3) including a 5α-cholestane derivative (entry 4). Since the products are configurationally stable under the reaction conditions, the predominate trans-disposition of the nitro group presumably reflects kinetic rather than thermodynamic factors.[13] Even alcohols prone to dehydration (entries 5 and 6) give cyclopropanes without complication. No allylic transposition or S_N2' products are detected in the closure leading to the conjugated cyclopropane in entry 7. However, a small amount (~10%) of alcohol displacement by diethyl hydrazinedicarboxylate, the byproduct of DEAD, is worthy of note.[14] The cyclizations of *threo*- and *erythro*-nitro alcohols (entries 8 and 9, respectively) are completely stereospecific (>95% as judged by ^1H NMR) and confirm the anticipated[12] inversion of configuration at the site of displacement. Hindered alcohols such as the one in entry 10 are unreactive and starting material is returned.

Reports of carbon–carbon bond formation via the Mitsunobu protocol are rare and largely limited to doubly activated methylenes.[15] This is mostly a consequence of

(13) The stereochemical stability of the products is due, in part, to the much lower acidity of α-nitrocyclopropanes ($pK_a \sim 27$) compared with acyclic analogues ($pK_a \sim 17$). See ref 10b.

(14) Interception of the intermediate alkoxyphosphonium salt by non-traditional nucleophiles has been observed, e.g.: Lumin, Sun; Falck, J. R.; Capdevila, J.; Karara, A. *Tetrahedron Lett.* **1992**, *33*, 2091.

(15) Macor, J. E.; Wehner, J. M. *Tetrahedron Lett.* **1991**, *32*, 7195. Wada, M.; Mitsunobu, O. *Ibid.* **1972**, 1279.

the paucity of carbon nucleophiles with pK_a values sufficiently low ($pK_a < 17$) for participation in the Mitsunobu reaction. The failure of the phenylsulfone ($pK_a \sim 25$)[16] in entry 11 to undergo cyclization is relevant in this regard.

General Procedure. Diethyl azodicarboxylate (0.5 mmol) is added dropwise to a stirring solution of triphenylphosphine (0.5 mmol) in anhydrous benzene (5 mL) at room temperature under an inert atmosphere and stirred for 15 min. To the resultant deep red, homogeneous mixture is added a solution of γ-nitroalkanol (0.33 mmol) in benzene (3 mL). Following complete consumption of the reactant (~1 h), the solvent is removed in vacuo and the residue is purified by silica gel chromatography to afford the corresponding α-nitrocyclopropanes in 75–98% yield (Table I).

(16) Bordwell, F. G. *Pure Appl. Chem.* **1977**, *49*, 963.

Acknowledgment. Supported by grants from the USPHS NIH (GM 31278) and the Robert A. Welch Foundation (I-782). Funds for the purchase of a mass spectrometer were provided by NIH (S10 RR05922).

Supplementary Material Available: Spectral and physical data for all α-nitrocyclopropanes in Table I (3 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Synthesis of Hexalithiobenzene

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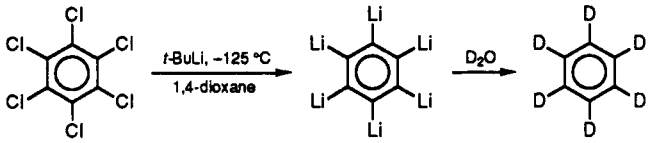
Summary: A new synthesis for hexalithiobenzene starting with hexachlorobenzene is reported.

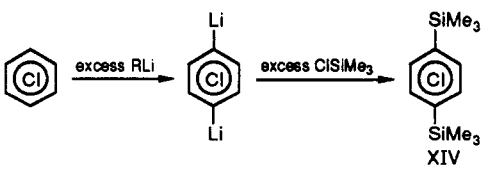
Recently we reported a new method for preparing polylithium organic compounds by lithium–halogen exchange which appears to be a new general synthesis for such compounds.[1] Previously, in 1978, an experiment in our laboratory established that hexalithiobenzene was a room-temperature stable compound.[2] However low yields (<1%) prevented purification and full characterization.

We now report a convenient laboratory synthesis for hexalithiobenzene in 53% yield.



(53% yield)

Previously Henry Gilman and co-workers attempted to prepare hexalithiobenzene using butyllithium and hexachlorobenzene, resulting in only disubstitution.[3] "The formation of pentachlorophenyllithium in the reaction of hexachlorobenzene with n-butyllithium at low temperature was mentioned above. We attempted to achieve polylithiation by treatment of hexachlorobenzene with several equivalents of n-butyllithium or t-butyllithium. No matter how large was the excess of organolithium reagent, after derivatization with trimelthylchlorosilane only 1,4-bis-(trimethylsilyl)-2,3,5,6-tetrachlorobenzene, XIV, was obtained (in over 50% yield)."



XIV

To successfully accomplish the hexalithiobenzene synthesis, one must seek conditions which favor lithium–halogen exchange over the competing coupling reactions and in addition create conditions to minimize cross-linking of partially lithium-substituted chlorobenzenes (which are also stable at room temperature).

Thus we have chosen to use *tert*-butyllithium since the bulky reagents are somewhat unfavorable for coupling reactions. The reaction between hexachlorobenzene and *tert*-butyllithium was conducted at the lowest temperature (to minimize vibrational energy leading to lithium–chlorine elimination) compatible with a significant reaction rate (usually less than −105 °C). The *tert*-butyllithium is kept highly concentrated (and in excess) in solution in a stirred round-bottom flask while hexachlorobenzene is slowly added via a solid addition funnel. Thus the halocarbon starting material is reacted very rapidly with the *tert*-butyllithium reagent before cross-linking or coupling reactions occur.

One gram of C_6Cl_6 (3.5 mmol) was slowly added to a slurry consisting of 40 mL of pentane, 49.6 mL (84 mmol) of 1.7 M *tert*-butyllithium, and 28.7 mL (337 mmol) of 1,4-dioxane, maintained at −125 °C. The reaction mixture was allowed to stir for 24 h. While other solvents are also useful, 1,4-dioxane has proven to be the most effective solvent for halobenzene reactions studied to date with respect to maximizing the lithium–halogen exchange reaction.

After 24 h (the optimum reaction time) the products were derivatized by addition of excess D_2O and the reaction temperature was slowly raised to room temperature. The deuteration products were analyzed by GC/MS. C_6D_6 was identified by ^{13}C and ^1H NMR and by HRMS ($C_6D_6^+$ m/z, calcd 84.084611, found 84.086183). Other products are polymeric species from cross-linking and coupling reactions.

Mass spectral data were obtained directly on the new hexalithiobenzene compound using laser desorption ionization/Fourier transform ion cyclotron resonance (LDI/FTICR) with a Nicolet Analytical Instruments FTMS 2000 spectrometer. Due to significant space charge distortion and high pressures (10^{-5} to 10^{-7} Torr) within the system, accurate mass detection was not possible.[4] Intense mo-

(1) Baran, J. R., Jr.; Lagow, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 9003.
(2) Shimp, L. A.; Chung, C.; Lagow, R. J. *Inorg. Chim. Acta* **1978**, *29*, 77.
(3) Haiduc, I.; Gilman, H. *Revue Roumaine de Chimie* **1971**, *16*(6), 907.

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