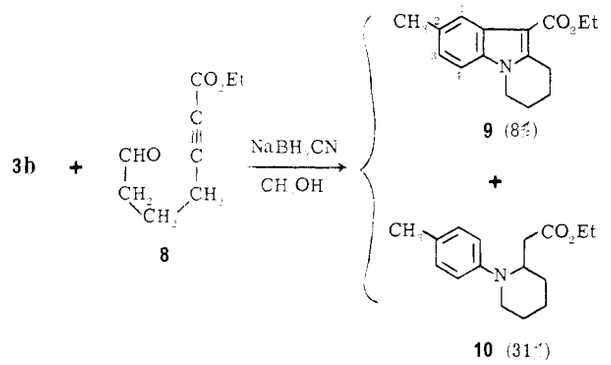
matropic rearrangement), thus forming an *N*-phenylpiperidine derivative.

The reductive cyclization of two *N*-arylhydroxylamines (**3b** and **3e**) with the homologue, ethyl 7-oxo-2-heptynoate (**8**), has also been studied briefly for comparison. Aldehyde ester **8**, prepared from 5-hexyn-1-ol as described above for **4**, was condensed with **3b** and **3e**, and the nitrone so formed was reduced with sodium cyanoborohydride in the same manner. Ethyl 2-methyl-6,7,8,9-tetrahydropyrido-[1,2-*a*]indole-10-carboxylate (**9**, mp 55.5–57 °C) was isolated from the former reaction in 8% yield. The major product (31%) was an unstable liquid identified as ethyl 1-(4-methylphenyl)piperidine-2-acetate (**10**).[19] The (*o*-



methoxyphenyl)hydroxylamine (**3e**) afforded the corresponding 4-methoxytetrahydropyridoindole (mp 117–118 °C)[9,20] in 12% yield.

The pyridoindole **9** and the piperidine acetate **10** very likely arise from competitive intramolecular Michael addition of the hydroxylamine intermediate (homologue of **6**) at oxygen and nitrogen, respectively. The piperidine *N*-oxide formed in the latter cyclization may undergo Polonovski-type rearrangement and twofold reduction with cyanoborohydride to give **10**. This pathway also competes to some extent in the reductive cyclizations with **4**, since the corresponding ethyl 1-arylpyrrolidine-2-acetates were isolated in small amounts from some of the preceding reactions (e.g., 10–20% of ethyl 1-(3-methylphenyl)-pyrrolidine-2-acetate from **3f** + **4**).

The reductive condensation of aromatic hydroxylamines with ethyl 6-oxo-2-hexynoate offers a short synthetic route to a variety of 2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole-9-carboxylates which may be of value in the preparation of mitomycin analogues. This reaction serves to illustrate the utility of the 1-aza-1′-oxa [3,3]sigmatropic rearrangement as a synthetic method for ortho alkylation and the rapid construction of complex heterocyclic ring systems.[5]

Acknowledgment. This investigation was supported in part by a research grant from the National Cancer Institute (CA 20436).

Registry No. 3a, 100-65-2; **3b**, 623-10-9; **3c**, 823-86-9; **3d**, 4546-20-7; **3e**, 35758-76-0; **3f**, 620-25-7; **4**, 71948-59-9; **5a**, 16916-14-6; **5b**, 71948-60-2; **5c**, 71948-61-3; **5d**, 71948-62-4; **5e**, 71948-63-5; **5f**, 71948-64-6; **5g**, 71948-65-7; **8**, 71948-66-8; **9**, 71948-67-9; **10**, 71948-68-0; 4-pentyn-1-ol, 5390-04-5; 4-pentynal, 18498-59-4; 4-pentynal ethylene acetal, 71948-69-1; ethyl 6-oxo-2-hexynoate ethylene acetal, 71974-88-4; 5-hexyn-1-ol, 928-90-5; 4-methoxytetrahydropyridoindole, 71948-70-4.

(19) IR (neat) 1725 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.13 (t, 3 H, J = 7 Hz, OCH_2CH_3), 1.62 (br s, 6 H, three CH_2), 2.20 (s, 3 H, $ArCH_3$), 2.28 (d, 2 H, J = 7 Hz, CH_2CO_2Et), 2.8–3.3 (br m, 2 H, NCH_2), 3.92 (br q, 3 H, J = 7 Hz, NCH and OCH_2CH_3), 6.65 (d, 2 H, J = 8 Hz, aryl H), 6.85 (d, 2 H, J = 8 Hz, aryl H); mass spectrum (70 eV) m/e (rel intensity) 261 (M^+, 10), 175 (15), 174 (100), 91 (10).

(20) ^1H NMR ($CDCl_3$) δ 1.39 (t, 3 H, J = 7 Hz, OCH_2CH_3), 1.65–2.20 (m, 4 H, $NCH_2CH_2CH_2$), 3.27 (t, 2 H, J = 7 Hz, CH_2), 3.87 (s, 3 H, OCH_3), 4.31 (q, 2 H, J = 7 Hz, OCH_2CH_3), 4.48 (t, 2 H, J = 7 Hz, NCH_2), 6.55 (d, 1 H, J = 8 Hz, H at C-3), 7.02 (t, 1 H, J = 8 Hz, H at C-2), 7.68 (d, 1 H, J = 8 Hz, H at C-1); mass spectrum (70 eV) m/e (rel intensity) 273 (M^+, 100), 245 (13), 244 (59), 228 (31), 201 (13), 200 (22), 185 (11), 184 (12).

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One-Step Synthesis of Complex Cyclopropanone Phenylthioketals by the Reaction of Sulfur-Stabilized Anions with Ketene Bis(phenylthio)acetal

Summary: Organolithium compounds which are stabilized by a phenylthio group lose the latter and form cyclopropanone phenylthioketals upon reaction with 1,1-bis(phenylthio)ethene; the latter is prepared by copper(I)-induced elimination of thiophenol from 1,1,1-tris(phenylthio)ethane, which is in turn generated by the reaction of acetic acid with a reagent formed by the reaction of trimethylaluminum with thiophenol.

Sir: We have recently revealed a remarkably efficient 1,3-elimination of thiophenol from 1,1,3-tris(phenylthio)-alkanes (**1**) induced by methyllithium in the presence of tetramethylethylenediamine (TMEDA) to produce cyclopropanone thioketals (**3**) in excellent yield (Scheme I);[1a] one important use of the products is their facile reduction to sulfur-stabilized cyclopropyl anions by lithium naphthalenide.[1b] We are now pleased to report that the presumed anionic intermediate (**2**)[1c] of the ring closure reaction can be produced in a connective manner by the reaction[2] of sulfur-stabilized anions (**4**) with ketene bis(phenylthio)acetal (**5**), a material which is now readily available (see below).[3] Examples are provided in eq 1–4.[4]

The lithio derivative[5] of **6** decolorized at 25 °C in the presence of **5**; we had previously prepared the product **7** by the nonconnective version of this ring closure.[1a] As hoped, the lithio derivative[6] of **8** reacted predominantly at the sulfur-bearing carbon atom to produce **9**; the mobility on TLC of the only other product leads us to believe that it possesses three phenylthio groups and it probably arises by attack of **5** on the γ position of the anion. It was gratifying to observe that the anions[7] of 1,3-bis(phenylthio)alkenes readily attack the ketene thioacetal even though the starting anion must be more highly stabilized than the intermediate **2**; substrate **10** was produced by the reaction of cyclohex-2-en-1-one with boron thiophenoxide

(1) (a) T. Cohen and W. M. Daniewski, *Tetrahedron Lett.*, 2991 (1978); (b) T. Cohen, W. M. Daniewski, and R. B. Weisenfeld, *ibid.*, 4465 (1978); (c) T. Cohen and J. R. Matz, *J. Org. Chem.*, in press.

(2) The addition of alkyllithiums to 2-methylene-1,3-dithiane has been known for some years: R. M. Carlson and P. M. Helquist, *Tetrahedron Lett.*, 173 (1969); D. Seebach, *Synthesis*, 17 (1969); D. Seebach, R. Bürstinghaus, B.-T. Gröbel, and M. Kolb, *Justus Liebigs Ann. Chem.*, 830 (1977). See also N. H. Andersen, P. F. Duffy, A. D. Denniston, and D. B. Grotjahn, *Tetrahedron Lett.*, 4315 (1978).

(3) T. Cohen, G. Herman, J. R. Falck, and A. J. Mura, Jr., *J. Org. Chem.*, **40**, 812 (1975).

(4) New compounds were characterized by ^1H NMR, IR, and mass spectroscopy and by their exact masses as determined by high-resolution mass spectroscopy. These data are in the supplementary material.

(5) T. Mukaiyama, K. Narasaka, and M. Furusato, *J. Am. Chem. Soc.*, **94**, 8641 (1972).

(6) J. F. Biellmann and J. B. Ducep, *Tetrahedron Lett.*, 5629 (1968); P. M. Atlani, J. F. Biellmann, S. Dube, and J. J. Vicens, *ibid.*, 2665 (1974).

(7) T. Cohen, D. A. Bennett, and A. J. Mura, Jr., *J. Org. Chem.*, **41**, 2506 (1976).

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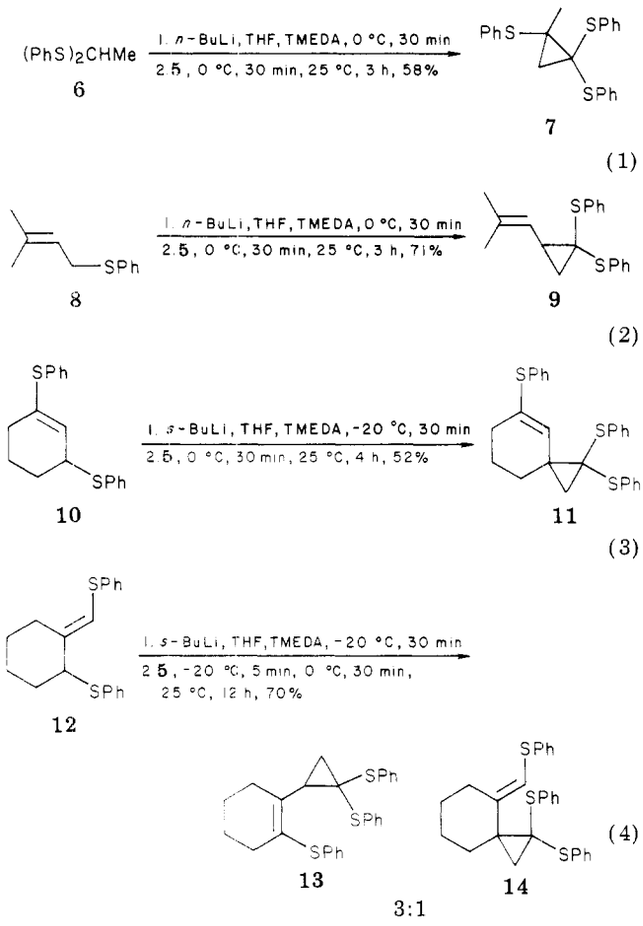
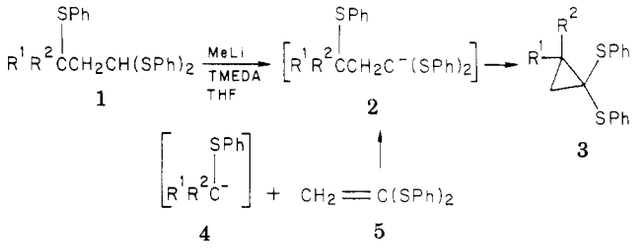


as described previously[7] and **12** was generated from the ketene bis(phenylthio)acetal derived from the reaction of cyclohexanecarboxylic acid with aluminum thiophenoxide.[8] A pure sample of **13** was obtained by silica chromatography of the product of eq 4. A pure sample of **14** has not yet been obtained; its structure has been assigned on the basis of its proton NMR spectrum as a mixture with **13** and the similarity of its TLC mobility with that of **13**.

Ketene thioacetal **5**, which should have multiple uses in organic chemistry, was prepared by an improvement of our earlier synthesis.[3] 1,1,1-Tris(phenylthio)ethane (**15**), which was previously prepared[3] by the methylation of tris(phenylthio)methyllithium, can be prepared somewhat more expeditiously by a modification of our procedure for converting esters to substituted ketene thioacetals.[8] To a solution containing 100 mL of 2.5 M trimethylaluminum (0.25 mol) in hexane and 200 mL of degassed toluene at 25 °C was added dropwise 76.8 mL (82.6 g, 0.750 mol) of thiophenol followed by 7.50 g (0.125 mol) of acetic acid. The mixture was heated at reflux for 2.5 h, cooled to 25 °C, and poured into 500 mL of 10% aqueous NaOH. The organic phase was washed with more alkali, dried, and evaporated to provide crude 1,1,1-tris(phenylthio)ethane (**15**). Recrystallization from benzene–ethanol provided 22.2 g (50%) of white crystals, mp 143–145 °C.

For the preparation of ketene thioacetal (**5**), a solution of 1.98 g (0.0056 mol) of **15** in 20 mL of THF was added dropwise within 1 min to a mixture of 2.9 g (0.0057 mol) of the cuprous triflate–benzene complex[9] and 1.3 mL (1.2 g, 0.011 mol) of 2,6-lutidine in 50 mL of dry benzene. The

Scheme I



mixture was stirred at 25 °C for 20 min during which time a yellow precipitate of cuprous thiophenoxide formed. The reaction mixture was added to a short column containing 100 g of silica gel and the product was eluted with ether to yield 1.34 g (98.5%) of spectroscopically pure **5** as a pale yellow oil.

$$CH_3CO_2H \xrightarrow[PhSH]{Me_3Al} \underset{\mathbf{15}}{CH_3C(SPh)_3} \xrightarrow[lutidine]{Cu^+} \underset{\mathbf{5}}{CH_2{=}C(SPh)_2}$$

The procedure for the preparation of **9** follows. To a stirred solution of 192 mg (1.08 mmol) of **8** and 137 mg (1.18 mmol) of TMEDA in 6 mL of THF at 0 °C was added 0.85 mL of a 1.35 M hexane solution of *n*-butyllithium (1.15 mmol) and the solution was stirred for 30 min. A solution of 269 mg (1.10 mmol) of **5** in 3 mL of THF was added to the yellow solution of 0 °C. The solution was stirred for 30 min at that temperature and for 3 h at 25 °C and it was then added to 50 mL of brine. Evaporation of the dried ether extract of the mixture and chromatography of the orange residue on 25 g of silica gel (elution with 100:1 hexanes–ethyl acetate) provided 243 mg (71%) of **9** as a yellow solid, mp 70.0–71.0 °C.[4] The other procedures were the same except for differences in times and temperatures, which are noted in eq 1, 3, and 4.

Because of the ready availability of the ketene thioacetal **5**[10] and of a wide variety of anions stabilized by the phenylthio group,[6-8,11] a large array of substituted cyclopropanone bis(phenylthio)ketals should be attainable by this procedure. The utility of the products is likely in view of the possibilities of reduced lithiation to sulfur-stabilized cyclopropyl anions[1b] and in the case of some of the vinylcyclopropanes[12] of [1,3]sigmatropic rearrangement to cyclopentenes, a type of rearrangement that should be greatly facilitated by the substitution pattern[13] especially if a diradical intermediate[14] is involved. Furthermore, greatly increased versatility of the concept could be envisioned by the use of other electrophilic olefins in place of the ketene thioacetal; testing of this concept is planned.

Acknowledgment. We thank Dr. Robert R. Hutchins for supplying compound **12**, Mssrs. Glen Herman, Daniel Ouellette, and Zenyk Kosarych for performing the mass spectral measurements, and the National Institutes of Health for support of this work.

(8) T. Cohen, R. E. Gapinski, and R. R. Hutchins, *J. Org. Chem.*, **44**, 3599 (1979).

(9) R. G. Salomon and J. K. Kochi, *J. Am. Chem. Soc.*, **95**, 3300 (1973); the benzene complex of cuprous triflate is now commercially available from Strem Chemicals, Inc., P. O. Box 108, Newburyport, Mass. 01950.

(10) During the preparation of this manuscript a synthesis of **5** was reported involving the reaction of formaldehyde with the lithio derivative of a boronic ester: A. Mendoza and D. S. Matteson, *J. Org. Chem.*, **44**, 1352 (1979).

(11) B.-T. Gröbel and D. Seebach, *Synthesis*, 357 (1977).

(12) For syntheses of vinylcyclopropanone dithioketals starting from dienes, see ref 13 and M. Braun and D. Seebach, *Chem. Ber.*, **109**, 669 (1976).

(13) Vinylcyclopropanone dithioketals have been rearranged to cyclopentenone dithioketals: E. J. Corey and S. W. Walinsky, *J. Am. Chem. Soc.*, **94**, 8932 (1972).

(14) H. G. Richey, Jr., and D. W. Shull, *Tetrahedron Lett.*, 575 (1976); P. H. Mazzocchi and H. J. Tamburin, *J. Am. Chem. Soc.*, **92**, 7220 (1970). For predictions of substituent effects on a concerted rearrangement, see: B. K. Carpenter, *Tetrahedron*, **34**, 1877 (1978).

Registry No. 5, 18889-01-5; 6, 13307-56-7; 7, 69519-88-6; 8, 10276-04-7; 9, 71987-46-7; 10, 60039-89-6; 11, 71948-55-5; 12, 71948-56-6; 13, 71948-57-7; 14, 71948-58-8; 15, 14859-20-2; thiophenol, 108-98-5; acetic acid, 64-19-7.

Supplementary Material Available: ^{1}H NMR, IR, and mass spectral data, as well as exact masses of the ring closure products for 7, 9, 11, 13, and 14 (2 pages). Ordering information is given on any current masthead page.

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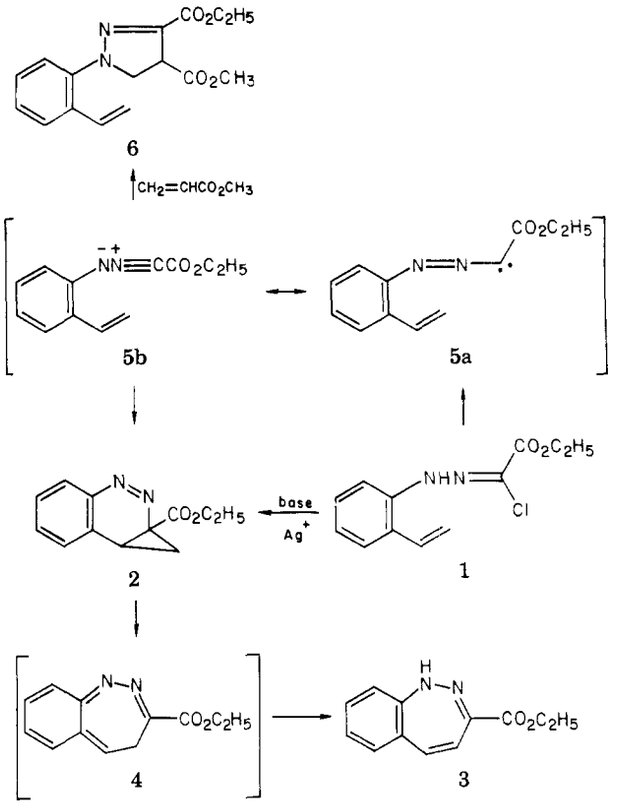
On the Stereochemical Aspects of the Intramolecular 1,1-Cycloaddition Reaction of Nitrilimines

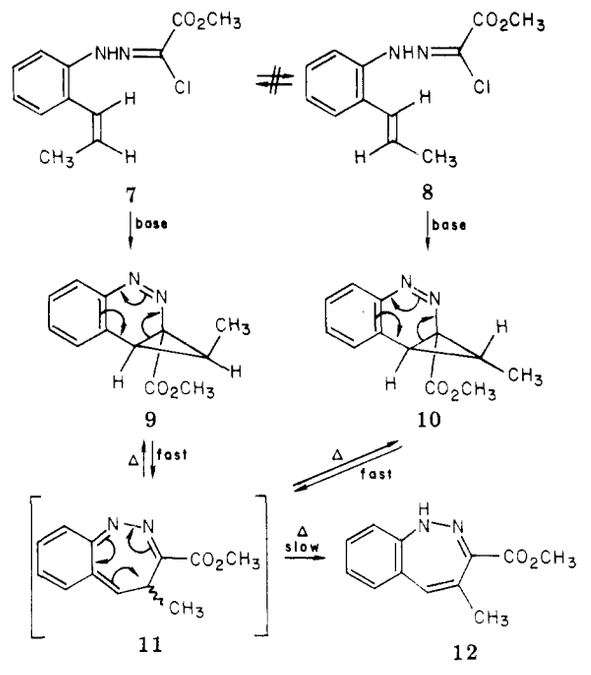
Summary: Treatment of *o*-vinylphenyl substituted chloroglyoxylate phenylhydrazones with base leads to nitrilimines as transient intermediates. These reactive 1,3-dipoles undergo intramolecular 1,1-cycloaddition with complete retention of configuration to give cyclopropa[*c*]-cinnolines.

Sir: Nitrilium betaines are a long known and thoroughly investigated class of 1,3-dipoles.[1,2] 1,3-Dipolar cycloaddition of this class of dipoles has been widely investigated[3,4] and in many cases has led to the synthesis of a variety of interesting heterocyclic compounds,[5] some of which would be tedious to synthesize by other routes. Recent results from our laboratory have shown that there are two pathways by which these dipoles can react with multiple π bonds.[6-9] The most frequently encountered path involves a "parallel-plane approach of addends" and can be considered to be an orbital symmetry allowed [4 + 2] concerted process.[1] The other path, designated as 1,1-cycloaddition, was first encountered with nitrile ylides[10] and operates only in certain intramolecular cases. It occurs when the p orbitals of the dipolarophile have been deliberately constrained to attack perpendicular to the nitrile ylide plane. Since our original report of this novel phenomenon appeared,[10] a related intramolecular carbene type of 1,1-cycloaddition of a nitrilimine has been reported by Garanti and co-workers.[11] As a further consequence of our interest in this area,[12] we thought it worthwhile to determine whether additional examples of carbenoid activity of nitrilimines could be uncovered. In this communicaton we wish to describe the stereochemical course of the intramolecular 1,1-cycloaddition reaction of *N*-(*o*-vinylphenyl) substituted nitrilimines to cyclopropa[*c*]-cinnolines.

Scheme I



Scheme II



Treatment of ethyl chloroglyoxylate 2-(*o*-vinylphenyl)-hydrazone (1) with base at 80 °C gave a 91% yield of ethyl 1*H*-1,2-benzodiazepine-3-carboxylate (3), mp 107–108 °C,

(1) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, 2, 565, 633.
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(8) Padwa, A.; Carlsen, P. H. J.; Ku, A. *J. Am. Chem. Soc.* **1977**, *99*, 2798.
(9) Padwa, A.; Kamigata, N. *J. Am. Chem. Soc.* **1977**, *99*, 1871.
(10) Padwa, A.; Carlsen, P. H. J. *J. Am. Chem. Soc.* **1975**, *97*, 3682.
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