Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. Spectra were determined with JEOL JNM-FX60Q NMR, Hewlett-Packard 5985 GC/MS, and Beckman Acculab-1 IR spectrometers. Microanalyses were performed by Galbraith Laboratories.

1,2,4,5-Tetraiodobenzene. Periodic acid (2.56 g, 11.2 mmol) was dissolved in 60 mL of concentrated H_2SO_4 while the mixture was stirred on ice. Crushed potassium iodide (5.58 g, 33.6 mmol) was added in small portions, followed by dropwise addition of benzene (1.00 mL, 11.2 mmol) to the resulting dark solution. After stirring to room temperature overnight, the thick, lavendar mixture was poured onto ice, and the resulting brownish precipitate filtered, triturated with methanol to remove I_2, and refiltered. The crude pink product (5.46 g, 84% yield) was moderately soluble in carbon disulfide and tetrahydrofuran and was crystallized from pyridine/ethanol, giving a 60% yield of off-white needles: mp 249–252 °C (lit.[6] mp 253 °C); ^{1}H NMR (CS_2 + $CDCl_3$) δ 8.23 (s); ^{13}C NMR δ 108.5 (s, CI), 147.1 (d, CH); MS, m/e 581.5 (M^+); small signal at 707.5 suggests less than 2% contamination with C_6I_5H; IR 3057 (w, CH), 1425, 1397, 1272, 1107, 982 (s), 869 cm^{-1}.

Anal. Calcd for $C_6I_4H_2$: C, 12.39; H, 0.35; I. 87.26. Found: C, 12.60; H, 0.26; I, 87.22.

Hexaiodobenzene. Periodic acid (3.82 g, 16.7 mmol), potassium iodide (8.35 g, 50.2 mmol), and benzene (0.50 mL, 5.58 mmol) were combined in 40 mL of sulfuric acid as described above. After stirring[9] for 6 h, the mixture was heated to 100 °C. After 10 h, the mixture was poured onto ice, filtered, washed with methanol, and finally washed with hot tetrahydrofuran to remove incompletely iodinated arenes. The orange crude product (3.40 g, 73% yield) was moderately soluble in *N*-methylpyrrolidinone and hot Me_2SO. Crystallization from pyridine/ethanol gave orange needles (45% yield) in two crops: mp 430 °C (dec with loss of I_2 starting about 370 °C) (lit.[5] mp >360 °C); ^{1}H NMR (Me_2SO-d_6) no signal; ^{13}C NMR δ 121.4 (CI); MS, m/e 833.3 (M^+); IR 1237, 1205 cm^{-1}.

Anal. Calcd for C_6I_6: C, 8.65; I, 91.35. Found: C, 8.77; I, 91.25.

Acknowledgment. I thank Dr. J. F. Parcher for the mass spectral analyses. This research was supported by the donors of the Petroleum Research Fund, administered by the American Chemical Society.

Registry No. Benzene, 71-43-2; periodic acid, 13444-71-8; potassium iodide, 7681-11-0; 1,2,4,5-tetraiodobenzene, 636-31-7; hexaiodobenzene, 608-74-2.

(8) Presented in part at the 186th National Meeting of the American Chemical Society, Washington, DC, Aug 1983.

(9) **Note Added in Proof**: Prof. Robert Hutchins has informed me that vigorous mechanical stirring is required when this procedure is performed on a large scale.

Thioimidate Methylides by the Desilylation Method: An Improved Synthesis of Pyrrolines and Pyrroles

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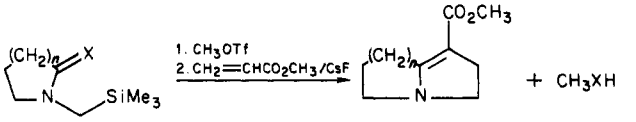
Received March 18, 1983

There are now several approaches to the generation of nonstabilized azomethine ylides by desilylation of α-trimethylsilyl iminium salts or equivalent species.[1-3] We had used an imidate methylide to assemble the retronecine nucleus in acceptable (51%) yield by trapping with methyl acrylate.[1b] However, other imidate ylide cycloadditions have proved inconsistent, and yields have often been low. For example, treatment of **1** with methyl triflate followed by $CsF/CH_2{=}CHCO_2CH_3$ affords a modest 37% yield of adduct **2**. We now report a substantial yield improvement by using the analogous thiolactam **3**. Under the usual conditions of ylide generation, enamine ester **2** is obtained in 66% yield.



1, X = O; n = 1
3, X = S; n = 1
4, X = S; n = 2

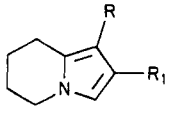
2, n = 1
5, n = 2

Table I. Cycloadducts from Imidate or Thioimidate Ylides + Dipolarophiles[a]

entry	starting material	dipolarophile	product(s)[c] (yield,[b] %)
11	**1**[b]	$CH_2{=}CHCO_2CH_3$	**2** (37)
22	**3**[c]	$CH_2{=}CHCO_2CH_3$	**2** (66)
33	**4**[c]	$CH_2{=}CHCO_2CH_3$	**5** (61)
4	**4**	$CH_3O_2CC{\equiv}CCO_2CH_3$	**6** (66) **9** (>90)
5	**4**	$HC{\equiv}CCO_2CH_3$	**7**[e] (31) **8**[e] (25) **10** (35)
6	**11**[d]	$CH_2{=}CHCO_2CH_3$	**13** (34)
7	**12**[c]	$CH_2{=}CHCO_2CH_3$	**13** (53)
8	**12**	$HC{\equiv}CCO_2CH_3$	**14**[e] (49) **15**[e] (20) **10** (53)
9	**16**[d]	$CH_2{=}CHCO_2CH_3$	complex
10	**17**[c]	$CH_2{=}CHCO_2CH_3$	**18** (56)

[a] Amide or thioamide + CH_3OTf/CH_2Cl_2; desilylation in situ, CsF/DME. [b] Yield of noncrystalline adduct, purified by preparative-layer chromatography. [c] From the amide + Lawesson's reagent,[8] >95% yield; see representative case in Experimental Section. [d] From the parent *N*-benzyl amide + NaH + Me_3SiCH_2I (see Experimental Section). [e] Isomers separated by preparative TLC, silica gel.

As seen from Table I, an improved yield of adducts is obtained in all cases (entries 1 vs. 2; 6 vs. 7; 9 vs. 10) where the thioimidate ylides have been compared with their oxygen analogues. The reasons for improved yields are probably related to (1) the relative ease of thioamide alkylation, (2) the greater stability of thioimidate salts, and (3) the tendency of the dipolarophile to scavenge the methyl mercaptan that is eliminated from the initial adduct. With $CH_3O_2CC{\equiv}CCO_2CH_3$ as dipolarophile (entry 4), the corresponding mercaptan adduct **9** can be isolated in >90% yield in addition to the pyrrole **6** (66%). With methyl propiolate as dipolarophile, the mercaptide adduct **10** is obtained.



6, R = R_1 = CO_2CH_3
7, R = CO_2CH_3; R_1 = H
8, R = H; R_1 = CO_2CH_3

$CH_3O_2CC(SCH_3){=}CHCO_2CH_3$

9

$CH_3SCH{=}CHCO_2CH_3$

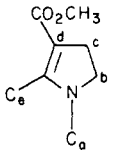
10

(1) (a) Vedejs, E.; Martinez, G. R. *J. Am. Chem. Soc.* **1979**, *101*, 6452. (b) Vedejs, E.; Martinez, G. R. *Ibid.* **1980**, *102*, 7993.

(2) Achiwa, K.; Sekiya, M. *Chem. Lett.* **1981**, 1213. Achiwa, K.; Sekiya, M. *Tetrahedron Lett.* **1982**, *23*, 2589. Terao, Y.; Imai, N.; Achiwa, K.; Sekiya, M. *Chem. Pharm. Bull.* **1982**, *30*, 367. Chen, S.-F.; Ullrich, J. W.; Mariano, P. S. *J. Am. Chem. Soc.* **1983**, *105*, 6160. Padwa, A.; Chen, Y.-Y. *Tetrahedron Lett.* **1983**, *24*, 3447.

(3) Smith, R.; Livinghouse, T. *J. Org. Chem.* **1983**, *48*, 1554.

Table II. NMR Characterization of Pyrroles and Pyrrolines[a]

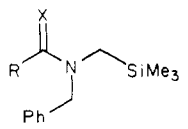


	OCH_3	H_a	H_b	H_c	H_d	H_e
2	3.65 (s)	3.01 (t, J = 7)	3.28 (t, J = 9)	3.02 (t, J = 9 Hz)		2.67 (t, J = 7)
5	3.63 (s)	2.96 (t, J = 5)	3.30 (t, J = 8)	2.68 (t, J = 8 Hz)		2.80 (t, J = 5)
6	3.78, 3.77 (s)	3.90 (t, J = 7)	7.02 (s)			2.95 (t, J = 7)
7	3.78 (s)	3.95 (t, J = 6)	6.52, 6.42	(ABq, J = 3)		3.08 (t, J = 6)
8	3.78 (s)	3.93 (t, J = 6)	7.12 (d, J = 1.5)		6.22 (d, J = 1.5)	2.73 (t, J = 6)
13	3.62 (s)	4.26 (s)	3.31 (t, J = 9)	2.27 (t, J = 9)		2.27 (s)
14	3.77	5.03 (s)	6.58, 6.53	(ABq, J = 3)		2.44 (s)
15	3.76 (s)	5.00 (s)	7.01 (s)		6.33 (s)	2.09 (s)
18	3.61 (s)	4.21 (s)	3.22 (t, J = 11)	2.64 (t, J = 11)		2.70 (t, J = 9)

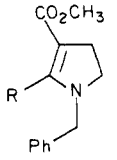
[a] 270-MHz NMR ($CDCl_3$) in ppm; J values are in hertz.

The condensation of thioimidate ylides with acetylenic dipolarophiles provides rapid access to pyrroles. However, the regiochemistry with the unsymmetrical $HC{\equiv}CCO_2CH_3$ is not as clean (entries 5 and 8) as with methyl acrylate as dipolarophile. It should be noted that the analogous cycloaddition of propiolate with munchnones also gives pyrroles directly.[4,5] The ethyl ester corresponding to **7** has been made with high selectivity by this method.[5]

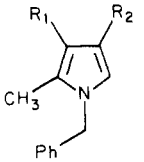
Entry 10, Table I, is significant because it shows that intermolecular ylide trapping with acrylate is more effective than intramolecular trapping by a simple unactivated alkene. No products derived from the internal adduct **19**



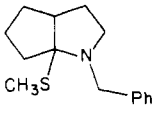
11, X = O; R = CH_3
12, X = S; R = CH_3
16, X = O; R = $(CH_2)_3CH{=}CH_2$
17, X = S; R = $(CH_2)_3CH{=}CH_2$



13, R = CH_3
18, R = $(CH_2)_3CH{=}CH_2$



14, R_1 = CO_2CH_3; R_2 = H
15, R_1 = H; R_2 = CO_2CH_3



19

have been detected with or without acrylate present. A recent report by Smith and Livinghouse describes a case where a similar intramolecular cycloaddition does occur.[3] In their example, a modified desilylation technique is used to generate a formamidine methylide.

Experimental Section

Representative Procedure: Amide → *N*-(Trimethylsilyl)methyl Amide → Thioamide → Pyrroline. *N*-Benzyl-*N*-[(trimethylsilyl)methyl]acetamide (11). A solution of *N*-benzylacetamide (0.15 g, 1.0 mmol) in dry Me_2SO (2 mL) under N_2 was added to NaH (0.027 g, 50% dispersion in oil, approximately 1.1 mmol) in dry Me_2SO (8 mL, distilled from CaH_2). After 90 min of vigorous stirring, (iodomethyl)trimethylsilane[7] (0.24 g, 1.1 mmol) was added, and the mixture was stirred for 0.5 h at 20 °C. Ether–water workup gave crude product, which was purified by filtration chromatography over 50 g of silica gel with ether. The product elutes faster than starting material, yield 0.14 g, 61%, and is sufficiently pure for the next step.

Thioamide 12. A solution of **11** (0.12 g, 0.52 mmol) in dry toluene (3 mL, distilled from CaH_2) was heated with Lawesson's reagent ((*p*-methoxyphenyl)thionophosphine sulfide dimer)[8] (0.13 g, 0.32 mmol) for 3 h at 100–110 °C with vigorous stirring under nitrogen. The bulk of the toluene was then removed by simple distillation, and the residue was purified by preparative-layer chromatography over silica gel with 20% ethyl acetate/hexane. The product was obtained at R_F 0.60, 0.13 g (99%), as a colorless oil: 200-MHz NMR ($CDCl_3$) benzyl singlets at 5.35 and 4.79 ppm, Me_3SiCH_2 at 3.74 and 3.16 ppm (*E*, *Z* thioamides), and CH_3–C at 2.69 ppm.

1-Benzyl-2-methyl-3-carbomethoxy-2-pyrroline (13). A solution of **12** (0.081 g, 0.32 mmol) in dry CH_2Cl_2 (4 mL, distilled from P_2O_5) was treated under nitrogen with methyl triflate (0.036 mL, 0.32 mmol) at 25 °C for 1 h. The solvent was removed under a nitrogen stream and replaced with dry dimethoxyethane (8 mL, distilled from sodium benzophenone). Methyl acrylate was added (0.086 mL, 0.96 mmol), and the solution was transferred under nitrogen pressure via a cannula into a flask containing powdered anhydrous CsF (0.146 g, 0.96 mmol, vacuum drived by repeated *gentle* heating with a small Bunsen flame until evolution of water vapor ceased, followed by 0.5 h, 20 °C all at 0.1 mm; strong heating causes formaton of brown decomposition products) and a magnetic stir bar. The mixture turned bright yellow at once. After stirring under nitrogen overnight, the solvent was removed (aspirator, *stench*!), and the residue was stirred with water (5 mL) and extracted with 3 × 5 mL of $CHCl_3$. After drying ($MgSO_4$) and evaporation (aspirator), the residual orange oil was separated into two zones by PLC on silica gel, 20% ethyl acetate/hexane. The R_f 0.6 band gave 0.017 g (38%) of $CH_3SCH_2CH_2CO_2CH_3$ and the R_f 0.4 band gave 0.039 g (53%) of **13** as a red oil: IR (neat) cm^{-1} 1670, 1585; NMR, see Table II.

The same standard procedures were used to prepare pyrroles and pyrrolines as shown in Table I.

Acknowledgment. This work was supported by PHS Grant CA17918 and by an NSF predoctoral fellowship to F.G.W.

Registry No. **1**, 76596-19-5; **2**, 87281-38-7; **3**, 87281-39-8; **4**, 87281-40-1; **5**, 87281-41-2; **6**, 87281-42-3; **7**, 87281-43-4; **8**, 87281-44-5; **9**, 87281-45-6; **10**, 13733-57-8; **11**, 87281-46-7; **12**, 87281-47-8; **13**, 87281-48-9; **14**, 87281-49-0; **15**, 87281-50-3; **16**, 87281-51-4; **17**, 87281-52-5; **18**, 87281-53-6; CH_3OTf, 333-27-7; $CH_2{=}CH(CH_2)_3CONHCH_2Ph$, 87281-54-7; $CH_2{=}CHCO_2CH_3$, 96-33-3; CsF, 13400-13-0; $CH_3O_2CC{\equiv}CCO_2CH_3$, 762-42-5; $HC{\equiv}CCO_2CH_3$, 922-67-8; *N*-benzylacetamide, 588-46-5; (iodomethyl)trimethylsilane, 4206-67-1.

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(7) Peterson, P. E.; Carol, S. *Synthesis* **1980**, 318.
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