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Novel Synthesis of Heterocycles Using Stannyl Anion Generated from $Me_3SiSnBu_3$ and F^-

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It has been found that stannyl anion, which is generated from $Me_3SiSnBu_3$ in the presence of R_4NX in DMF, can react with an aryl or vinyl halide to produce an aryl or vinyl anion.[1] The reaction procedure is very simple, and the aryl or vinyl anion generated can react intramolecularly with an aldehyde, ketone, or ester carbonyl group in a chain to give a cyclized product in good yield. During the course of our studies, we have found that F^- is the most effective as the halide ion of R_4NX.[1b] Now we report a novel synthesis of heterocycles by the reaction of the aryl or vinyl anion generated with an imide carbonyl group.

To a DMF solution of the imide **1a** and TASF[2] [$(Et_2N)_3S^+Me_3SiF_2^-$] was added $Me_3SiSnBu_3$[3] at −50 °C. This solution was stirred at the same temperature for 3 h giving the desired cyclized product **2a** in 76% yield. Although the reaction proceeded in the presence of CsF instead of TASF at 0 °C, the yield of **2a** decreased to 27% and the dehalogenation product **3a** was obtained in 23% yield. On the other hand, treatment of **1b** with $Me_3SiSnBu_3$ and TASF did not afford good results, but instead using CsF improved the yield of the desired product **2b** (81% yield). Hydrogenation of the crude product **2b** with 10% Pd/C in the presence of TsOH afforded compound **4**. However, treatment of **5** with $Me_3SiSnBu_3$ and TASF or CsF did not afford the cyclized product, and only the dehalogenation product **6** was obtained (78% yield).

Subsequently, vinyl iodide **9a**, which was prepared from succinimide (**7a**) and vinyl iodide **8**[4] in the presence of KF–Celite[5] in CH_3CN upon heating, was treated with $Me_3SiSnBu_3$ and CsF in DMF at 0 °C. The cyclized product **10a**, whose structure was confirmed by its NMR and mass spectra, was a polar substance and could not be separated from DMF. Thus, the crude product **10a** was treated with *p*-TsOH in MeOH at room temperature in order to convert it to the methoxylated compound **13**. However, the acyl pyrrole derivative **11a** was obtained in 59% yield *via* the acyliminium salt **10a′**. Hydrogenation of **11a** with 10% Pd/C in EtOH gave the pyrrolizinone derivative **12a** in 77% yield.

Scheme I

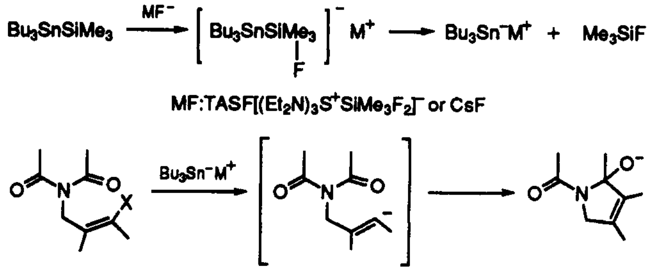
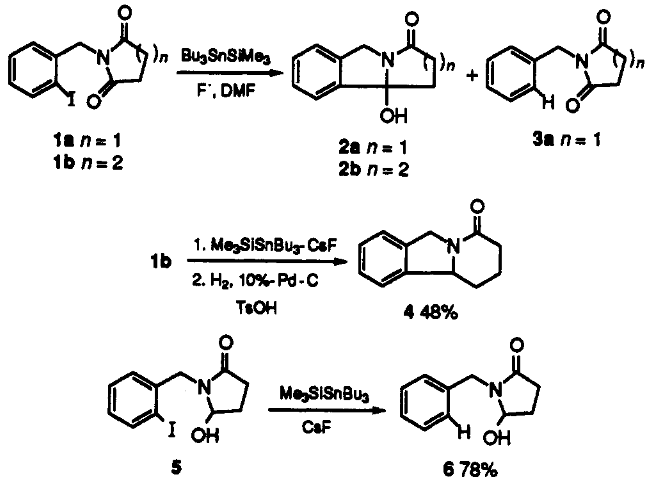


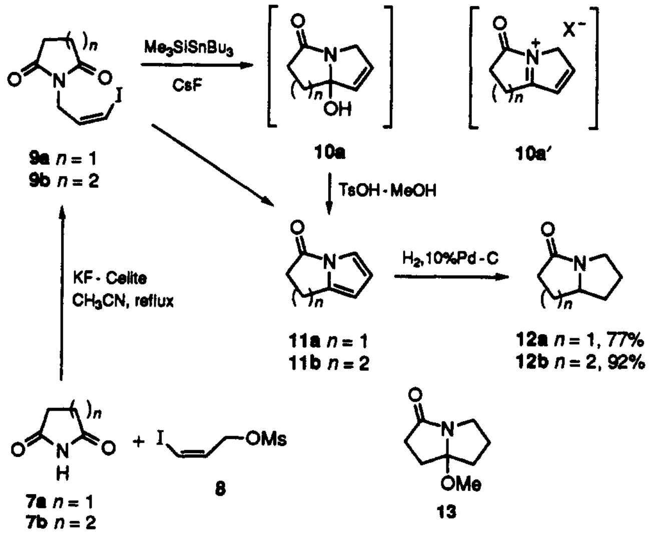
Table I. Reaction of 1 with $Me_3SiSnBu_3$ in the Presence of F^-

run	substrate	F^-	temp (°C)	2 (%)	3 (%)
1	**1a**	TASF	−50	76	
2	**1a**	CsF	0	27	23
3	**1b**	TASF	−50	44	
4	**1b**	CsF	0	81	

Scheme II



Scheme III



On the other hand, the vinyl iodide **9b**, which was obtained from glutarimide (**7b**) and vinyl iodide **8**, was treated with $Me_3SiSnBu_3$–CsF in DMF at 0 °C. In this case, the acyl pyrrole **11b** was obtained directly in 74% yield, which was hydrogenated with 10% Pd/C in EtOH to give the indolizidine derivative **12b** in 92% yield. Treatment of **12b** with $LiAlH_4$ afforded δ-coniceine (**14**)

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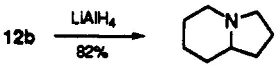
in 75% yield, whose structure was confirmed by the melting point of its known picrate.[6]

$$\mathbf{9a} \xrightarrow[\text{2. TsOH-MeOH}]{\text{1. Me}_3\text{SiSnBu}_3\text{-CsF}} \underset{59\%}{\mathbf{11a}}$$



δ-coniceine (14)

These results indicate that cyclization of an aryl or vinyl iodide having an imide in the chain provides heterocyclic compounds in good yield. The reaction procedure is simple, and the reaction proceeds smoothly at 0 °C.

Experimental Section

Solvents were distilled under argon from sodium benzophenone ketyl (THF), CaH$_2$ (DMF, Et$_3$N), or P$_2$O$_5$ (CH$_2$Cl$_2$). Me$_3$SiSnBu$_3$[3] and TASF[2c] were prepared by the reported procedure. The solvent (THF) of TASF (1 M THF solution) was replaced with DMF before the reaction was carried out. NMR spectra were recorded at 100 MHz. Melting points are uncorrected.

General Procedure for the Cyclization of an Aryl or Vinyl Iodide. To a solution of the substrate (1 equiv) and TASF or CsF (2 equiv) was added Me$_3$SiSnBu$_3$ at an appropriate temperature, and the solution was stirred at the same temperature until the starting material disappeared on TLC. Ether was added to the reaction mixture, and the organic layer was washed with aqueous 10% NH$_4$OH solution and then brine. The organic layer was dried over Na$_2$SO$_4$ and was concentrated. The residue was purified by chromatography on silica gel.

Cyclization of 1a. The crude product, which was prepared from **1a** (46.4 mg, 0.147 mmol), TASF (0.3 mL, 0.3 mmol), and Me$_3$SiSnBu$_3$ (0.1 mL, 0.286 mmol) in DMF (1 mL) at -50 °C, was purified by chromatography on silica gel [hexane–ethyl acetate–NEt$_3$ (100:100:1)] to give **2a** (21.8 mg, 76%): IR (Nujol) 3292, 1667, 1590 cm^{-1}; ^{1}H NMR (C$_6$D$_6$) δ 1.6–2.4 (m, 4H), 2.6–2.9 (m, 1H), 3.99 and 4.49 (ABq, J = 10.5 Hz, 2H), 6.6–7.6 (m, 4H); MS m/z 189 (M$^+$), 171 (M$^+$ - H$_2$O); HRMS m/z calcd for C$_{11}$H$_{11}$NO$_2$ 189.0890, found 189.0779.

Cyclization of 1b. The crude product, which was prepared from **1b** (206 mg, 0.626 mmol), CsF (189 mg, 1.24 mmol), and Me$_3$SiSnBu$_3$ (0.44 mL, 1.26 mmol) in DMF (4 mL) at 0 °C, was purified by chromatography on silica gel [hexane–ethyl acetate–NEt$_3$ (100:100:1)] to give **2b** (103 mg, 81%): IR (Nujol) 3317, 1620, 1590 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.4–2.0 (m, 4H), 2.4–2.7 (m, 3H), 4.58 and 4.97 (ABq, J = 16.1 Hz, 2H), 7.2–7.4 (m, 4H); MS m/z 203 (M$^+$), 185 (M$^+$ - H$_2$O, bp): HRMS m/z calcd for C$_{12}$H$_{13}$NO$_2$ 203.0946, found 203.0934.

Cyclization of 9a. To a solution of **9a** (147 mg, 0.554 mmol) and CsF (145 mg, 0.955 mmol) in DMF (1 mL) was added Me$_3$SiSnBu$_3$ (0.34 mL, 0.974 mmol) at 0 °C, and the solution was stirred for 2 h at the same temperature. A solution of p-TsOH (44.3 mg, 0.233 mmol) in MeOH (1 mL) was added to the reaction mixture, and the solution was stirred for 2 h. Ether was added, and the ether layer was washed with aqueous NaHCO$_3$ solution and then brine, dried over Na$_2$SO$_4$, and concentrated. The residue was purified by chromatography on silica gel (hexane–ethyl acetate = 1:1) to give the acyl pyrrole **11a** (39.9 mg, 59%): IR (Nujol) 1734 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 3.03 (s, 4H), 5.96 (dd, J = 1.1, 2.9 Hz, 1 H), 6.46 (dd, J = 2.9, 3.2 Hz, 1 H), 7.05 (dd, J = 1.1, 3.2 Hz, 1 H); MS m/z 121 (M$^+$), 93 (M$^+$ - CO), 80; HRMS m/z calcd for C$_7$H$_7$NO 121.0528, found 121.0503.

Cyclization of 9b. The crude product, which was prepared from **9b** (61.4 mg, 0.220 mmol), CsF (67.0 mg, 0.441 mmol), and Me$_3$SiSnBu$_3$ (0.15mL, 0.429 mmol) in DMF (1 mL) at 0 °C, was purified by chromatography on silica gel (hexane–ether = 1:1) to give the acyl pyrrole **11b** (21.9 mg, 74%): IR (Nujol) 1719 cm^{-1}; ^{1}H NMR (100 MHz) (CDCl$_3$) δ 1.8–2.2 (m, 2H), 2.6–3.0 (m, 4 H), 5.97 (dd, J = 1.46, 3.29 Hz, 1 H), 6.21 (dd, J = 3.3, 3.4 Hz, 1 H), 7.35 (dd, J = 1.5, 3.4 Hz, 1 H); MS m/z 135 (M$^+$), 80; HRMS m/z calcd for C$_8$H$_9$NO 135.0684, found 135.0667.

Hydrogenation of the Cyclized Product 2b. Crude **2b** (83.2 mg), 10% Pd/C (78.6 mg), and p-TsOH (9.0 mg, 0.047 mmol) was stirred in CH$_2$Cl$_2$ (3 mL) under hydrogen for 56 h. After filtration, the solvent was removed, and the residue was purified by chromatography on silica gel (ethyl acetate) to give **4** (36.8 mg, 48% yield from **1b**): IR (Nujol) 1629 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.4–2.3 (m, 4H), 2.3–2.6 (m, 2H), 4.53 and 5.11 (ABq, J = 15.4, 2H), 4.6–4.9 (m, 1H), 7.1–7.4 (m, 4 H); MS m/z 187 (M$^+$), 159 (M$^+$ - CO), 117 (bp); HRMS m/z calcd for C$_{12}$H$_{13}$NO 187.0997, found 187.0991.

Hydrogenation of 11a. A solution of the acyl pyrrole **11a** (31.1 mg, 0.231 mmol) and 10% Pd/C (61.6 mg) in EtOH (1mL) was stirred under hydrogen for 1 h. The undissolved material was filtered off, and the filtrate was concentrated. The residue was purified by chromatography on silica gel (hexane–ethyl acetate (1:1)) to give a colorless oil of **12a** (22.2 mg, 77%): IR (Nujol) 1674 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.0–4.1 (m, 11H); MS m/z 125 (M$^+$), 97 (M$^+$ - CO), 69: HRMS m/z calcd for C$_7$H$_{11}$NO 125.0841, found 125.0834.

Hydrogenation of 11b. A solution of the acylpyrrole **11b** (10.1 mg, 0.231 mmol) and 10% Pd/C (20.6 mg) in EtOH (2mL) was stirred under hydrogen for 5 h. The solution was filtered, and the filtrate was concentrated. The residue was purified by chromatography on silica gel (ethyl acetate–MeOH (1:1)) to give **12a** as a colorless oil (9.6 mg, 92%): IR (Nujol) 1621 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.0–2.5 (m, 10 H), 3.2–3.7 (m, 3H); MS m/z 139 (M$^+$), 111 (M$^+$ - CO), 83, 70; HRMS m/z calcd for C$_8$H$_{13}$NO 139.0997, found 139.0978.

δ-Coniceine (13). A solution of **12a** (47.9 mg, 0.354 mmol) and LiAlH$_4$ (53.4 mg, 1.41 mmol) in THF (1.0 mL) was stirred for 4 h at room temperature. To the reaction mixture was added Na$_2$SO$_4$·10H$_2$O, and the solution was stirred overnight. Undissoved material was filtered off, and 3.5% HCl-EtOH (0.5 mL) was added to the filtrate. The solvent was evaporated to give δ-coniceine hydrochloride (46.9 mg, 82%). δ-Coniceine picrate: mp 218–221 °C (lit.[6] mp 225–228 °C); MS m/z 125 (M$^+$), 124 (bp), 97, 83; HRMS m/z calcd for C$_8$H$_{15}$N 125.1205, found 125.1205. Anal. Calcd for C$_{14}$H$_{18}$N$_4$O$_7$: C, 47.46; H, 5.12; N, 15.81. Found; C, 47.11; H, 4.90; N, 15.54.

Supplementary Material Available: ^{1}H-NMR spectra of all new compounds (7 pages). This material is contained in 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.

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