Preparation of 1-(4-Cyanophenyl)-1-phenyl-2,2,2-trifluoroethyl Tosylate. The titled compound was synthesized from butyllithium, 4-bromobenzonitrile, α,α,α-trifluoroacetophenone, and tosyl chloride following the general procedure for the preparation of *p*-nitrobenzoates. Esterification at room temperature for 24 h followed by separation and recrystallization gave 65% yield of the tosylate: mp 88–88.5 °C; IR (KBr) 2232 (m) (CN), 1376 (s) and 1171 (s) (O_3SAr), 1194 cm^{-1} (s) (CF_3); ^1H NMR (CCl_4) δ 2.42 (3 H, s, CH_3), 7.30 (8 H, m), 7.59 (5 H, s, C_6H_5). Anal. ($C_{22}H_{16}NO_3F_3S$) C, H, N.

Acknowledgment. We are indebted to the National Science Council for financial support of this work.

Registry No. PNBCl, 122-04-3; $PhC(O)CF_3$, 434-45-7; *t*-Bu_2CO, 815-24-7; *t*-$BuC(O)CH_3$, 75-97-8; 4-$CF_3C_6H_4Br$, 402-43-7; PhBr, 108-86-1; 4-CNC_6H_4Br, 623-00-7; 3-$CF_3C_6H_4Br$, 401-78-5; *i*-PrCl, 75-29-6; Ph_2CO, 119-61-9; BzCl, 98-88-4; TsCl, 98-59-9; $Ph_2C(4\text{-}CF_3C_6H_4)OC(O)\text{-}4\text{-}C_6H_4NO_2$, 108418-82-2; $Ph_3COC(O)Ph$, 17714-77-1; $PhC(CF_3)(4\text{-}CNC_6H_4)OSO_2\text{-}4\text{-}C_6H_4Me$, 108418-83-3; $Ph_2C(CF_3)OC(O)\text{-}4\text{-}C_6H_4jNO_2$, 108418-84-4; *t*-$Bu_2C(4\text{-}CF_3C_6H_4)OC(O)\text{-}4\text{-}C_6H_4NO_2$, 40544-07-8; $CH_3C(t\text{-}Bu)(Ph)OC(O)\text{-}4\text{-}C_6H_4NO_2$, 42044-42-8; $CH_3C(t\text{-}Bu)(3\text{-}CF_3C_6H_4OC(O)\text{-}4\text{-}C_6H_4NO_2$, 108418-85-5; cyclopentanone, 120-92-3; adamantanone, 700-58-3; 1-[[(4-nitrophenyl)carbonyl]oxy]-1-[3-(trifluoromethyl)phenyl]cyclopentane, 108418-86-6; 2-[[(4-nitrophenyl)carbonyl]oxy]-2-isopropyladamantane, 38432-73-4.

Preparation of Enaminones by Two-Carbon Homologation of Amides with Lithium (Triphenylsilyl)acetylide

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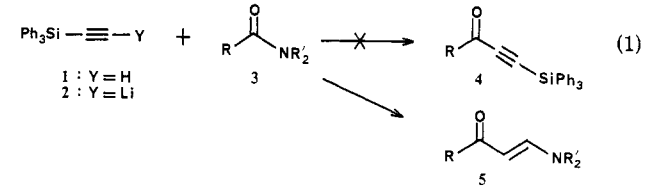
Enaminones[1] constitute a class of compounds that are versatile for the synthesis of heterocyclic or aromatic compounds.[2] They are used in some other useful synthetic transformations.[3] Therefore, a variety of their preparative methods have been reported thus far.[4]

During the course of our recent investigations,[5] we encountered an unexpected formation of enaminones during the reaction of lithium (triphenylsilyl)acetylide (**2**) with carboxamides (eq 1): attempted reaction of **2** with amide



(1)

3 gave none of the expected alkynone **4**, although the starting material was completely consumed. TLC inspection indicated the formation of a highly polar product which was isolated and identified as the two-carbon-inserted enaminone **5**. This outcome can be understood by the following sequence of events: the initial formation of the silylalkynone followed by the Michael-type addition of in situ-formed lithium amide and subsequent protiodesilylation.[6] A D_2O-quenching experiment showed the double incorporation of deuterium into the product (Figure 1), where D^α underwent gradual replacement by a proton under certain conditions such as the purification on silica gel TLC. Intrigued by these observations and also considering the synthetic utility of enaminones, we briefly surveyed the scope of the present unexpected reaction.

Table I represents some aspects of the reaction. While amides with a Me_2N or pyrrolidino group were smoothly converted to the enaminones **5** (entries 1, 2, 4, 5), the amides bearing bulkier amino groups such as Et_2N (entry 3) or Ph_2N (not shown) gave none of the corresponding enaminones. Concerning the substituents on silicon, *triphenyl* is essential for smooth enaminone formation, and other silylacetylides (e.g. *t*-$BuMe_2SiC{\equiv}CLi$) gave the normal product **4**.[7,8]

Aside from these features, application to the two-carbon ring expansion of cyclic amides (entries 6–8) is notable: five to seven-membered *N*-methyl lactams underwent this two-carbon insertion to afford the corresponding medium-ring azacycles **5f–h**.[9] In these cases, a slight modification of the reaction conditions (method B; see Experimental section) was necessary, that is, (1) the use of $BF_3{\cdot}OEt_2$,[10] which is essential for the addition reaction to proceed, and (2) the use of a less polar solvent mixture (hexane–THF, 5/1) for the improvement of the yields.[11]

Experimental Section

General. Infrared (IR) spectra were recorded on a JASCO A-202 spectrometer. ^1H NMR spectra were measured on a Varian EM 390 spectrometer at 90 MHz. ^{13}C NMR spectra were measured on a JEOL GX 400 spectrometer at 100 MHz. The chemical shifts are expressed in parts per million downfield from internal tetramethylsilane (δ = 0). Mass spectra (MS) were obtained with a Hitachi M-80 spectrometer. All experiments were carried out under an atmosphere of dry argon. For thin-layer chromatography (TLC) analysis, Merck precoated plates (silica gel 60 GF 254, 0.25 mm) were used. The products were purified by preparative TLC

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(2) (a) Meyers, A. I.; Reine, A. H.; Sircar, J. C.; Singh, S.; Weidman, H.; Fitzpatrick, M. *J. Hetrocycl. Chem.* **1968**, *5*, 151. (b) Iida, H.; Yuasa, Y.; Kibayashi, C. *J. Am. Chem. Soc.* **1978**, *100*, 3598. (c) Barton, D. H. R.; Dressaire, G.; Willis, B. J.; Barrett, A. G. M.; Pfeffer, M. *J. Chem. Soc., Perkin Trans. 1* **1982**, 665. (d) Takeuchi, N.; Okada, N.; Tobinaga, S. *Chem. Pharm. Bull.* **1983**, *31*, 4355.

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(5) Suzuki, K.; Ohkuma, T.; Miyazawa, M.; Tsuchihashi, G. *Tetrahedron Lett.* **1986**, *27*, 373.

(6) Reaction of $MeCOC{\equiv}CSiPh_3$ (prepared by the Friedel–Crafts reaction, i.e., $AcCl—Ph_3SiC{\equiv}CSiPh_3—AlCl_3$: Newman, H. *J. Org. Chem.* **1973**, *38*, 2254) with lithium salt of pyrrolidine in THF gave almost quantitative yield of the corresponding enaminone **5**.

(7) Reaction of Me_3Si- or *t*-$BuMe_2Si$-acetylide gave the corresponding alkynone **4**, while Ph_2MeSi-acetylide gave a varying mixture of **4** and **5** depending on the conditions. For the related examples of Me_3Si cases, see: Cupps, T. L.; Boutin, R. H.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 3972.

(8) Since the Michael addition of amines to alkynones is known,[4c,d] the transformation (**3**→**5**) is formally possible simply by using $LiC{\equiv}CH$. However, this protocol appeared to be inefficient in this context, where the use of excess reagents or forcing conditions led to the complex mixture of products.

(9) For related ring expansion of lactones, see: Schreiber, S. L.; Kelly, S. E. *Tetrahedron Lett.* **1984**, *25*, 1757.

(10) Yamaguchi, M.; Waseda, T.; Hirao, I. *Chem. Lett.* **1983**, 35.

(11) The reaction using $BF_3{\cdot}OEt_2$ should be stopped with aqueous acids, such as CH_3COOH, $(COOH)_2$, etc. Substantial decomposition of the products occurred with MeOH or H_2O quenching.

0022-3263/87/1952-2929$01.50/0

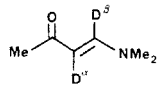
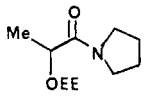
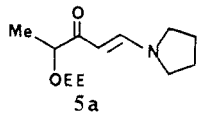
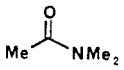
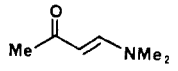
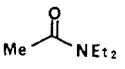
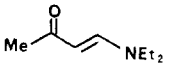
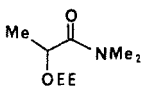
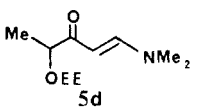
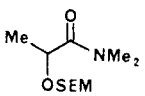
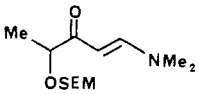
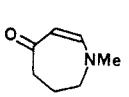
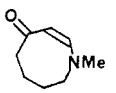
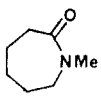
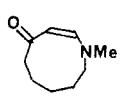


Figure 1.

Table I[a]

entry	reactants	products[b]	method[c]	yield, %
1	 3a	 5a	A	82
2	 3b	 5b	A	68
3	 3c	 5c	A[d], B[e]	
4	 3d	 5d	A	78
5	 3e	 5e	A	80
6	 3f	 5f	B	70
7	 3g	 5g	B	42
8	 3h	 5h	B	28

[a] EE = $CH(CH_3)OCH_2CH_3$, SEM = $CH_2OCH_2CH_2Si(CH_3)_3$. [b] Geometry of the double bond is determined as depicted on the basis of the coupling constant. [c] Method A: 2/THF. Method B: 2-BF_3·OEt_2/THF–hexane (v/v 1/5) (see Experimental Section). [d] No reaction. [e] Complex mixture of products formed.

using Wako silica gel B-5F. Tetrahydrofuran (THF) was distilled from benzophenone ketyl immediately before use. Amides **3b, c** and lactams **3f–h** were obtained from commercial sources; the amides **3a, d, e** were prepared from ethyl lactate by aminolysis and subsequent protection.

Preparation of 5a (Method A). To a solution of 1 (284 mg, 1.0 mmol) in THF (2 mL) was added *n*-BuLi (1.5 M hexane; 0.67 mL) at −78 °C, and the mixture was stirred for 15 min. Amide **3a** (172 mg, 0.8 mmol) in THF (2 mL) was then added to the mixture, and stirring was continued for 5 h at −45 °C. After MeOH was added, the reaction mixture was gradually warmed to room temperature and evaporated. The resulting oily residue was chromatographed on silica gel TLC (hexane/acetone, 50/50) to afford enaminone **5a** (158 mg, 82%) as a colorless oil: ^1H NMR (CCl_4) δ 1.0–1.5 (m, 9 H), 1.65–2.3 (m, 4 H), 3.1–4.05 (m, 7 H), 4.4–4.7 (m, 1 H), 5.1 (d, 0.6 H, J = 13.5 Hz), 5.2 (d, 0.4 H, J = 13.5 Hz), 7.6 (d, 1 H, J = 13.5 Hz); IR (neat) 1645 cm^{-1}; HRMS, m/z 241.1651, calcd for $C_{13}H_{23}NO_3$ 241.1675.

Enaminones **5b, d, e** were prepared in essentially the same manner as described above and their physical properties are listed below.

5b: oil; ^1H NMR (CCl_4) δ 1.9 (s, 3 H), 2.85 (s, 6 H), 4.85 (d, 1 H, J = 13.5 Hz), 7.25 (d, 1 H, J = 13.5 Hz); IR (neat) 1660 cm^{-1}; HRMS, m/z 113.0846, calcd for $C_6H_{11}NO$ 113.0840.

5d: oil; ^1H NMR (CCl_4) δ 1.0–1.4 (m, 9 H), 2.95 (s, 6 H), 3.25–3.65 (m, 2 H), 3.65–4.05 (m, 1 H), 4.4–4.75 (m, 1 H), 5.15 (d, 0.6 H, J = 13.5 Hz), 5.3 (d, 0.4 H, J = 13.5 Hz), 7.4 (d, 0.4 H, J = 13.5 Hz), 7.45 (d, 0.6 H, J = 13.5 Hz); IR (neat) 1655 cm^{-1}; HRMS, m/z 215.1516, calcd for $C_{11}H_{21}NO_3$ 215.1519.

5e: oil; ^1H NMR (CCl_4) δ 0.0 (s, 9 H), 0.6–1.0 (m, 2 H), 1.2 (d, 3 H, J = 6 Hz), 2.9 (br s, 6 H), 3.35–3.6 (m, 2 H), 3.8 (q, 1 H, J = 6 Hz), 4.45 (d, 1 H, J = 9 Hz), 4.55 (d, 1 H, J = 9 Hz), 5.2 (d, 1 H, J = 13.5 Hz), 7.35 (d, 1 H, J = 13.5 Hz); IR (neat) 1655 cm^{-1}; HRMS, m/z 273.1772, calcd for $C_{13}H_{27}NO_3$ 273.1759.

Preparation of 5f (Method B). To a THF (2 mL) solution of $LiC{\equiv}CSiPh_3$ (**2**) (1.0 mmol), prepared in the same manner as described in method A, was added BF_3·OEt_2 (142 mg, 1.0 mmol) in THF (0.5 mL), and the mixture was diluted with hexane (12.5 mL). To this solution was then added amide **3f** (79 mg, 0.8 mmol) in THF–hexane (1/5 v/v; 1 mL), and the mixture was stirred for 5 h at −45 °C. The reaction was quenched with 50% aqueous CH_3COOH (0.5 mL)[11] and gradually warmed up to room temperature. Solvents were evaporated in vacuo, and the residue was chromatographed on silica gel TLC (EtOH/acetone, 50/50) to afford **5f** as white solids: mp 81.5–82 °C; ^1H NMR ($CDCl_3$) δ 1.9–2.25 (m, 2 H), 2.9 (s, 3 H), 3.15 (t, 2 H, J = 7.5 Hz), 3.6 (t, 2 H, J = 7.5 Hz), 5.2 (d, 1 H, J = 9 Hz), 9.15 (d, 1 H, J = 9 Hz); ^{13}C NMR ($CDCl_3$) δ 20.6, 29.9, 33.1, 54.8, 94.5, 168.5, 187.0; IR (neat) 1610, 1580 cm^{-1}; HRMS; m/z 125.0825, calcd for $C_7H_{11}NO$, 125.0839.

Cyclic enaminones **5g** and **5f** were prepared by this method, and their physical properties are listed below.

5g: oil; ^1H NMR (CCl_4) δ 1.55–2.1 (m, 4 H), 2.9 (s, 3 H), 2.95 (t, 2 H, J = 7.5 Hz), 3.3 (t, 2 H, J = 7 Hz), 4.85 (d, 1 H, J = 7 Hz), 9.4 (d, 1 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 19.2, 23.1, 25.5, 40.1, 51.7, 76.9, 98.9, 164.5, 185.8; IR (neat) 1600, 1560 cm^{-1}; HRMS, m/z 139.1007, calcd for $C_8H_{13}NO$ 139.0993.

5h: oil; ^1H NMR (CCl_4) δ 1.4–1.85 (m, 6 H), 2.8–3.1 (m, 2 H), 2.95 (s, 3 H), 3.35–3.6 (m, 2 H), 4.75 (d, 1 H, J = 7 Hz), 9.35 (d, 1 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 26.0, 27.3, 27.4, 28.8, 41.0, 54.8, 101.0, 169.8, 186.8; IR (neat) 1605, 1560 cm^{-1}; HRMS, m/z 153.1150, calcd for $C_9H_{15}NO$ 153.1152.

Acknowledgment. Financial support from the Ministry of Education, Science and Culture of Japan, is deeply acknowledged.

Registry No. **1**, 6229-00-1; **3a**, 108344-13-4; **3b**, 127-19-5; **3d**, 96642-85-2; **3e**, 108344-14-5; **3f**, 872-50-4; **3g**, 931-20-4; **3h**, 2556-73-2; **5a**, 108344-15-6; **5b**, 1190-91-6; **5d**, 108344-16-7; **5e**, 108344-17-8; **5f**, 108344-18-9; **5g**, 108344-19-0; **5h**, 108344-20-3.

Toxicants from Mangrove Plants. 3. Heritol, a Novel Ichthyotoxin from the Mangrove Plant *Heritiera littoralis*[1]

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An ethnobotanical survey of mangrove vegetation in Southeast Asia revealed[2] that certain plants possess toxic

