containing pure **3** were combined, and the solvent was removed under reduced pressure to yield pure **3** [3.28 g (90%)] as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.94 (s, py H-3, 2 H), 3.61 (t, J = 7.1 Hz, CH_2O, 2 H) 3.36 (s, OCH_3, 3 H), 2.84 (t, J = 7.1 Hz, 2 H, py CH_2, 2 H), 1.33 (s, CCH_3, 18 H); ^{13}C NMR ($CDCl_3$) δ 167.4 (py C-2), 147.2 (py C-4), 115.7 (py C-3), 72.8 (CH_2O), 58.6 (OCH_3), 37.6 (CCH_3), 36.2 (py-CH_2), 30.3 (CCH_3). Anal. Calcd for $C_{16}H_{27}NO$: C, 77.06; H, 10.91. Found: C, 77.13; H, 10.93.

4-Vinyl-2,6-di-*tert*-butylpyridine (4). To a chilled (-78 °C) THF (150 mL) solution containing **3** (3.50 g, 14.0 mmol) was added, in one portion, potassium *tert*-butoxide (3.15 g, 28.0 mmol). The cooling bath was removed, and the mixture was allowed to warm to room temperature and react for 2.5 h. The mixture was diluted with diethyl ether (200 mL) and H_2O (75 mL), and the layers were separated. The aqueous layer was back-extracted with diethyl ether (75 mL). The diethyl ether solutions were combined and washed with H_2O (100 mL) and finally brine (100 mL). The organic layer was dried (K_2CO_3) and filtered, and the solvents were removed under reduced pressure to afford crude **4** [2.60 g (85%)] as a colorless oil. Purification of **4** was achieved by flash chromatography on basic alumina (4 × 8 cm) with hexanes. Removal of the solvent under reduced pressure gave analytically pure **4** [2.49 g (82%)] as a clear oil: ^{1}H NMR ($CDCl_3$) δ 7.08 (s, py H-3, 2 H), 6.67 (dd, J = 10.8, 17.6 Hz, C*H*=CH_2, 1 H), 5.91 (d, J = 17.6 Hz, =CH_2, 1 H), 5.38 (d, J = 10.8 Hz, =CH_2, 1 H), 1.33 (s, CCH_3, 18 H); ^{13}C NMR ($CDCl_3$) δ 167.9 (py C-2), 144.6 (py C-4), 136.3 (*C*H=CH_2), 116.6 (=CH_2), 112.5 (py C-3), 37.7 (CCH_3), 30.3 (CCH_3). Anal. Calcd for $C_{15}H_{23}N$: C, 82.89; H, 10.67. Found: C, 82.85; H, 10.71.

Suspension Polymerization of 4 with Styrene and Divinylbenzene. A 250-mL three-neck Morton flask equipped with a mechanical stirrer and condenser was charged with a degassed aqueous (60 mL) solution of PVP (500 mg) and then vigorously stirred. A degassed solution containing styrene (490 mg, 4.8 mmol), divinylbenzene (119 mg), and **4** (357 mg, 1.6 mmol) was cannulated into the rapidly stirred PVP solution to form an emulsion. With continued stirring, a degassed toluene (2 mL) solution of AIBN (50 mg, 4 mol %) was added by cannula, and the suspension was heated at 65 °C for 20 h. The suspension was cooled and diluted with methanol (50 mL). Stirring was continued for 30 min, and then the mixture was transferred to a beaker. The beads were allowed to settle, and the supernatant liquid was decanted. The beads were washed/stirred/decanted with methanol (2 × 50 mL), tetrahydrofuran (2 × 150 mL), benzene (100 mL), and finally methanol (100 mL). The polymer was dried under reduced pressure at 65 °C for 24 h to afford beads [0.52 g (52%)] ranging in size from 80 to 300 μm. Anal. Calcd: N, 2.21. Found: N, 2.25.

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Registry No. **1**, 38222-83-2; **3**, 107082-94-0; **4**, 81869-04-7; $ClCH_2OCH_3$, 107-30-2; (divinylbenzene)(styrene)(4-vinyl-2,6-di-*tert*-butylpyridine)(copolymer), 107054-29-5.

Conjugate Reduction of α,β-Acetylenic Ketones and Esters by Diisobutylaluminum Hydride–Hexamethylphosphoric Triamide

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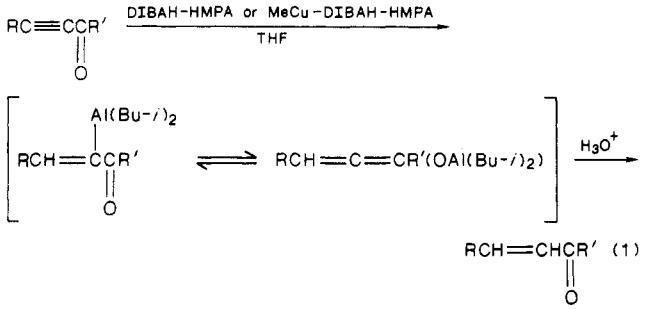
Recently we have reported an efficient and selective methylcopper- (MeCu-) catalyzed conjugate reduction of α,β-olefinic carbonyl compounds by diisobutylaluminum hydride (DIBAH) in the presence of hexamethylphosphoric triamide (HMPA) as a ligand to aluminum, where aluminum enolate intermediates generated by the hydralumination of α,β-unsaturated carbonyl compounds by DIBAH are involved.[1] In the present study, we tried to extend the scope of this novel reducing reagent; i.e., we investigated the conjugate reduction of α,β-acetylenic ketones and esters by the DIBAH–HMPA and the MeCu–DIBAH–HMPA systems (eq 1). Although catalytic



hydrogenation has been known to effect the cis-conjugate reduction of α,β-acetylenic carbonyl compounds (vide post),[2] only a few examples of the conjugate reduction by metal hydrides or complex metal hydrides are known. The reduction of methyl propiolate with the Bu_3SnH–MeOH system gives methyl acrylate in a low yield.[3] The conjugate reduction of methyl 2-butynoate and methyl phenylpropiolate is effected by the use of a large amount of the reducing reagent $NaAlH_2(OCH_2CH_2OCH_3)_2$–CuBr,[4] while the complex metal hydrides such as LiCuHR[5] and $LiBH(s\text{-}Bu)_3$[6] have been reported not to be able to accomplish the conjugate reduction of α,β-acetylenic carbonyl compounds.

First, factors influencing the conjugate reduction of α,β-acetylenic ketone were examined using 2-methyl-4-nonyn-3-one (**1**) as a representative substrate. The results are summarized in Table I. In the presence of 3 equiv of HMPA to 1 equiv of aluminum, the conjugate reduction of **1** by DIBAH alone took place smoothly at 0 °C to give 2-methyl-4-nonen-3-one (**9**) quantitatively. At -50 °C the reduction proceeded very slowly. Addition of a catalytic amount of MeCu (10 mol %) to the DIBAH–HMPA system accelerated the reaction remarkably to effect the quantitative conjugate reduction at -50 °C. The reduction by DIBAH alone without HMPA caused the usual carbonyl reduction to give the corresponding propargyl alcohol. Thus, HMPA alters remarkably the reducing reactivity of DIBAH to suppress completely the carbonyl reduction and to effect the conjugate reduction selectively. An equimolar amount of HMPA to DIBAH is sufficient to manifest its effect. This finding suggests that HMPA functions not as a cosolvent but as a ligand to aluminum.[1] Stereochemistry of the resultant carbon–carbon double bond of the conjugate reduction product **9** depends on the presence or absence of MeCu. The (*E*) isomer predominates in the DIBAH–HMPA system. On the other hand, the MeCu–DIBAH–HMPA system favors the formation of the (*Z*) isomer, although the selectivity is not high. Several attempts to improve the (*Z*) stereochemistry by employing other copper(I) compounds and solvents (toluene, diethyl ether) were unsuccessful. The stereochem-

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Table I. Conjugate Reduction of 2-Methyl-4-nonyn-3-one (1) by DIBAH-HMPA and MeCu-DIBAH-HMPA[a]

MeCu/1	DIBAH/1	HMPA/DIBAH	solvent	temp, °C	time, h	yield conj redn product BuCH=CHCOPr-*i* (9),[b] % (*Z*:*E*)	unreact substr, %
0	2.0	2.9	THF	0	2	100 (21:79)	0
0	1.5	3.8	THF	−50	2	12	88
0.1	1.5	3.8	THF	−50	2	100 (60:40) (48:32)[c]	0
0.1	1.5	1.0	THF	−50	2	100 (54:46)	0
0.5	2.0	2.9	THF	−50	1	83 (67:33)	0
0	1.5	0	THF	0	0.5	0[d]	0
0.1	1.5	3.8	toluene	−50	2	94 (39:61)	0
0.1	1.5	3.8	Et_2O	−50	2	100 (43:57)	0
t-BuCu 0.1	1.5	3.8	THF	−50	2	100 (53:47)	0
PhCu 0.1	1.5	3.8	THF	−50	2	100 (58:42)	0
CuI 0.1	1.5	3.8	THF	−50	2	100 (53:47)	0

[a] 1, 1 mmol; solvent, THF (5 mL). [b] Yield was determined by GLC using an internal standard. [c] Values are isolated yields of (*Z*) and (*E*) isomers, respectively. [d] 2-Methyl-4-nonyn-3-ol was produced quantitatively.

Table II. Conjugate Reduction of α,β-Acetylenic Ketones and Esters by DIBAH-HMPA and MeCu-DIBAH-HMPA[a]

α,β-acetylenic ketone or ester (S)	MeCu/S	DIBAH/S	HMPA/DIBAH	solvent	temp, °C	time, h	yield conj redn product,[b] % (*Z*:*E*)	unreact substr, %
HC≡CCOPr (2)	0	1.5	1.0	THF	0	1	H_2C=CHCOPr (10), 99	0
BuC≡CCOPh (3)	0	1.5	2.0	THF	0	2	BuCH=CHCOPh (11), 93 (53:47)	0
	0.1	1.5	2.0	THF	−50	2	99 (58:42) (51:41)[c]	0
MeC≡C$(CH_2)_4$C≡C-COPr-*i* (4)	0.1	2.0	2.9	THF	−50	3.5	MeC≡C$(CH_2)_4$CH=CHCOPr-*i* (12), (37:26)[c]	0
PhC≡CCOPr-*i* (5)	0	2.0	2.9	THF	0	2	PhCH=CHCOPr-*i* (13), 21 (62:38)	79
	0.5	2.0	2.9	THF	−50	2	65 (75:25)	35
HC≡CCO_2Me (6)	0	1.5	1.3	toluene	0	1	H_2C=$CHCO_2$Me (14), 100	0
MeC≡CCO_2Me (7)	0	1.5	1.3	THF	−20	2	MeCH=$CHCO_2$Me (15), 0	94
	0.1	1.5	1.3	toluene	−20	1	58	4
	0.1	1.5	1.3	Et_2O	−40	1	54	24
Me$(CH_2)_4$C≡C-CO_2Me (8)	0.1	2.0	1.0	THF	−50	1	Me$(CH_2)_4$CH=$CHCO_2$Me (16), (7:12)[c]	53

[a] S, 1 mmol; solvent, THF (5 mL). [b] Yield was determined by GLC using an internal standard. [c] Values are isolated yields of (*Z*) and (*E*) isomers, respectively.

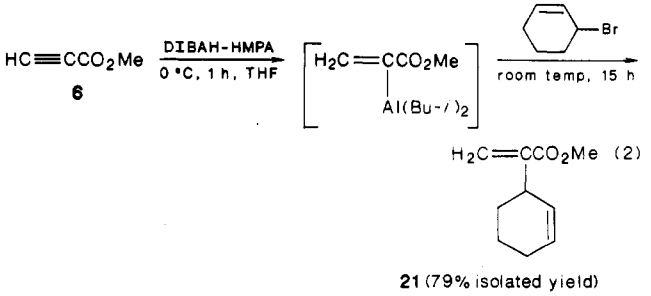
istry of **9** was determined by the 400-MHz ^{1}H NMR coupling constant of two olefinic protons: J = 11.5 Hz for the (*Z*) isomer and J = 15.8 Hz for the (*E*) isomer.

The results of the conjugate reduction of other α,β-acetylenic ketones are shown in Table II. The conjugate reduction of β-unsubstituted α,β-acetylenic ketone **2** and β-alkyl-substituted α,β-acetylenic phenyl ketone **3** proceeded quantitatively. However, β-phenyl substitution disturbed the reaction. Chemoselective conjugate reduction of the α,β-acetylenic ketone having the nonconjugated carbon–carbon triple bond (**4**) is noteworthy, which cannot be accomplished by the conventional catalytic hydrogenation. For example, the catalytic hydrogenation of 1-oxo-1-phenyl-4-penten-2-yne produces 1-oxo-1-phenyl-2-(*Z*)-pentene.[7] The conjugate reduction of β-unsubstituted α,β-acetylenic ester **6** proceeded quite satisfactorily by DIBAH alone in the presence of the HMPA ligand. However, β-alkyl substitution decreased the reactivity. The stereochemistry of the conjugate reduction of α,β-acetylenic ester was examined using methyl 2-octynoate (**8**), but the stereoselectivity was not high.

The present study provides the first example of the efficient conjugate reduction of α,β-acetylenic ketone and ester to α,β-olefinic ketone and ester, respectively, by the metal hydride compound. Because of the easy availability of α,β-acetylenic ketones by the acylation of terminal acetylenes,[8] the present conjugate reduction of α,β-acetylenic ketones offers a facile preparative method of β-unsubstituted and β-monosubstituted α,β-enones.

Another feature of the present reduction is a vinylaluminum intermediate. As is shown in eq 1, the conjugate reduction of α,β-acetylenic carbonyl compound by DIBAH–HMPA may be reasonably assumed to involve an (α-carbonylvinyl)aluminum intermediate.[9] Utilization of this vinylaluminum intermediate in organic synthesis discriminates the present conjugate reduction of α,β-acetylenic carbonyl compounds from that employing the catalytic hydrogenation.[2,7]

The (α-carbomethoxyvinyl)aluminum intermediate generated easily from **6** by DIBAH–HMPA was trapped by 3-bromocyclohexene to produce methyl 2-(2-cyclohexenyl)propenoate (**21**) in a good yield (eq 2), which is



21 (79% isolated yield)

a precursor of α-methylene-γ-butyrolactone.[10] Other

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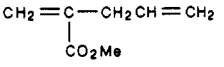
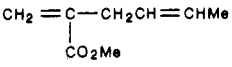
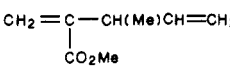
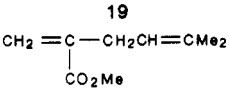
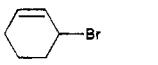
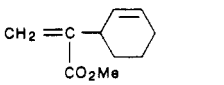
(9) The (α-carboalkoxyvinyl)copper intermediates generated by the conjugate addition of organocuprates to α,β-acetylenic esters are proposed to be equilibrated with the copper allenolate intermediates. See: Marino, J. P.; Linderman, R. J. *J. Org. Chem.* **1983**, *48*, 4621.

Table III. Allylation of (α-Carbomethoxyvinyl)aluminum Intermediate CH_2=C(CO_2Me)Al(Bu-*i*)$_2$ with Allylic Bromides[a]

allylic bromide	α-allylated methyl acrylate	isol yield by PLC, %
CH_2=$CHCH_2Br$	 17	53
MeCH=$CHCH_2Br$[b]	 18	
	 19	72 (18:19 = 68:32)[d]
Me_2C=$CHCH_2Br$	 20	66
	 21	79 (90)[c]

[a] The (α-carbomethoxyvinyl)aluminum intermediate was prepared by the reaction of **6** (2.00 mmol), DIBAH (3.00 mmol), and HMPA (6.00 mmol) in THF (10 mL) at 0 °C for 1 h except for the reaction with 3-bromocyclohexene where 1.00 mmol of **6** was used. Allylation was carried out at room temperature for 15 h using 4.00 mmol of allylic bromide. [b] The mixture with 14% CH_2=CHCH(CH_3)Br was used. [c] The yield in parentheses was determined by GLC. [d] The ratio was determined by GLC.

allylic bromides also can be used (Table III). Previously (α-carboethoxyvinyl)cuprate [CH_2=C(CO_2Et)CuC≡CBuLi] has been developed, but its formation requires a multistep manipulation.[10] Thus, the hydralumination of **6** by DIBAH–HMPA offers the simple way of generating the β-unsubstituted (α-carboalkoxyvinyl)metal intermediate. On the other hand, the (α-butyrylvinyl)aluminum intermediate generated from **2** by DIBAH–HMPA did not react with allyl bromide under the similar condition. To our knowledge, the present study provides the first example of the generation of the alkenylaluminum intermediate having a carbonyl functionality by means of the hydralumination of acetylenic compounds.[11]

Experimental Section

IR spectra were determined on a Hitachi 260-50 grating spectrophotometer. ^{1}H NMR spectra were recorded on either a Hitachi R-20B (60-MHz) or JEOL JNM-JX-400 (400-MHz) instrument. ^{13}C NMR spectra were obtained on a Hitachi R-100 spectrometer. All chemical shifts are reported in δ downfield from internal tetramethylsilane. Coupling constants (*J*) are reported in hertz. Mass spectra were obtained on a JEOL DX-300 instrument. Gas chromatographic analyses (GLC) were made on a Shimadzu 4CPT instrument. GLC quantitative analyses of reaction products were made with internal standards with calibration based upon authentic samples employing a 20% silicone DC 550 on Celite 545 column or a 20% poly(ethylene glycol) (PEG) 20M on Celite 545 column.

Reactions were carried out under an atmosphere of nitrogen. Cuprous iodide was obtained from Nakarai Chemicals, Ltd., and used without further purification. Diisobutylaluminum hydride (DIBAH) in hexane and methyllithium in ether were obtained from Aldrich Chemical Co. Tetrahydrofuran (THF) was distilled from lithium aluminum hydride under nitrogen. α,β-Acetylenic ketones **1**, **3**, **4**, and **5** were prepared according to the published method.[8] Hexamethylphosphoric triamide (HMPA) was distilled from calcium hydride under reduced pressure. Unsubstituted α,β-acetylenic ketone **2** was prepared by oxidation of 1-hexyn-3-ol.[12] α,β-Acetylenic esters **6** and **7** were commercial reagents and were distilled under nitrogen after drying over Drierite. Methyl 2-octynoate (**8**) was prepared by the reaction of commercially available 2-octynoic acid and diazomethane.[13] Allyl bromide, 1-bromo-2-butene, 4-bromo-2-methyl-2-butene, and 3-bromocyclohexene were commercial reagents and were distilled under nitrogen after drying over Drierite. 1-Bromo-2-butene contained 14% 3-bromo-1-butene.

The conjugate reduction products methyl acrylate (**14**) and methyl crotonate (**15**) were isolated by GLC and identified by the agreement of their GLC retention times and IR spectra with those of the commercially available authentic samples. The conjugate reduction products hexen-3-one (**10**) and 4-methyl-1-phenylpenten-3-one (**13**) were isolated by GLC and identified by the following spectral data. Compound **10**:[14] IR (liquid film, cm^{-1}) 1718, 1680, 1620; ^{1}H NMR (60 MHz, $CDCl_3$) 0.90 (t, 3 H), 1.67 (sext, 2 H), 2.53 (t, 2 H) 5.83 (t, 1 H), 6.23 (d, 2 H); mass spectrum, M$^+$ at *m/e* 98. Compound (*E*)-**13**:[15] IR (liquid film, cm^{-1}) 1690, 1660, 1610; ^{1}H NMR (400 MHz, $CDCl_3$) 1.19 (d, *J* = 7.0, 6 H), 2.94 (sept, *J* = 6.9, 1 H), 6.82 (d, *J* = 16.1, 1 H), 7.61 (d, *J* = 16.1, 1 H), 7.3–7.6 (m, 5 H); mass spectrum, M$^+$ at *m/e* 174. Compound (*Z*)-**13**: IR (liquid film, cm^{-1}) 1685, 1600; ^{1}H NMR (400 MHz, $CDCl_3$) 1.11 (d, *J* = 7.0, 6 H), 2.68 (sept, *J* = 7.0, 1 H), 6.25 (d, *J* = 12.7, 1 H), 6.83 (d, *J* = 12.7, 1 H), 7.3–7.6 (m, 5 H); mass spectrum, M$^+$ at *m/e* 174.

The conjugate reduction products of methyl 2-octynoate (**8**) were isolated by preparative-layer chromatography (PLC) [silica gel; hexane–ether (10:1, v/v) as eluent] and identified by the following spectral data. (*E*)-Methyl 2-octenoate [(*E*)-**16**]:[16] ^{1}H NMR (400 MHz, $CDCl_3$) 0.91 (t, *J* = 7.1, 3 H), 1.3–1.5 (m, 6 H), 2.20 (quart of d, *J* = 7.4, 1.4, 2 H), 3.72 (s, 3 H), 5.82 (dt, *J* = 15.6, 1.5, 1 H), 6.98 (dt, *J* = 15.6, 7.0, 1 H); mass spectrum M$^+$ at *m/e* 156. (*Z*)-Methyl 2-octenoate [(*Z*)-**16**]: IR (liquid film, cm^{-1}) 1720, 1625; ^{1}H NMR (400 MHz, $CDCl_3$) 0.89 (t, *J* = 7.0, 3 H), 1.3–1.5 (m, 6 H), 2.65 (quart of d, *J* = 7.5, 1.7, 2 H), 3.71 (s, 3 H), 5.77 (dt, *J* = 11.6, 1.7, 1 H), 6.24 (dt, *J* = 11.6, 7.5, 1 H); mass spectrum M$^+$ at *m/e* 156.

The spectral data of **10**, (*E*)-**13**, (*E*)-**16**, and the following compound (*E*)-**11** are compatible with those of the literature.

Conjugate Reduction of 2-Methyl-4-nonyn-3-one (1). To a stirred suspension of CuI (0.0190 g, 0.100 mmol) in 5 mL of THF cooled to 0 °C was added an ether solution of methyllithium (0.100 mmol). A yellow precipitate of methylcopper was formed. The mixture was cooled to −50 °C. HMPA (1 mL) and a hexane solution of DIBAH (1.50 mmol) were added successively. The reaction mixture was stirred for 30 min at −50 °C, and **1** (0.183 mL, 1.00 mmol) was added. After being stirred for 2 h, the mixture was treated with 3 mL of 1 N HCl solution followed by 15 mL of ether. The separated ether solution was washed three times with 3 mL of 1 N HCl solution, 3 mL of saturated $NaHCO_3$ solution, and 3 mL of water. The ether solution was dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified on a silica gel plate (20 × 20 × 0.2 cm) employing hexane–ether (10:1, v/v) as eluent to give two fractions. The front fraction gave (*Z*)-2-methyl-4-nonen-3-one [(*Z*)-**9**]: 74 mg (48%); IR (liquid film, cm^{-1}) 1695, 1620; ^{1}H NMR (400 MHz, $CDCl_3$) 0.90 (t, *J* = 7.2, 3 H), 1.10 (d, *J* = 7.0, 6 H), 1.30–1.45 (m, 4 H), 2.61 (quart of d, *J* = 7.3, 1.7, 2 H), 2.62 (sept, *J* = 6.9, 1 H), 6.11 (dt, *J* = 11.5, 7.1, 1 H), 6.19 (dt, *J* = 11.5, 1.5, 1 H); mass spectrum, M$^+$ at *m/e* 154. The rear fraction gave (*E*)-2-methyl-4-nonen-3-one [(*E*)-**9**]: 49 mg (32%); IR (liquid film, cm^{-1}) 1690, 1670, 1620; ^{1}H NMR (400 MHz, $CDCl_3$) 0.92 (t, *J* = 7.2, 3 H), 1.11 (d, *J* = 7.0, 6 H), 1.35 (sext, *J* = 7.5, 2 H), 1.46 (quint,

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J = 7.8, 2 H), 2.23 (quart of d, J = 7.0, 1.6, 2 H), 2.83 (sept, J = 6.9, 1 H), 6.16 (dt, J = 15.8, 1.5, 1 H), 6.88 (dt, J = 15.8, 7.0, 1 H); mass spectrum, M^+ at m/e 154.

Conjugate Reduction of 1-Phenyl-2-heptyn-1-one (3). The reaction was carried out as described above, using 1.00 mmol of **3**. The crude product obtained after workup was purified by PLC [silica gel, benzene–chloroform (10:1, v/v) as eluent] to give two fractions. The front fraction gave (*Z*)-1-phenyl-2-hepten-1-one [(*Z*)-**11**]: 97 mg (51%); IR (liquid film, cm^{-1}) 1680, 1615; ^1H NMR (400 MHz, $CDCl_3$) 0.91 (t, J = 7.2, 3 H), 1.37 (sext, J = 7.4, 2 H), 1.47 (quint, J = 7.5, 2 H), 2.63 (quart of d, J = 7.4, 1.7, 2 H), 6.33 (dt, J = 11.6, 7.4, 1 H), 6.80 (dt, J = 11.6, 1.8, 1 H), 7.40–8.00 (m, 5 H); mass spectrum, m/e (relative intensity) 81 (21), 91 (12), 105 (100), 120 (12), 131 (18), 134 (15), 145 (58), 159 (106), 188 (M^+, 46). The rear fraction gave (*E*)-1-phenyl-2-hepten-1-one [(*E*)-**11**]:[17] 76 mg (41%); IR (liquid film, cm^{-1}) 1670, 1620; ^1H NMR (400 MHz, $CDCl_3$) 0.94 (t, J = 7.3, 3 H), 1.39 (sext, J = 7.5, 2 H), 1.52 (quint, J = 7.7, 2 H), 2.33 (quart of d, J = 7.0, 1.3, 2 H), 6.88 (dt, J = 15.4, 1.5, 1 H), 7.07 (dt, J = 15.4, 6.9, 1 H), 7.4–8.0 (m, 5 H); mass spectrum, m/e (relative intensity) 81 (6), 91 (2), 105 (100), 120 (7), 131 (2), 134 (2), 145 (9), 159 (5), 188 (M^+, 7).

Conjugate Reduction of 2-Methyl-4,10-dodecadiyn-3-one (4). The reaction was carried out as described above, using 0.72 mmol of **4**. The crude product obtained after workup was purified by PLC [silica gel; hexane–ethyl acetate (8:1, v/v) as eluent] to give two fractions. The front fraction gave (*Z*)-2-methyl-2-dodecen-10-yn-3-one [(*Z*)-**12**]: 52 mg (37%); IR (liquid film, cm^{-1}) 2050, 1685, 1610; ^1H NMR (400 MHz, $CDCl_3$) 1.10 (d, J = 7.0, 6 H), 1.45–1.55 (m, 4 H), 1.77 (t, J = 2.6, 3 H), 2.1–2.2 (m, 2 H), 2.62 (sept, J = 7.0, 1 H), 2.63 (quart, J = 7.1, 2 H), 6.11 (dt, J = 11.5, 7.1, 1 H), 6.21 (dt, J = 11.5, 1.5, 1 H); mass spectrum, m/e (relative intensity) 55 (31), 57 (20), 71 (67), 79 (57), 93 (100), 107 (32), 121 (46), 135 (30), 149 (40), 163 (58), 177 (57), 192 (M^+, 1.5). The rear fraction gave (*E*)-2-methyl-2-dodecen-10-yn-3-one [(*E*)-**12**]: 36 mg (26%); ^1H NMR (400 MHz, $CDCl_3$) 1.11 (d, J = 6.8, 6 H), 1.45–1.65 (m, 4 H), 1.78 (t, J = 2.6, 3 H), 2.1–2.2 (m, 2 H), 2.24 (quart of d, J = 7.1, 1.3, 2 H), 2.83 (sept, J = 6.9, 1 H), 6.18 (dt, J = 15.8, 1.5, 1 H), 6.85 (dt, J = 15.8, 6.9, 1 H); mass spectrum, m/e (relative intensity) 55 (31), 57 (26), 71 (8), 79 (63), 93 (100), 107 (14), 121 (34), 135 (7), 149 (35), 163 (20), 177 (39), 192 (M^+, 0.90).

Reaction of the (α-Carbomethoxyvinyl)aluminum Intermediate with 3-Bromocyclohexene. To a stirred solution of THF (5 mL) and HMPA (0.522 mL, 3.00 mmol) cooled to 0 °C was added a hexane solution of DIBAH (1.50 mmol). After 0.5 h, methyl propiolate (0.089 mL, 1.00 mmol) was added. The reaction mixture was stirred for 1 h, and then 3-bromocyclohexene (0.244 mL, 2.10 mmol) was added. The mixture was allowed to warm to room temperature, stirred for 15 h, treated with 3 mL of 1 N HCl solution, and extracted with 15 mL of ether. The organic layer was washed three times with 3 mL of 1 N HCl solution, 3 mL of saturated $NaHCO_3$ solution, and 3 mL of water. The ether solution was dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by PLC [silica gel; hexane–ether (1:1, v/v) as eluent] to give methyl 2-(2-cyclohexenyl)propenoate (**21**): 132 mg (79%); IR (liquid film, cm^{-1}) 1730, 1625, 950, 730; ^1H NMR (60 MHz, $CDCl_3$) 1.3–1.8 (m, 4 H), 1.8–2.3 (m, 2 H), 3.33 (m, 1 H), 3.73 (s, 3 H), 5.3–6.3 (m, 4 H); mass spectrum, M^+ at m/e 166. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.86; H, 8.60.

Other allylation products **17–20** were similarly obtained and identified as follows. Compound **17**: IR (liquid film, cm^{-1}) 1720, 1625, 995, 940, 915; ^1H NMR (60 MHz, $CDCl_3$) 3.07 (d, 2 H), 3.76 (s, 3 H), 4.8–5.3 (m, 2 H), 5.57 (s, 1 H), 5.6–6.0 (m, 1 H), 6.20 (s, 1 H); mass spectrum, M^+ at m/e 126. Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.67; H, 8.14. Compound **18**: IR (liquid film, cm^{-1}) 1725, 1630, 970, 945; ^1H NMR (60 MHz, $CDCl_3$) 1.5–1.8 (m, 3 H), 2.98 (d, 2 H), 3.75 (s, 3 H), 5.3–5.6 (m, 2 H), 5.55 (s, 1 H), 6.16 (s, 1 H); mass spectrum, M^+ at m/e 140. Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.74; H, 8.81. Compound **19**: IR (liquid film, cm^{-1}) 1720, 1625, 990, 945, 915; ^1H NMR (60 MHz, $CDCl_3$) 1.20 (d, 3 H), 3.1–3.7 (m, 1 H), 3.76 (s, 3 H), 4.8–5.3 (m, 2 H), 5.55 (s, 1 H), 5.5–6.1 (m, 1 H), 6.19 (s, 1 H); mass spectrum, M^+ at m/e 140. Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.67; H, 8.81. Compound **20**: IR (liquid film, cm^{-1}) 1730, 1635, 950; ^1H NMR (60 MHz, $CDCl_3$) 1.64 (s, 3 H), 1.74 (s, 3 H), 3.00 (d, 2 H), 3.76 (s, 3 H), 4.9–5.3 (m, 1 H), 5.54 (s, 1 H), 6.14 (s, 1 H); mass spectrum, M^+ at m/e 154. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.88; H, 9.23.

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A Short Synthesis of (*S*)-(+)-Tylophorine

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Tylophorine (**6**) is one of a group of selectively toxic alkaloids whose structures represent the fusion of a polymethoxyphenanthrene or -stilbene with indolizidine or quinolizidine.[2] Tylophorine has been synthesized in racemic form through a number of approaches,[3] and one optically active preparation has recently been reported.[4]

We describe here a short enantiospecific synthesis of tylophorine illustrative of yet another alternative route to preparation of β-arylalkylamines based on Friedel–Crafts acylations with *N*-(trifluoroacetyl)-α-amino acid chlorides and anhydrides.[5]

Results and Discussion

The reaction sequence employed is outlined in Scheme I. The key step was the first, wherein 2,3,6,7-tetramethoxyphenanthrene (**1**)[6] was acylated with 1.2 equiv of (*S*)-*N*-(trifluoroacetyl)prolyl chloride (**2**) in boiling CH_2Cl_2.[5a,b] Crystalline ketone **3** was obtained in 51% yield after flash chromatographic separation from residual **1**, *N*-(trifluoroacetyl)proline (from hydrolysis of excess **2**), and an unidentified minor byproduct. The regiochemistry was anticipated from a preliminary demonstration that acetylation of **1** takes place cleanly at the 9-position. The

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