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LITHIUM N-BENZYLTRIMETHYLSILYLAMIDE (LSA): A NEW REAGENT FOR CONJUGATE ADDITION - ENOLATE TRAPPING REACTIONS

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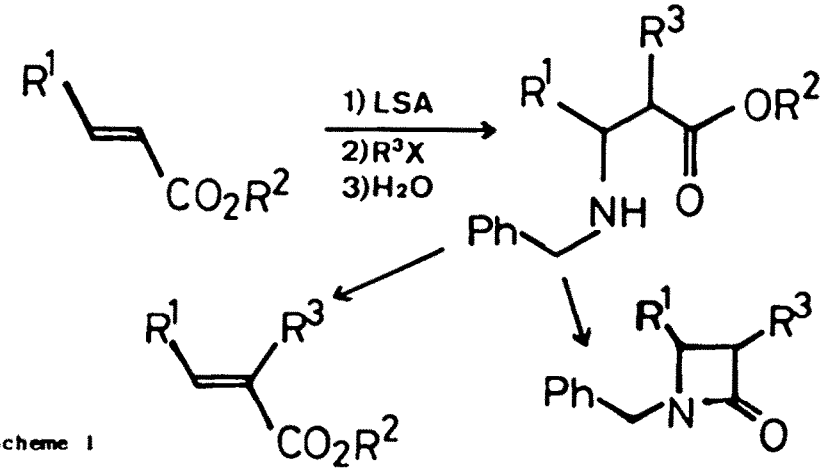
Abstract-Lithium N-benzyltrimethylsilylamide (LSA) adds to crotonates in a 1,4-manner, though the reaction of ordinary lithium amides with α,β-unsaturated carbonyl compounds is accompanied with a 1,2-addition and hydrogen abstraction at the γ-position. The conjugate addition via LSA followed by enolate trapping with electrophiles produces the corresponding α-substituted β-amino esters, which are, in turn, converted into β-lactams and α-substituted α,β-unsaturated esters.

Lithium amides R_2NLi are ordinarily used as strong bases for deprotonation of organic compounds. However, nucleophilic reactions of R_2NLi, such as conjugate addition to α,β-unsaturated esters, have received little attention from a synthetic point of view.[1-3] We report that lithium N-benzyl-trimethylsilylamide [$LiN(CH_2Ph)SiMe_3$] (LSA)[4] reacts with α,β-unsaturated esters in a 1,4-manner to produce the corresponding β-amino ester enolates, which are trapped by electrophiles such as alkyl halides and aldehydes. The resulting α-substituted β-amino esters can be converted into the β-lactams or into the α-substituted α,β-unsaturated esters (Scheme I).



Scheme I

RESULTS AND DISCUSSION

Conjugate addition. The reactions of methyl crotonate (1) with various kinds of lithium amides were investigated to elucidate the regioselectivity toward α,β-unsaturated ester. The results are summarized in Table 1. LSA was an efficient reagents for the conjugate addition; by-products such as 3 and 4 were not detected. It was reported that LDA gave 2 in good yields without contamination of 3 and 4.[1-3] Our experiments revealed that LDA produced significant amounts of 4 as a by-product; the n-octylated derivative of 4 was isolated since isolation of 4 itself was difficult owing to its volatile characteristics. Further, the isopropyl group of LDA can not be removed in the subsequent process and thus this reagent is not suitable for the preparation of β-lactams. The silylsubstituted amines such as Bn(t-BuMe$_2$Si)NH, Bn(Ph$_2$MeSi)NH, Bn(Ph$_3$Si)NH, and Bn(t-BuPh$_2$Si)NH were prepared from the reaction of benzylamine with the corresponding chlorosilanes.[5] The conjugate adduct 2 was obtained along with 3 via Bn(t-BuMe$_2$Si)NLi or Bn(Ph$_2$MeSi)NLi. When Bn(Ph$_3$Si)NLi or Bn(t-BuPh$_2$Si)NLi was used, several unidentified materials were produced. Other lithium amides such as BnNHLi and Bn$_2$NLi, in which Bn group can be replaced by H in the subsequent process, also afforded both 1,4- and 1,2-adducts. The deprotonation reaction leading to 4 took place with (TMS)$_2$NLi.

1

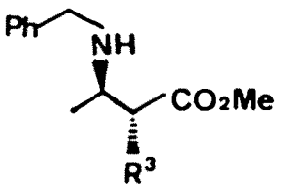
2 3 4

Table 1. Reaction of methyl crotonate with lithium amides (Bn = CH$_2$Ph)

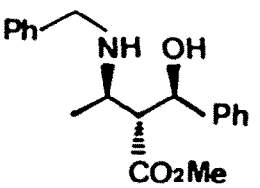
R$_2$NLi	isolated product, %		
	2	3	4
LDA(iPr$_2$NLi)	44[b]	-	14[a]
LSA(Bn(TMS)NLi)	88	-	-
BnNHLi	20	60	-
Bn$_2$NLi	18[b]	-	-
Bn(t-BuMe$_2$Si)NLi	61	7	-
Bn(Ph$_2$MeSi)NLi	30	6	
(TMS)$_2$NLi	-	-	9[a]

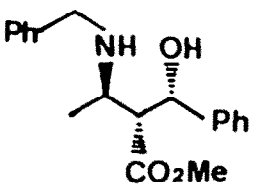
a) Instead of H$_3$O$^+$, octyl iodide was added. The octylated derivative of 4 was isolated in the indicated yields. b) Isolated as iPr$_2$N or Bn$_2$N adducts, respectively.

Conjugate addition-enolate trapping reaction. By using LSA, the conjugate addition to **1** followed by treatment with various electrophiles was studied. With n-octyl iodide, a 59:41 mixture of the anti (**5a**) and syn (**5b**) isomers was isolated in 81% yield. The isomer ratio depended upon the additives; the presence of HMPA gave a 89:11 mixture in 96% yield and the presence of TMEDA produced a 77:23 mixture in 78% yield. It should be noted that the TMS group of LSA is removed during work-up procedures. With methyl iodide, a 52:48 mixture of **6a** and **6b** was obtained in an essentially quantitative yield. With benzaldehyde, the adduct (**7**) was obtained in 97% yield; the ratio of four isomers (**7a**, **b**, **c**, **d**) was 57:24:17:2. Unfortunately, the stereochemistry of these isomers has not yet been determined.

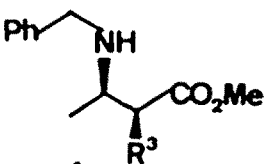


5a: R^3 = n-C_8H_{17}
6a: R^3 = Me

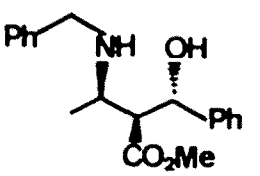


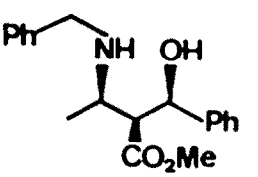


7a, b, c, d

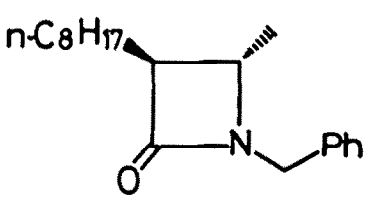


5b: R^3 = n-C_8H_{17}
6b: R^3 = Me

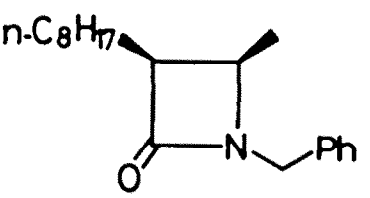




β-Lactam synthesis. The anti β-amino ester (**5a**) was converted into **8a** in 90% yield via hydrolysis followed by dehydration [KOH/aqueous MeOH; PPh_3, $(PyS)_2$/MeCN].[6] Quite similarly, **5b** gave **8b** in 74% yield. The stereochemistry of **8a** and **b**, in turn the stereostructure of **5a** and **b**, was determined by their ^1H n.m.r. coupling constant: (**8a**) $J_{3,4}$ 2.0Hz; (**8b**) $J_{3,4}$ 5.3Hz.



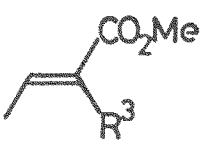
8a

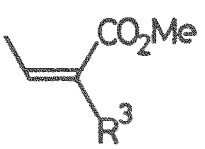


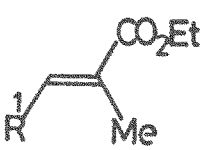
8b

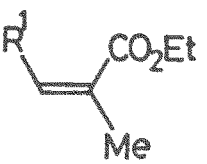
α-Alkylated α,β-unsaturated ester. The β-amino esters underwent β-elimination[7-9] via quarternization-base treatment to produce the corresponding α-alkylated α,β-unsaturated esters. N-Methylation of **5a** with MeI/K_2CO_3 followed by treatment with silica gel produced a 86 : 14 mixture of the E (**9a**) and Z (**9b**) isomers in 90% yield. Similar treatment of **5b** again gave a 91 : 9 mixture of **9a** and **9b** in 86% yield. The three-step sequence, conjugate addition of LSA to **1** - enolate trapping with octyl iodide - β-elimination,

afforded a 88 : 12 mixture of **9a** and **9b** in 72% total yield. The conjugate addition of LDA to **1** followed by enolate trapping with octyl iodide and subsequent treatment with silica gel[10] gave a 93 : 7 mixture of **9a** and **9b** in 56% total yield. Therefore, the synthetic equivalent of the α-carbanion of an α,β-unsaturated ester can be generated by conjugate addition of a nitrogen nucleophile (R_2NLi); LDA, as well as LSA, is also useful for this purpose. Quite similarly, a 88 : 12 mixture of **11a** and **11b** was obtained in 52% yield via the three-step sequence with LDA. The α-benzylated derivative **10** (**10a**/**10b** = 87/13) was produced in 74% yield via LSA. Other α,β-unsaturated esters such as ethyl 4-methyl-2-pentenoate[11] and ethyl 2-decenoate also underwent the conjugate addition of LDA - trapping with MeI - β-elimination, giving **12** (E/Z = 95/5, 33%) and **13** (E/Z = 88/12, 69%), respectively. Consequently, the three-step sequence via LSA or LDA provides a new synthetic procedure for trisubstituted enoates.







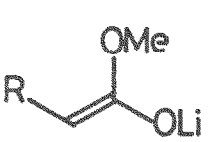


9a; R^3 = n-C_8H_{17} **9b**; R^3 = n-C_8H_{17} **12a**; R^1 = i-Pr **12b**; R^1 = i-Pr

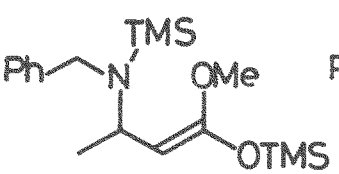
10a; R^3 = CH_2Ph **10b**; R^3 = CH_2Ph **13a**; R^1 = n-C_7H_{15} **13b**; R^1 = n-C_7H_{15}

11a; R^3 = $CH_2CH{=}C(CH_3)_2$ **11b**; R^3 = $CH_2CH{=}C(CH_3)_2$

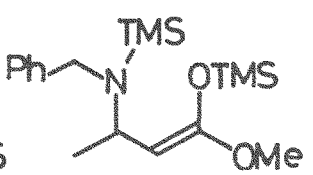
Stereochemistry of intermediate enolate. The stereoselectivity of the conjugate addition - enolate trapping with octyl iodide depended upon the additives; the presence of HMPA increased the anti-isomer. To help clarify the origin of the anti-stereoselectivity, we intended to isolate the intermediate enolate. The conjugate adduct of LSA to **1** was trapped with Me_3SiCl. It is well known that kinetic deprotonation of esters with lithium dialkylamides produces the Z-enolate (**14**).[12] Therefore, it was anticipated that E-**15** would be produced predominantly in our case. The intermediate O-silylated ketene acetal **15** was isolated as a single isomer. We attempted to assign the E or Z configuration by using a NOE technique, but the attempt was unsuccessful.[13] At present, we are unable to clarify the relation between the syn-anti stereoselectivity of **5**-**7** and the E-Z stereochemistry of **15**.



14 (Z-enolate)



E-**15**



Z-**15**

EXPERIMENTAL

^{1}H NMR spectra were recorded with a Varian EM-390, XL-200, or Jeol GX-400 instruments with TMS as internal standard. IR spectra were recorded with a Hitachi 215 spectrophotometer. Mass spectra were recorded with a Hitachi M-52 or Jeol DX-303 spectrometer. Elemental analyses were performed by the Tohoku University Microanalytical Center.

Preparation of silylated amines. N-(Trimethylsilyl)benzylamine was prepared according to the literature procedure;[14] ^{1}H NMR (CCl_4) δ 0.19 (s, 9), 0.45-1.08(br, 1), 4.00(d, J=7.9Hz, 2), 7.05-7.35(m, 5). Other amines were prepared by the procedure of Narula and Kapur.[5]

N-(t-Butyldimethylsilyl)benzylamine. bp 92.5°C/2.5mmHg; ^{1}H NMR (CCl_4) δ 0.17 (s, 6), 0.38-0.92 (m, 1), 1.05 (s, 9), 4.06 (d, J = 7.8Hz, 2), 7.12-7.38 (m, 5); IR (CCl_4) 3040, 2970, 2940, 2870, 1650, 1500, 1470, 1405, 1260, 830cm^{-1}; MS calcd for $C_{13}H_{23}NSi$ m/z 221.1600, found m/z 221.1609.

N-(Diphenylmethylsilyl)benzylamine. bp 215°C/0.5mmHg; ^{1}H NMR(CCl_4) δ 0.56 (s, 3), 0.85-1.38 (br, 1), 3.95 (d, J=7.5Hz, 2), 6.92-7.65 (m, 15); IR (CCl_4) 3070, 3030, 1455, 1430, 1400, 1260, 1120, 700cm^{-1}; MS calcd for $C_{20}H_{21}NSi$ m/z 303.1443, found m/z 303.1482.

N-(t-Butyldiphenylsilyl)benzylamine. bp 233°C/0.5 mmHg; ^{1}H NMR (CCl_4) δ 0.93-1.30 (br, 1), 1.04 (s, 9), 3.90 (d, J=7.5Hz, 2), 6.93-7.73(m, 15); IR (CCl_4) 3080, 2940, 2865, 1470, 1455, 1430, 1405, 1390, 1110, 700cm^{-1}; MS calcd for $C_{23}H_{27}NSi$ m/z 345.1913, found m/z 345.1866.

N-(Triphenylsilyl)benzylamine. mp 85.0°C; ^{1}H NMR (CCl_4) δ 1.43 (bt, J=3.8Hz, 1), 4.05(d, J=3.8Hz, 2), 6.96-7.67(m, 20H); IR(KBr) 3390, 3075, 1430, 1405, 1120, 845, 740, 700cm^{-1}. Anal. Calcd for $C_{25}H_{23}NSi$:C, 82.14; H, 6.34; N, 3.83. Found: C, 81.97; H, 6.46; N, 3.60.

Reaction of 1 with lithium amides. The reaction of LSA is representative. In a 20ml flask under Ar atmosphere were placed N-(TMS)-benzylamine (0.431ml, 2.2mmol) and dry THF (5ml). The flask was cooled to -78°C, and then BuLi-hexane solution (1.38ml, 2.2mmol) was added. The resulting solution was stirred for 30min, and then a THF (3ml) solution of 1 (0.212ml, 2mmol) was slowly added. The color changed to pale yellow. The stirring was continued for another 30min at this temperature. The reaction was quenched with a THF solution of HOAc. A saturated solution of $NaHCO_3$ was added to make the solution basic. Extraction with ether, washing with brine, drying with K_2CO_3, condensation, and a chromatography by using silica gel gave the product.

Methyl 3-(benzylamino)butanoate (2). ^{1}H NMR (CCl_4) δ 1.11 (d, J=6.2Hz, 3), 1.50 (s, 1), 2.28(dd, J=6.2, 15.2Hz, 1), 2.36 (dd, J=6.2, 15.2Hz, 1), 3.05 (ddq, J=6.2, 6.3, 6.3Hz, 1), 3.59 (s, 3), 3.72 (s, 2), 7.00-7.28(m, 5); IR (neat) 3330, 1735, 1605, 1440, 1195, 1175, 740 cm^{-1}; MS calcd for $C_{12}H_{17}NO_2$ m/z 207.1259, found m/z 207.1257.

N-Benzyl-2-butenamide (3). ^{1}H NMR (CCl_4) δ 1.83 (dd, J=1.7, 6.8 Hz, 3), 4.47 (d, J=5.9 Hz, 2), 5.43-5.83 (br, 1), 5.75 (dq, J=1.7, 16.5 Hz, 1), 6.83 (dq, J=6.8, 16.5 Hz, 1), 7.24(S, 5); IR (KBr) 3270, 1670, 1625, 1560, 1430, 970cm^{-1}, MS calcd for $C_{11}H_{13}NO$ m/z 175.0997, found m/z 175.0998.

Methyl 3-(N, N-dibenzylamino)butanoate. ^{1}H NMR (CCl_4) δ 1.09 (d, J=6.2 Hz, 3), 2.14 (dd, J=7.2, 13.8 Hz, 1), 2.53 (dd, J=7.2, 13.8 Hz, 1), 3.25 (ddq, J=6.2, 13.8, 13.8Hz, 1), 3.43 (s, 3), 3.38, 3.58(2d, J=13.5Hz, 4), 6.90-7.33 (m, 10); IR(CCl_4) 3045, 1745, 1458, 1195, 700cm^{-1}; MS calcd for $C_{19}H_{23}NO_2$ m/z 297.1729, found m/z 297.1744.

Methyl 3-(N, N-diisopropylamino)butanoate. ^{1}H NMR (CCl_4) δ 0.96 (d, J=6.6Hz, 6), 1.03 (d, J=6.6Hz, 6), 1.06 (d, J=6.5Hz, 3), 2.14 (dd, J=7.0, 13.5Hz, 1), 2.37 (dd, J=7.6, 13.5Hz, 1), 3.07 (hep, J=6.6Hz, 2), 3.39(ddq, J=6.5, 7.0, 7.6 Hz, 1), 3.55 (s, 3); IR (CCl_4) 1745, 1465, 1440, 1400, 1220cm^{-1}; MS calcd for $C_{11}H_{23}NO_2$ m/z 201.1729, found m/z 201.1727.

Methyl 2-octyl-3-butenoate. ^{1}H NMR (CCl_4) δ 0.75-1.02 (m, 3), 1.02-1.54 (bs, 14), 2.89 (m, 1), 3.61 (s, 3), 5.05 (m, 2), 5.68 (m, 1); IR (CCl_4) 1735, 1455, 1435, 990, 920, 700cm^{-1}; MS calcd for $C_{13}H_{24}O_2$ m/z 212.1776, found m/z 212.1800.

Conjugate addition - enolate trapping reactions. The conjugate addition of LSA was performed as described above. After stirring at -78°C for 1hr, MeI (1.59ml, 25mmol) was added. The reaction mixture was allowed to warm to room temperature, and then quenched with aqueous NH_4Cl. The product was isolated via the usual work-up procedure.

Methyl 3-(benzylamino)-2-methylbutanoate. ^{1}H NMR ($CDCl_3$)(as a 52 : 48 mixture of diastereomers **6a** and **b**) δ 0.83-0.93 (m, 1), 1.07(d, J=6.7Hz, 3), 1.10 (d, J=6.4Hz, 3), 1.13 (d, J=7.0Hz, 3), 1.17 (d, J=6.9Hz, 3), 1.21-1.34 (m, 1), 2.58(dq, J=6.8, 6.9Hz, 1), 2.63 (dq, J=5.0, 7.0 Hz, 1), 2.92 (dq, J=5.0, 6.4Hz, 1), 2.99 (dq, J=6.7, 6.8Hz, 1), 3.67 (s, 3), 3.68 (s, 3), 3.78 (2d, J=13.2Hz, 2), 3.80(2d, J=13.2Hz, 2), 7.20-7.34 (m, 10); IR (CCl_4) 3400, 1740, 1457, 1200cm^{-1}; MS calcd for $C_{13}H_{19}NO_2$ m/z 221.1416, found m/z 221.1413.

Methyl 3-(benzylamino)-2-octylbutanoate. **5a** (anti); ^{1}H NMR (CCl_4) δ 0.75-1.00 (m,3), 1.05(d, J=6.3Hz, 3), 1.12-1.72 (m, 14), 1.03-1.72 (br, 1), 2.13-2.41 (m, 1), 2.81 (dq, J=6.3, 6.3Hz, 1), 3.60 (s, 3), 3.64, 3.80 (2d, J=13.5Hz, 2), 7.00-7.28 (bs, 5); IR (neat) 3340, 3040, 2940, 2870, 1735, 1460, 1440, 1380, 1200, 1165cm^{-1}; MS calcd for $C_{20}H_{33}NO_2$ m/z 319.2512, found m/z 319.2484.
5b (syn); ^{1}H NMR (CCl_4) δ 0.74-0.97 (m, 3), 1.05 (d, J=6.0Hz, 3), 1.11-1.80 (m, 14), 1.11-1.80 (br, 1), 2.23-2.52 (m, 1), 2.76 (dq, J=5.3, 6.0Hz, 1), 3.60 (s, 3), 3.73 (s, 2), 7.00-7.30 (bs, 5); IR (CCl_4) 3340, 3040, 2940, 2870, 1735, 1605, 1455, 1440, 1380, 1200, 1165cm^{-1}; MS calcd for $C_{20}H_{33}NO_2$ m/z 319.2512, found m/z 319.2490.

Methyl 2-(1-benzylaminoethyl)-3-hydroxy-3-phenylpropanoate. Three isomers (**7a, b, c**) were isolated as a pure form, though **7d** was contaminated with **7a**. **7a**; ^{1}H NMR (CCl_4) δ 1.20 (d, J=6.3Hz, 3), 2.60 (dd, J=3.5, 3.5Hz, 1), 2.99 (dq, J=3.5, 6.3Hz, 1), 3.02 (s, 3), 3.64, 3.95 (2d, J=13.4Hz, 2), 4.95 (d, J=3.5Hz, 1), 7.00-7.38 (m, 10); IR(CCl_4) 3150, 2940, 1730, 1455, 1195, 1170cm^{-1}; MS calcd for $C_{19}H_{23}NO_3$ m/z 313.1678, found m/z 313.1681. **7b**; ^{1}H NMR (CCl_4) δ 1.11 (d, J=6.2Hz, 3), 2.37 (dd, J=9.0, 9.0Hz, 1), 3.22 (S, 3), 3.24 (dq, J=6.2, 9.0 Hz, 1), 3.76, 3.88 (2d, J=12.6Hz, 2), 4.80 (d, J=9.0Hz, 1), 6.97-7.40 (m, 10); IR (CCl_4) 3100, 3040, 2960, 1730, 1455, 1435, 700cm^{-1}; MS calcd for $C_{19}H_{23}NO_3$ m/z 313.1678, found m/z 313.1699. **7c**; ^{1}H NMR (CCl_4) δ 1.14 (d, J=6.5Hz, 3), 2.73 (dd, J=4.7, 6.3Hz, 1), 3.02 (dq, J=6.3, 6.5Hz, 1), 3.46 (s, 3), 3.74 (s, 2), 5.03 (d, J=4.7Hz, 1), 7.17 (bs, 10); IR (CCl_4) 3310, 3075, 3040, 2960, 1725, 1603, 1495, 1455, 1440cm^{-1}; MS calcd for $C_{19}H_{23}NO_3$ m/z 313.1678, found m/z 313.1687. **7d**; ^{1}H NMR (CCl_4) δ 1.19 (d, J=6.3Hz, 3), 2.60 (dd, J=2.7, 4.2Hz, 1), 2.78 (dq, J=2.7, 6.3Hz, 1), 3.53, 3.79 (2d, J=12.2Hz, 2), 3.68 (s, 3), 5.16 (d, J=4.2Hz, 1), 6.93-7.33 (m, 10); IR (CCl_4) 3150, 3030, 2930, 1730, 1495, 1450, 1435, 1165, 695cm^{-1}; MS calcd for $C_{19}H_{23}NO_3$ m/z 313.1678, found m/z 313.1690.

β-Lactam sythesis. Hydrolysis of **5** (128mg, 0.4mmol) was performed with MeOH (2.5ml), H_2O (0.5ml) and KOH (2 pellets). The mixture was kept at

40°C for 36hr. Neutralization with 1.4N HCl, followed by evaporation of MeOH and H_2O, gave a white precipitate. The mixture of this acid, CH_3CN (40ml), Ph_3P (133.6mg, 0.48mmol), and $(PyS)_2$ (108.4mg, 0.48mmol) was refluxed for 2 days under nitrogen. Condensation followed by purification via a silica gel column chromatography by using hexane-ether-CH_2Cl_2 (1:1:1) as an eluant produced **8**.

trans 1-Benzyl 4-methyl-3-octyl-2-azetidinone (**8a**). ^{1}H NMR (CCl_4) δ 0.71-1.00 (m, 3), 1.18 (d, J=6.0Hz, 3), 1.07-1.78 (m, 14), 2.44-2.68 (m, 1), 3.09 (dq, J=2.0, 6.0Hz, 1), 3.93, 4.50 (2d, J=15.0Hz, 2), 7.19 (bs, 5); IR (neat) 2970, 2930, 2860, 1750, 1400, 730, 700cm^{-1}; MS calcd for $C_{19}H_{29}NO$ m/z 287.2249, found m/z 287.2240. The cis-isomer (**8b**); ^{1}H NMR (CCl_4) δ 0.74-1.00 (m, 3), 1.07 (d, J=6.3Hz, 3), 1.12-1.67 (m, 14H), 2.99 (dt, J=5.1, 5.3Hz, 1), 3.53 (dq, J=5.3, 6.3Hz, 1), 3.97, 4.48 (2d, J=15.0Hz, 2), 7.19 (bs, 5); IR (CCl_4) 2920, 2850, 1735, 1445, 1365, 700cm^{-1}; MS calcd for $C_{19}H_{29}NO$ m/z 287.2249, found m/z 287.2252.

α-Alkylated α,β-unsaturated ester. Preparation of **9a**, **b** is representative. The α-octylated enoate **5** (158mg, 0.49mmol) was placed in a 10ml flask, and then MeOH (1.5ml) and K_2CO_3 (0.35g) were added. The mixture was cooled to 0°C and then MeI (0.25ml, 4mmol) was added. The mixture was kept at room temperature for 15hr. Water was added and K_2CO_3 was dissolved. Ether extraction gave the methylated derivative. This N-benzyl-N-methylamino derivative (133.4mg, 0.4mmol) was refluxed with SiO_2 (0.04-0.063mm, 270mg) in toluene (2.9ml). After 60hr, the β-elimination was completed.

Methyl 2-octyl-2-butenoate (**9**). The trans-isomer (**9a**) was contaminated with the cis-isomer (**9b**). The spectral data was based on a 93:7 mixture. ^{1}H NMR (CCl_4) δ 0.73-1.07 (m, 3), 1.2? (bs, 12), 1.79 (d, J=7.2Hz, 3), 2.10-2.37 (m, 2), 3.64 (s, 3), 6.69 (q, J=7.2Hz, 1); IR (CCl_4) 2960, 2935, 2860, 1715, 1460, 1440cm^{-1}; MS calcd for $C_{13}H_{24}O_2$ m/z 212.1776, found m/z 212.1759. The trans-configuration was assigned by the chemical shifts of the olefinic Me and H[15] (1.79 and 6.69, respectively); the corresponding chemical shifts of the cis-isomer appeared at 1.92 (dt, J=1.2, 7.2Hz) and 5.87 (q, J=7.2Hz). Further, photochemical irradiation of a 93:7 mixture of **9a** and **b** produced a 50 : 50 mixture of both isomers.

Methyl 2-benzyl-2 butenoate (**10**). The stereochemistry was determined as described above. ^{1}H NMR (CCl_4) δ 1.86 (d, J=7.1Hz, 3), 3.60 (s, 2), 3.62 (s, 3), 6.89 (q, 1, =CH), 5.90 (m, the cis isomer), 6.93-7.25 (bs, 5); IR (neat) 3100, 3075, 3040, 2960, 1715, 1650, 820, 740cm^{-1}; MS calcd for $C_{12}H_{14}O_2$ m/z 190.0994, found m/z 190.1000.

Methyl 2-ethylidene-5-methyl-4-hexenoate (**11**). ^{1}H NMR (CCl_4) δ 1.63 (bs, 6), 1.80 (d, J=7.1Hz, 3), 2.93 (bd, J=6.9Hz, 2), 3.64 (s, 3), 4.92 (m, 1), 6.68 (q, 1, =CH), 5.87 (m, the cis isomer); IR (neat) 2930, 2860, 1720, 1650, 1440, 1285, 1235, 850cm^{-1}; MS calcd for $C_{10}H_{16}O_2$ m/z 168.1150, found m/z 168.1154.

Ethyl 2,4-dimethyl-2-pentenoate (**12**). The ^{1}H NMR spectra was in good agreement with the reported data.[16]

Ethyl 2-methyl-2-undecenoate (**13**). ^{1}H NMR (CCl_4) δ 0.74 (m, 3), 1.27 (t, J=7.1Hz, 3), 1.32 (bs, 10), 1.79 (d, J=1.5Hz, 3), 2.13 (m, 2), 4.11 (q, J=7.1Hz, 2), 6.60 (dt, J=1.5, 7.2Hz, 1, =CH), 5.80 (m, the cis isomer); IR (neat) 2960, 2940, 2860, 1715, 1650, 1465, 1270cm^{-1}; MS calcd for $C_{13}H_{24}O_2$ m/z 212.1776, found m/z 212.1756.

O-Silylated ketene acetal (**15**). After the conjugate addition of LSA to **1**, 1 eq of TMSCl was added at -78°C. The reaction was allowed to warm

to room temperature. The solvent was removed under vacuum. The ketene acetal was obtained along with LiCl. ^{1}H NMR (THF-d_8 at -78°C) 0.13 (s, 9, $OSiMe_3$), 0.24 (s, 9, $NSiMe_3$), 1.01 (d, J=6.8Hz, 3, CH_3CN), 3.29 (s, 3, OMe), 3.58 (d, J=9.5Hz, 1, CHCN), 3.93-4.10 (m, 1, CHN), 4.03 (s, 2, CH_2Ph), 7.13-7.36 (m, 5, Ph).

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