EFFECT OF TIN(II) TRIFLATE ON REACTIONS OF α-ETHOXYCARBAMATES WITH ENOLATES

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Abstract - Reactions of α-ethoxycarbamates (α-ethoxylated derivatives of *N*-ethoxycarbonylpyrrolidine, -piperidine, and -hexamethyleneimine) with various enolates (enol acetates, enol ethers, or tin(II) enolates of ketones) in the presence of tin(II) triflate are described.

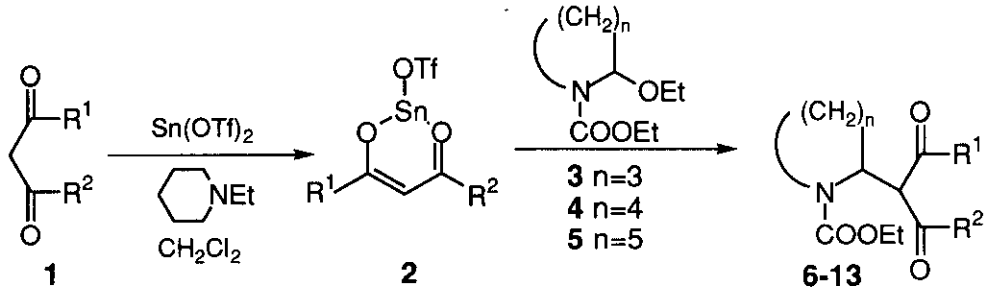
Tin(II) triflate [$Sn(OTf)_2$; stannous trifluoromethanesulfonate] was shown by the Mukaiyama group[1] useful for converting ketones to divalent tin enolates, with which a new type aldol condensation with high stereoselectivity was conducted. Reactions of the tin(II) enolates of C4-chiral 3-acyl-1,3-thiazolidine-2-thiones with acyl iminium ions, formed *in situ* from ω-acetoxylactams (four- ~ six-membered rings), were carried out by the Nagao group[2] for the chiral synthesis of bicyclic alkaloids each possessing a nitrogen atom at ring juncture. Aside from the work of these two groups, nothing apparently has been reported on tin(II) triflate.

In the previous paper,[3] tin(II) triflate was shown effective for converting α-ethoxy-*N*-ethoxycarbonylpyrrolidine to the corresponding acyl

iminium intermediate, which was made to react with tin(IV) acetylides as a new method for introducing acetylene groups at the α-position of the pyrrolidine ring. Additional applications and limitations of reactions of α-ethoxycarbamates with various enolates in the presence of tin(II) triflate are discussed in the following.

Carbon-carbon bond formation at the α-position of cyclic amine by reactions of α-methoxycarbamates with active methylene compounds or electron-rich olefins (enol esters and enol ethers) has already been demonstrated by Shono *et al.*[4] In these reactions, Lewis acids such as

Table I. Reactions of α-Ethoxycarbamates with Active Methylene Compounds in the Presense of $Sn(OTf)_2$

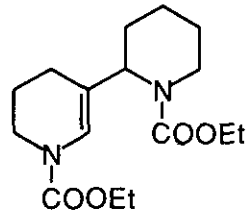


Run	Carbamate (3-5)	Nucleophile (1)	Product (6-13)*		(Yield, %)
1	**3**	R^1=Me, R^2=OMe	**6**	n=3, R^1=Me, R^2=OMe	(78)
2	**3**	R^1=Me, R^2=O^{t}Bu	**7**	n=3, R^1=Me, R^2=O^{t}Bu	(87)
3	**3**	R^1=Me, R^2=OBzl	**8**	n=3, R^1=Me, R^2=OBzl	(79)
4	**3**	R^1=Ph, R^2=OEt	**9**	n=3, R^1=Ph, R^2=OEt	(59)
5	**3**	R^1=R^2=OMe	**10**	n=3, R^1=R^2=OMe	(67)
6	**4**	R^1=Me, R^2=OMe	**11**	n=4, R^1=Me, R^2=OMe	(70)
7	**4**	R^1=Ph, R^2=O^{t}Bu	**12**	n=4, R^1=Ph, R^2=O^{t}Bu	(68)
8	**5**	R^1=Me, R^2=OMe	**13**	n=5, R^1=Me, R^2=OMe	(80)

*There appears to be only one product judging from the nmr spectrum and tlc spot.

boron trifluoride etherate and titanium(IV) chloride are used to convert α-methoxycarbamates to acyl iminium ions with a structure similar to **22**. In this study, Shono's reactions were carried out to examine the effects of tin(II) triflate. Reactions of α-ethoxycarbamates with active methylene compounds and electron-rich olefins in the presence of tin(II) triflate are listed in Tables I and II, respectively. It is evident from these Tables that tin(II) triflate could function as boron trifluoride and titanium(IV) chloride to give α-substituted cyclic amines (**6-20**) in moderate or high yields.

In the case of active methylene compounds (Table I), tin(II) enolate (**2**) was prepared beforehand using tin(II) triflate (1.1 eq.), *N*-ethylpiperidine (1.2 eq.), and an active methylene compound (1 eq.). The successive addition of carbamates (**3-5**) to the solution of this mixture gave the desired products (**6-13**). From carbamates (**3** and **5**) of five- and seven-membered rings, only products and starting carbamates were obtained, while from carbamate (**4**) of six-membered ring, dimer[5] (**21**) was obtained along with the expected product. More than the stoichiometric amount of tin(II) triflate was required for these reactions.[6] Excess tin(II) triflate may possibly facilitate the formation of acyl iminium ion (**22**) from carbamates (**3-5**). Tin(IV) chloride or tri-*n*-butylmethoxytin instead of tin(II) triflate gave low product yields (15-0%). Tin(II) triflate may be weaker as a Lewis acid than titanium(IV) chloride and zinc(II) chloride because the same reactions have been



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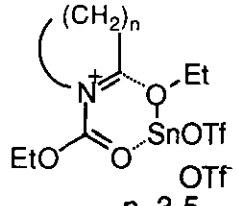
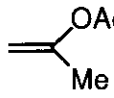
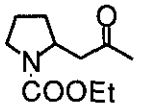
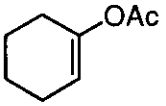
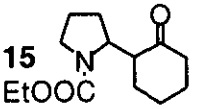
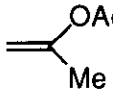
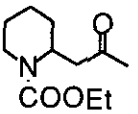
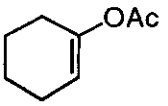
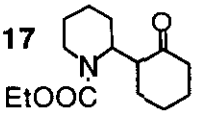
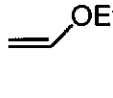
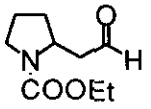
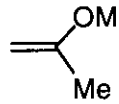
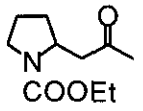
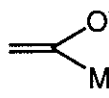
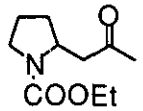
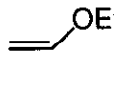
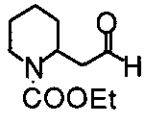
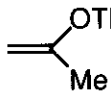
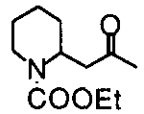
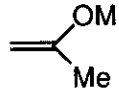
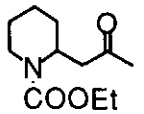
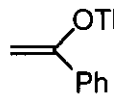
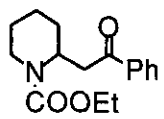


22 n=3-5

Table II. Reactions of α-Ethoxycarbamates with Electron-rich Olefins in the Presence of $Sn(OTf)_2$

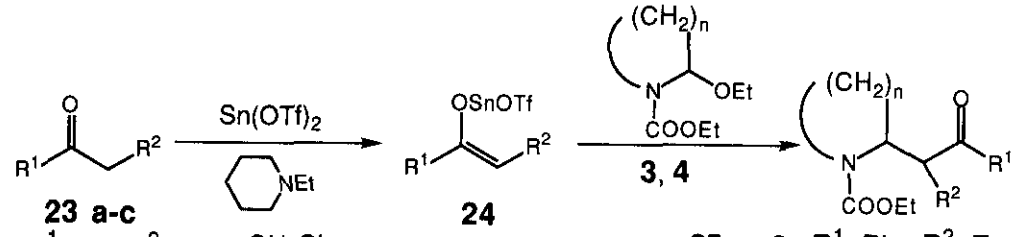
Run	Carbamates	Olefin	Reaction Conditions	Product	(Yield, %)
1	**3**		23°C, 24 h	**14** 	(62)
2	**3**		23°C, 24 h	**15** 	(61)
3	**4**		-78 ~ 23°C	**16** 	(0)
4	**4**		-78 ~ 23°C	**17** 	(0)
5	**3**		23°C, 14 h	**18** 	(62)
6	**3**		23°C, 1 h	**14** 	(54)
7	**3**		-78°C, 2 h	**14** 	(35)
8	**4**		-78°C, 5 h	**19** 	(68)
9	**4**		-78°C, 8 h	**16** 	(43)
10	**4**		-78°C, 5 h	**16** 	(70)
11	**4**		-78°C, 5 h	**20** 	(61)

shown to proceed in the presence of 0.3 equivalent of titanium(IV) chloride and zinc(II) chloride.[4]

For electron-rich olefins, acyl iminium ions (**22**) were prepared beforehand and the succesive olefin addition gave the desired products as shown in Table II. Reactions of enol acetates (Runs 1-4 in Table II) required more stringent reaction conditions (room temperature and long reaction time) compared to those of enol ethers (Runs 5- 11). Reactions of **3** (five-membered ring) with enol acetates thus afforded the sought products (**14** and **15**) in moderate yields. Those of **4** (six-memberd ring) with enol acetates gave only dimer (**21**) with no desired products (Runs 3 and 4). The properties of six-membered acyl iminium ions would be the reason for this and it thus follows that these ions each couple with two molecules at room temperature before enol acetate attacks. With various enol ethers, the reactions proceeded smoothly at lower temperature to give the expected products (Runs 5-11) regardless of five- or six-membered rings. Reactions of tin(II) enolates, prepared *in situ* from ketone (**23**, 1.0 eq.), tin(II) triflate (2.3 eq.), and *N*-ethylpiperidine (1.5 eq.) in dichloromethane, with carbamates (**3** and **4**) were carried out and results are shown in Table III. Methyl ketone (Run 4) afforded no product owing to the difficulty of tin enolate (**24**) formation from methyl ketone. The reactions in Table III greatly depend on the solvent,[1] thus, tetrahydrofuran instead of dichloromethane gave no product.

α-Acetonyl cyclic amines (**14**, **16**, and **28**) are important intermediates in alkaloid synthesis.[7] The hydrolysis and decarboxylation of acetoacetates (**6**, **11**, and **13**), alternative routes to the direct synthesis of **14**, **16**, and **28** as shown in Table II, were thus carried out and the results are given in Table IV. Surprisingly, reactions under these acidic or basic conditions failed to give satisfactory results, the yields being low or moderate (0-49%). No desired product at all was obtained by the

Table III. Reactions of α-Ethoxycarbamates with Ketones in the Presence of $Sn(OTf)_2$



23 a-c
a R^1=Ph, R^2=Et
b R^1=n-Pr, R^2=Et
c R^1=Ph, R^2=H

24

25 n=3, R^1=Ph, R^2=Et
26 n=4, R^1=n-Pr, R^2=Et
27 n=4, R^1=Ph, R^2=Et

Run	Ketone	Carbamate	Product *	(Yield%)
1	**23a**	**3**	**25**	(41)
2	**23b**	**4**	**26**	(65)
3	**23a**	**4**	**27**	(70)
4	**23c**	**4**	**20**	(0)

*^{1}H-Nmr spectra of products **25-27**, whose separation was not possible by glc and hplc, showed them to be a mixture of diastereomers.

hydrolysis of ester (**11**) including a six-membered ring under acidic conditions. Treatment of *tert*-butyl acetoacetate (**7**) with trifluoroacetic acid gave **14** in 40% yield. The hydrogenolysis of benzyl acetoacetate (**8**) over 5% palladium-carbon in ethanol gave **14** in 65% yield. This neutral conditions would thus appear best for obtaining ketones from acetoacetates.

Table IV. Hydrolysis and Decarboxylation of Acetoacetates

6 n=3
11 n=4
13 n=5

14 n=3
16 n=4
28 n=5

Run	Acetoacetates	Conditions*	Product (Yield, %)
1	**6**	A	**14** (39)
		B	**14** (28)
2	**11**	A	**16** (trace)
		B	**16** (12)
3	**13**	A	**28** (25)
		B	**28** (49)

* A: 2%HCl-EtOH, reflux B: 5%NaOH-EtOH, reflux

The present results indicate that tin(II) triflate converts α-ethoxy-carbamates (**3**, **4**, and **5**) to acyl iminium ions (**22**), which react with electron-rich olefins or tin(II) enolates formed from active methylene compounds or ketones to give α-substituted cyclic amine derivatives in good yields. It is significant that tin(II) triflate:$Sn(OTf)_2$ functions to form both acyl iminium ion (electrophile) and tin(II) enolate (nucleophile) in the same vessel and can be handled more easily as a Lewis acid than fuming titanium(IV) chloride or boran trifluoride-etherate.

EXPERIMENTAL

All melting points were determined by micro-melting apparatus (Yanagi-moto) without correction. Ir and mass spectra were measured on Hitachi 200-10 spectrophotometer and Hitachi M-80 spectrometer, respectively.

^{1}H-Nmr spectra were recorded on a Varian EM-390 instrument. Chemical shifts were recorded in ppm downfield from the internal standard (tetra-methylsilane). Chromatographic separations were made using a silica gel (Wako-gel C-200) column. Thin-layer chromatography (tlc) was carried out with pre-coated silica gel plates (Kiesel Gel 60F-254, Merck). α-Ethoxycarbamates (**3**, **4**, and **5**) were prepared as previously reported.[8]

General Procedure for Reactions of α-Ethoxycarbamates (**3**, **4**, and **5**) with Active Methylene Compounds (**1**) (Table I) --- A suspension of $Sn(OTf)_2$ (458 mg, 1.1 mmol) and *N*-ethylpiperidine (138 mg, 1.2 mmol) in dry CH_2Cl_2 (4 ml) was cooled at 0 °C under an Ar atmosphere. To this suspension was added a solution of active methylene compound (**1**) (1.0 mmol) in dry CH_2Cl_2 (2 ml), followed by stirring at 0 °C for 30 min. A solution of α-ethoxycarbamate (**3-5**) (1.3 mmol) in dry CH_2Cl_2 (5 ml) was added dropwise over a period of 5 min. The reaction mixture was stirred at 0 °C for 30 min and then at room temperature for 1 h. The reaction mixture was quenched with pH 7 phosphate buffer solution (10 ml) and extracted with ether several times. The extract was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give an oil. Chromatographic separation of the oil on silica gel by elution with hexane-acetone (5:1) gave the desired product which was purified by distillation to obtain pure **6-13** as shown in Table I. Spectral data for **6-13** are shown in Table V.

General Procedure for Reactions of α-Ethoxycarbamates (**3** and **4**) with Enol Acetates or Enol Ethers (Table II) --- A typical procedure for **14** is as follows: A solution of **3** (187 mg, 1.0 mmol) in CH_2Cl_2 (3 ml) was added dropwise at 0 °C over a period of 5 min to a suspension of $Sn(OTf)_2$ (458 mg, 1.1 mol) in CH_2Cl_2 (2 ml) under an Ar atmosphere, followed by stirring at 0 °C for 30 min. A solution of isopropenyl acetate (110 mg, 1.1

mol) in CH_2Cl_2 (2 ml) was added at 0 °C to this mixture for 5 min, followed by stirring for 1 h at the same temperature. The reaction mixture was stirred at room temperature for 1 day, quenched with pH 7 phosphate buffer solution (10 ml), and extracted with ether several times. The combined ether extracts were washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give an oil, which, on distillation, gave 123 mg (62.0 %) of **14** as a colorless oil. Compounds (**14-20**) were prepared under the conditions specified in Table II and spectral data of compounds in Table II are shown in Table V.

General Procedure for Reactions of α-Ethoxycarbamates (**3** and **4**) with Ketones (**23**) (Table III) --- A typical procedure for **27** is as follows: A suspension of $Sn(OTf)_2$ (5.18 g, 12.5 mmol) and *N*-ethylpiperidine (918 mg, 8.12 mmol) in CH_2Cl_2 (15 ml) was cooled at 0 °C under an Ar atmosphere. A solution of 4-heptanone (612 mg, 5.41 mmol) in CH_2Cl_2 (5 ml) was added dropwise for 5 min, followed by stirring at 0 °C for 1 h. After cooling the reaction mixture to -10 °C, a solution of **4** (1.09 g, 7.03 mol) in CH_2Cl_2 (5 ml) was added dropwise for 5 min, followed by stirring for 4 h at the same temperature. The mixture was quenched with water and extracted with ether several times. The extract was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give an oil, which was chromatographed on silica gel by elution with hexane-acetone (15:1) and then distilled under reduced pressure to give 1.01 g (70%) of **27** as a colorless oil. Compouds (**25** and **26**) were prepared in the same method.

Preparation of **14** from Diester (**6** and **8**) --- Method A (by acidic conditions): A solution of **6** (129 mg, 0.5 mmol) in 2% HCl-ethanol (10 ml) was refluxed overnight and evaporated under reduced pressure. The residue was extracted by ether. The extract was washed with 3% $NaHCO_3$ solution and brine, dried over $MgSO_4$, and evaporated under reduced

Table V. Physical Properties of α-Substituted Pyrrolidine, Piperidine, and Hexametyleneimine Derivatives*

7. bp 112-115 °C (4 mmHg), ms *m/z* 299 (M^+), ir (neat) 1690, 1710, 1740 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.27 (3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 1.46 (9H, s, $OC(C\underline{H}_3)_3$), 1.65-2.15 (4H, m, $C\underline{H}_2C\underline{H}_2$), 2.23 (3H, s, $COC\underline{H}_3$), 3.12-3.65 (2H, m, $C\underline{H}_2N$), 4.11 (2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 3.90-4.20 (1H, m, $COC\underline{H}CO$), 4.30-4.50 (1H,m, $C\underline{H}N$).*Anal.* Calcd for $C_{15}H_{25}NO_5$: C, 60.18;H,8.42; N, 4.68. Found: C, 60.03; H, 8.70; N, 4.52.

8. oil, ms *m/z* 333 (M^+), ir ($CHCl_3$) 1690, 1710, 1740 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.27 (3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 1.55-2.35 (4H, m, $C\underline{H}_2C\underline{H}_2$), 2.20 (3H, s, $COC\underline{H}_3$), 2.90-3.76 (2H, m, $C\underline{H}_2N$), 4.13 (2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 3.87-4.30 (1H, m, $COC\underline{H}CO$), 4.31-4.61 (1H, m, $C\underline{H}N$), 5.19 (2H, s, $C\underline{H}_2Ph$), 7.37 (5H, s, Ph). *Anal.* Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.71; H, 7.03; N, 4.18.

9. bp 150 °C (4 mmHg), ms *m/z* 333 (M^++1), ir (neat) 1690, 1710, 1740 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.21 (3H, t, *J*=7.5 Hz, $CH_2C\underline{H}_3$), 1.26 (3H, t, *J*=7.5 Hz, $CH_2C\underline{H}_3$), 1.50-2.58 (4H, m, $C\underline{H}_2C\underline{H}_2$), 2.68-3.78 (2H, m, $C\underline{H}_2N$), 4.13 (2H, q, *J*=7.5 Hz, $C\underline{H}_2CH_3$), 4.16 (2H, q, *J*=7.5 Hz, $C\underline{H}_2CH_3$), 4.35-4.75 (1H, m, $COC\underline{H}CO$), 4.84-5.60 (1H, m, $C\underline{H}N$), 7.37-7.78 (2H, m, Ph), 7.84-8.18 (2H, m, Ph). *Anal.* Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.74; H, 6.98; N, 4.17.

10. bp 115-118 °C (5 mmHg), ms *m/z* 273 (M^+), ir (neat) 1690, 1725 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.25 (3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 1.72-2.30 (4H, m, $C\underline{H}_2C\underline{H}_2$), 3.15-3.80 (2H, m, $C\underline{H}_2N$), 3.70 (6H, s, $OC\underline{H}_3$ X 2), 4.15 (2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 3.90-4.20 (1H, m, $COC\underline{H}CO$), 4.30-4.50 (1H, m, $C\underline{H}N$). High ms calcd for $C_{12}H_{19}NO_6$: 273.1211. Found: 273.1214.

11. bp 110-112 °C (4 mmHg), ms *m/z* 271 (M^+), ir (neat) 1690, 1710, 1740 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.24 (3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 1.39-2.15 (6H, m, $C\underline{H}_2$ X 3), 2.24 (3H, s, $COC\underline{H}_3$), 2.65-3.15 (1H, m, $\underline{H}CHN$), 3.65 (3H, s, $OC\underline{H}_3$), 4.14 (2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 3.85-4.30 (2H, m, $HC\underline{H}N$, $COC\underline{H}CO$), 4.85-5.20 (1H, m, $C\underline{H}N$). High ms calcd for $C_{13}H_{21}NO_5$: 271.1418: Found: 271.1425.

12. oil, ms *m/z* 318 (M^+-$C(CH_3)_3$), ir (neat) 1690, 1730 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.26 (3H, t, *J*=7 Hz, $CH_2C\underline{H}_3$), 1.36 (9H, s, Bu), 1.46-2.03 (6H, m, $C\underline{H}_2$ X 3), 2.49-3.13 (1H, m, $\underline{H}CHN$), 3.99 (2H, q, *J*=7 Hz, $C\underline{H}_2CH_3$), 3.74-4.24 (2H, m, $HC\underline{H}N$, $COC\underline{H}CO$), 5.06-5.39 (1H, m, $C\underline{H}N$), 7.39-7.66 (3H, m,

Ph), 7.86-8.09 (2H, m, Ph). *Anal.* Calcd for $C_{21}H_{29}NO_5$: C, 67.18; H, 7.79; N, 3.73. Found: C, 66.97; H, 7.88; N, 3.70.

13. bp 120 °C (5 mmHg), ms *m/z* 285 (M^+), ir (neat) 1690, 1710, 1740 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.25 (3H, t, *J*=7 Hz, CH_2CH_3), 1.43-2.17 (8H, m, CH_2 X 4), 2.26 (3H, s, $COCH_3$), 2.63-3.43 (2H, m, CH_2N), 3.73 (3H, s, OCH_3), 3.93-4.37 (2H, m, COCHCO), 4.13 (2H, q, *J*=7 Hz, CH_2CH_3), 4.37-4.87 (1H, m, CHN). *Anal.* Calcd for $C_{14}H_{23}NO_5$: C, 58.93; H, 8.13; N, 4.91. Found: C, 58.49; H, 8.23; N, 4.85.

15. oil, ms *m/z* 239 (M^+), ir (neat) 1700, 1710 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.25 (3H, t, *J*=7 Hz, CH_2CH_3), 1.20-2.38 (12H, m, CH_2CH_2, CH_2 X 4), 2.33 (2H, br, $COCH_2$), 2.83-3.93 (3H, m, COCH, CH_2N), 4.10 (2H, q, *J*=7 Hz, CH_2CH_3), 4.26 (1H, br, CHN). *Anal.* Calcd for $C_{13}H_{21}NO_3$: C, 65.24; H, 8.85; N, 5.85. Found: C, 65.33; H, 8.71; N, 5.76.

16. oil, ms *m/z* 213 (M^+), ir (neat) 1690, 1705 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.22 (3H, t, *J*=7 Hz, CH_2CH_3), 1.40-1.80 (6H, m, CH_2 X 3), 2.20 (3H, s, $COCH_3$), 2.60-3.30 (3H, m, CH_2CO, HCHN), 4.15 (2H, q, *J*=7 Hz, OCH_2), 4.80 (1H, m, HCHN). *Anal.* Calcd for $C_{11}H_{19}NO_3$: C, 61.94; H, 8.98; N, 6.57. Found: C, 61.80; H, 9.04; N, 6.43.

18. bp 75 °C (5 mmHg), ms *m/z* 185 (M^+), ir (neat) 1700 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.26 (3H, t, *J*=7 Hz, CH_2CH_3), 1.54-3.16 (6H, m, CH_2CH_2, CH_2CO), 3.45 (2H, t, *J*=7 Hz, CH_2N), 4.12 (2H, q, *J*=7 Hz, CH_2CH_3), 4.15-4.45 (1H, m, CHN), 9.81 (1H, m, CHO). *Anal.* Calcd for $C_9H_{15}NO_3$: C, 58.36; H, 8.16; N, 7.56. Found: C, 58.54; H, 8.23; N, 7.39.

19. bp 100 °C (5 mmHg), ms *m/z* 199 (M^+), ir (neat) 1695, 1730 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.26 (3H, t, *J*=7 Hz, CH_2CH_3), 1.64 (6H, br, CH_2 X 3), 2.34-3.04 (3H, m, $COCH_2$, HCHN), 4.14 (2H, q, *J*=7 Hz, CH_2CH_3), 3.67-4.34 (1H, m, HCHN), 4.67-5.10 (1H, m, CHN), 9.74-9.94 (1H, m, CHO). *Anal.* Calcd for $C_{10}H_{17}NO_3$: C, 60.28; H, 8.60; N, 7.03. Found: C, 60.44; H, 8.90; N, 6.97.

20. bp 150-153 °C (5 mmHg), ms *m/z* 275 (M^+), ir (neat) 1690 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.18 (3H, t, *J*=7 Hz, CH_2CH_3), 1.13-1.91 (6H, m, CH_2 X 3), 2.57-3.37 (1H, m, HCHN), 3.23 (2H, d, *J*=9 Hz, $COCH_2$), 3.47-4.10 (1H, m, HCHN), 4.09 (2H, q, *J*=7 Hz, CH_2CH_3), 4.67-5.07 (1H, m, CHN), 7.30-8.13 (5H, m, Ph). *Anal.* Calcd for $C_{16}H_{21}NO_3$: C, 69.46; H, 7.69; N, 5.09. Found: C, 69.19; H, 7.76; N, 5.08.

25. bp 143-145 °C (4 mmHg), ms *m/z* 303 (M^+), ir (neat) 1670, 1695 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 0.84 (3H, t, *J*=7 Hz, CH_2CH_3), 1.27 (3H, t, *J*=7 Hz, OCH_2CH_3), 1.40-2.20 (6H, m, CH_2 X 3), 2.51-3.09 (1H, m, COCH), 3.10-

3.76 (2H, m, C$\underline{H}_2$N), 4.17 (2H, q, J=7 Hz, OC$\underline{H}_2$CH3), 3.73-4.46 (1H, m, C$\underline{H}$N), 7.34-7.73 (3H, m, $\underline{Ph}$), 7.80-8.00 (2H, m, $\underline{Ph}$). *Anal.* Calcd for $C_{16}H_{22}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.29; H, 8.02; N, 4.71.

26. bp 150-153 °C (3 mmHg), ms *m/z* 303 (M^+), ir (neat) 1660, 1690 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 0.84 (3H, t, J=7 Hz, CH2C$\underline{H}_3$), 1.27 (3H, t, J=7 Hz, OCH2C$\underline{H}_3$), 1.40-2.10 (8H, m, C$\underline{H}_2$CH3, C$\underline{H}_2$ X 3), 2.51-3.06 (1H, m, COC$\underline{H}$), 4.17 (2H, q, J=7 Hz, OC$\underline{H}_2$CH3), 3.04-4.42 (2H, m, C$\underline{H}_2$N), 4.48-4.90 (1H, m, C$\underline{H}$N), 7.34-7.73 (3H, m, $\underline{Ph}$), 7.84-8.13 (2H, m, $\underline{Ph}$). *Anal.* Calcd for $C_{18}H_{25}NO_3$: C, 71.25; H, 8.31; N, 4.62. Found: C, 71.34; H, 8.37; N, 4.59.

27. bp 118-120 °C (4 mmHg), ms *m/z* 269 (M^+), ir (neat) 1685, 1700 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 0.69-1.07 (6H, m, J=7 Hz, CH2C$\underline{H}_3$ X 2), 1.24 (3H, t, J=7 Hz, OCH2C$\underline{H}_3$), 1.10-2.10 (10H, m, C$\underline{H}_2$CH3, C$\underline{H}_2$ X 3, COCH2C$\underline{H}_2$), 2.40 (2H, q, J=7 Hz, COC$\underline{H}_2$), 2.50-3.20 (2H, m, COC$\underline{H}$, $\underline{H}$CHN), 4.12 (2H, t, J=7 Hz, OC$\underline{H}_2$CH3), 3.80-4.30 (2H, m, $\underline{H}$CHN), 4.30-4.62 (1H, m, C$\underline{H}$N). *Anal.* Calcd for $C_{15}H_{27}NO_3$: C, 66.88; H, 10.10; N, 5.20. Found: C, 66.46; H, 10.15; N, 5.17.

28. oil, ms *m/z* 227 (M^+), ir (neat) 1690, 1710 cm^{-1}, ^{1}H-nmr ($CDCl_3$) δ 1.27 (3H, t, J=7 Hz, CH2C$\underline{H}_3$), 1.47-2.20 (8H, m, C$\underline{H}_2$ X 4), 2.16 (3H, s, COC$\underline{H}_3$), 3.47-4.10 (2H, m, C$\underline{H}_2$N), 4.13 (2H, q, J=7 Hz, C$\underline{H}_2$CH3), 4.23-4.63 (1H, m, C$\underline{H}$N). High ms calcd for $C_{12}H_{21}NO_3$: 227.1520. Found: 227.1598.

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* The physical data of compounds **6** and **14** are described in our paper.[5]

pressure to give an oil, which was purified by chromatography on silica gel by elution with CH_2Cl_2 to give 39 mg (39%) of **14** as a colorless oil. **28** was obtained from **13** by the same method in 25% yield. Method B (by alkaline conditions): **14**, **16**, and **28** were also obtained in 28, 12, and 49% yields by alkaline hydrolysis (5% NaOH-ethanol, reflux, overnight) of **6**, **11**, and **13**, respectively. Method C (under the neutral conditions): The catalytic hydrogenation of **8** (166 mg, 0.5 mmol) in ethanol (25 ml) over 5% Pd-C, followed by chromatography on silica gel by elution with hexane-ethyl acetate (25:1) gave 65 mg (65%) of **14**.

ACKNOWLEDGEMENT

The authors express their appreciation to Lederle (Japan) Co. Lit. for providing the tin(II) triflate and their helpful comments.

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Received, 20th December, 1993