Lithium Bromide/Triethylamine Induced Cycloaddition of *N*-Alkylidene 2-Amino Esters and Amides to Electron-Deficient Olefins with High Regio- and Stereoselectivity

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The imines of 2-amino esters and amides derived from glycine, alanine, and valine are deprotonated by the action of a lithium halide and triethylamine (or DBU). The resulting anionic intermediates undergo highly regio- and stereoselective cycloadditions with a variety of olefins activated by carbonyl-type substituents to produce stereochemically defined derivatives of proline esters or amides. The scope and limitations of this novel cycloaddition are discussed.

Thermal tautomerization of the imines of 2-amino esters[1] or nitriles[2] offers a simple access to azomethine ylides. By this process N-protonated (or N-unsubstituted) azomethine ylides of ester- or cyano-stabilized types can be generated. The ylides are captured as cycloadducts, pyrrolidines or pyrrolines, if such reactive dipolarophiles as maleimides, maleates, or fumarates are present.

The azomethine ylides thermally generated from the imines of glycine ester undergo stereoselective cycloadditions to highly activated cyclic dipolarophiles such as maleimides and maleic anhydride, regardless of substitution at the α-position of the imines, to lead to the exclusive formation of endo cycloadducts of the *E,E*-ylides (or syn ylides).[1a,3] However, their cycloadditions to acyclic olefin dipolarophiles such as maleates and fumarates are no longer stereoselective.[1b,4] Though the cycloadditions to acrylates as unsymmetrically substituted olefins proceed in a regioselective manner, the endo selectivity and/or the *E,E* specificity with respect to dipoles are poor.[4] Furthermore reactivity, regio- and stereoselectivities, and stereospecificity of these azomethine ylide dipoles to other unsymmetrically substituted olefins remain unsolved.[5]

We have recently discovered that the treatment of *N*-(1-cyanoalkyl) imines with a metallic base such as LDA, *n*-BuLi, or EtMgBr generates highly reactive intermediates, which we believe are N-metalated azomethine ylides.[6] The cycloadditions of the metalated ylides to olefins take place in a perfectly regio- and stereoselective manner to furnish 4,5-*cis*-1-pyrrolines after the elimination of the cyano moiety.

There are several examples known for the N-metalated species of azomethine ylides,[7] but the ylide precursors employed in the precedents are structurally limited and therefore their synthetic applications are not clear.

The present article presents a simple and general access to N-metalated azomethine ylides of ester- and amide-stabilized types or the related anionic species such as metal enolates, etc. The imines of 2-amino esters or amides are deprotonated by the action of a lithium halide and triethylamine (or DBU). The resulting anionic species show an enhanced reactivity in 1,3-dipolar cycloadditions. Their diastereoselective cycloadditions to a variety of olefins offer a convenient access to stereochemically defined derivatives of proline esters and amides.

Results and Discussion

The deprotonation of *N*-alkylidene 2-amino esters has been investigated by several research groups. When these imines are deprotonated with sodium or potassium alkoxides or Triton B in protic (methanol, ethanol) or aprotic solvents (benzene, THF) and the resulting species are trapped with electron-deficient olefins,[1a,8] the products are mostly the corresponding Michael adducts. Competitive formation of the Michael adducts and the stereoselective cycloadducts is also known.[8d] In this case, the base-catalyzed cyclization of the Michael adducts was ruled out as a possible route to the cycloadducts and a concerted 1,3-anionic cycloaddition is the proposed mechanism.

According to the procedure used in our successful activation of *N*-alkylidene 2-amino nitriles with LDA,[6] we first applied a similar activation method to methyl (benzylideneamino)acetate (**1a**). When treated with LDA in dry THF at −78 °C, the solution of **1a** immediately turned bright red. All attempts to trap this colored intermediate with methyl acrylate or *N*-methylmaleimide ended in failure. The use of other bases such as *n*-BuLi, NaH, EtMgBr, EtMgBr plus HN(*i*-Pr)$_2$, and a variety of Lewis acids plus LDA[9] led to a complex reaction mixture or very poor yields of the expected cycloadducts. Presumably instability of the olefins under the reaction conditions is responsible for the failure. The olefins with electron-

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(2) (a) Tsuge, O.; Ueno, K. *Heterocycles* **1982**, *19*, 1411. (b) Tsuge, O.; Kanemasa, S.; Yorozu, K.; Ueno, K. *Chem. Lett.* **1985**, 1601. (c) Tsuge, O.; Ueno, K.; Kanemasa, S.; Yorozu, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1809.

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(4) Grigg, R.; Kemp, J. *Tetrahedron Lett.* **1980**, *21*, 2461.

(5) Heating methyl (benzylideneamino)acetate (**1a**) or methyl 2-(benzylideneamino)propanoate (**1b**) with methyl crotonate under reflux in xylene for 6 h produced about 40% or 10%, respectively, of the corresponding cycloadducts together with the recovered imine **1a** (60%) or **1b** (90%). The major cycloadduct in each case was **2f** or **3d** (^{1}H NMR, our unpublished result).

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(7) (a) Casella, L.; Gullotti, M.; Pasini, A.; Psaro, R. *Synthesis* **1979**, 150. (b) Grigg, R.; Gunaratne, H. Q. N. *J. Chem. Soc., Chem. Commun.* **1982**, 384. (c) Casella, L.; Gullotti, M.; Melani, E. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1827. (d) Joucla, M.; Foucheet, B.; Hamelin, J. *Tetrahedron* **1985**, *41*, 2707. (e) Grigg, R.; Devlin, J. *J. Chem. Soc., Chem. Commun.* **1986**, 631. (f) Grigg, R.; Sridharan, V.; Thianpatanagul, S. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1669.

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(9) After the treatment of **1a** with LDA at −78 °C, a Lewis acid ($SnCl_2$, $SnCl_4$, $ZnCl_2$, or Et_2AlCl) and then methyl acrylate were added. The reaction was monitored by TLC and conducted at this temperature for several hours.

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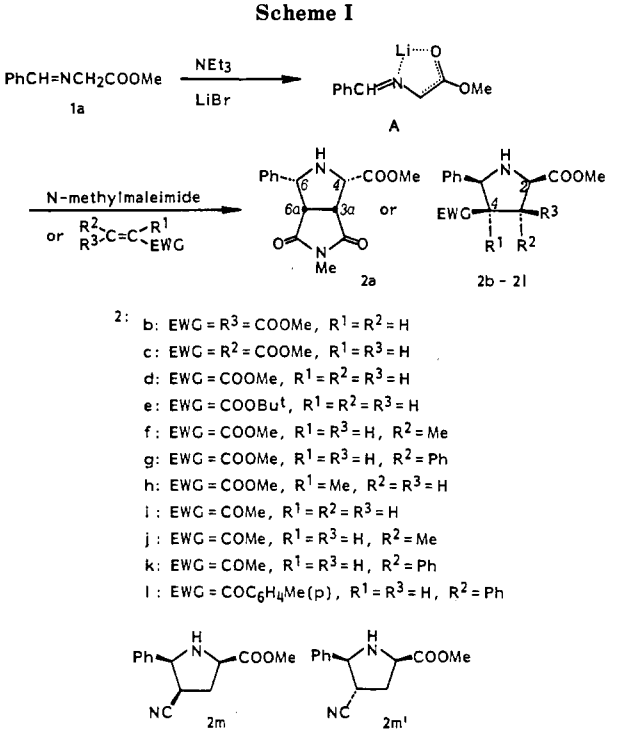
Table I. LiBr/NEt_3-Induced Cycloaddition of Methyl (Benzylideneamino)acetate (1a) to Electron-Deficient Olefins[a]

entry	olefin	LiBr (equiv)	NEt_3 (equiv)	time/h	product	EWG	R^1	R^2	R^3	yield,[b] %
1	*N*-methylmaleimide	1.5	1.2	17	**2a**					45
2	*N*-methylmaleimide	0.1	0.1	28	**2a**					83
3	dimethyl maleate	1.5	1.2	21	**2b**	COOMe	H	H	COOMe	44
4	dimethyl fumarate	1.5	1.2	22	**2c**	COOMe	H	COOMe	H	70
5	methyl acrylate	1.5	1.2	21	**2d**	COOMe	H	H	H	82
6	*tert*-butyl acrylate	1.5	1.2	24	**2e**	$COOBu^t$	H	H	H	71
7	methyl crotonate	1.5	1.2	23	**2f**	COOMe	H	Me	H	91
8	methyl cinnamate	1.5	1.2	22	**2g**	COOMe	H	Ph	H	77
9	methyl methacrylate	1.5	1.2	24	**2h**	COOMe	Me	H	H	91
10	3-buten-2-one	1.5	1.2	30	**2i**	COMe	H	H	H	20
11	3-buten-2-one	0.1	0.1	72	**2i**					35
12	(*E*)-3-penten-2-one	1.5	1.2	8	**2j**	COMe	H	Me	H	77
13	(*E*)-4-phenyl-3-buten-2-one	1.5	1.2	24	**2k**	COMe	H	Ph	H	59
14	(*E*)-1-(*p*-tolyl)-3-phenylpropenone	1.5	1.2	24	**2l**	COC_6H_4Me-*p*	H	Ph	H	73
15	acrylonitrile	1.5	1.2	28	**2m** + **2m′**					91[c]

[a] All reactions were carried out in dry THF at room temperature. [b] Yields of isolated products. [c] **2m**, 26%; **2m′**, 65%.

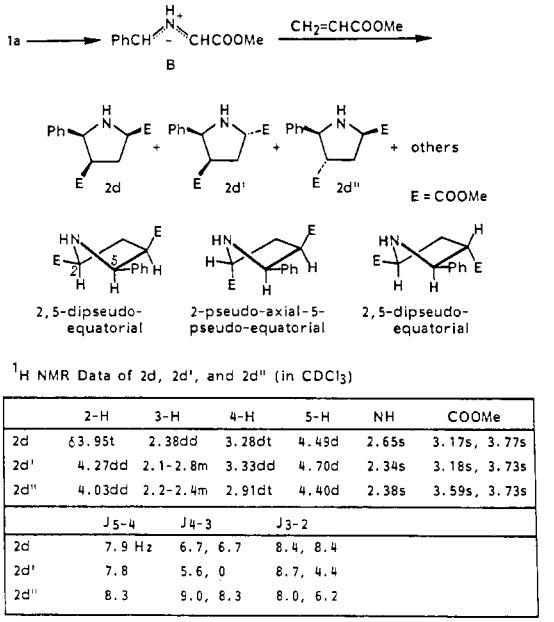
Scheme I



withdrawing substituents undergo polymerization under these highly basic conditions more readily than the desired cycloaddition.[10]

This suggested the use of a weaker base which is basic enough to deprotonate **1a** but does not initiate the undesired polymerization. A combination of a metal halide and a tertiary amine was tried since this combination has been effectively employed in the olefination with base-labile 2-oxoalkylphosphonates or 2-phosphoryl esters.[11] To our delight, the treatment of **1a** with lithium bromide and triethylamine in dry THF at room temperature generated the anionic intermediate, A which was captured by *N*-methylmaleimide to lead to an excellent yield of the expected cycloadduct **2a** as a single isomer (Scheme I).

Scheme I and Table I summarize the cycloaddition reactions of **1a** with a variety of electron-deficient olefins



^1H NMR Data of 2d, 2d′, and 2d″ (in $CDCl_3$)

	2-H	3-H	4-H	5-H	NH	COOMe
2d	δ3.95t	2.38dd	3.28dt	4.49d	2.65s	3.17s, 3.77s
2d′	4.27dd	2.1-2.8m	3.33dd	4.70d	2.34s	3.18s, 3.73s
2d″	4.03dd	2.2-2.4m	2.91dt	4.40d	2.38s	3.59s, 3.73s

	J_{5-4}	J_{4-3}	J_{3-2}
2d	7.9 Hz	6.7, 6.7	8.4, 8.4
2d′	7.8	5.6, 0	8.7, 4.4
2d″	8.3	9.0, 8.3	8.0, 6.2

Figure 1. Assignment of the stereostructures of **2d**, **2d′**, and **2d″**.

under similar conditions. Symmetrically substituted olefins (entries 1–4), unsymmetrically substituted olefinic esters (entries 5–9), and ketones (entries 10–14) all reacted with **1a** in a highly regio- and stereoselective manner to produce cycloadducts **2a–l**. The reactions were carried out under nitrogen in dry THF[12] at room temperature by using a slight excess of lithium bromide (1.5 equiv) and triethylamine (1.2 equiv) to an equimolar mixture of imine **1a** and an olefin. The reaction rates seem to be independent upon reactivity of the olefins used, indicating that the intermediate species are captured as they are generated. In the reactions with *N*-methylmaleimide and 3-buten-2-one, which are very sensitive to base-catalyzed polymerization, use of catalytic amounts of lithium bromide and triethylamine (each 0.1 equiv) is effective (entries 2 and 11).

The stereochemistries of **2** were determined on the basis of spectroscopic data. Assignment of the cycloadduct of methyl acrylate **2d** is as follows: The thermal tautomerization of **1a** generated the N-protonated azomethine ylide B, which was captured by methyl acrylate. In contrast to the above case, this thermal cycloaddition exhibited poor

(10) This polymerization can be significantly inhibited by the addition of water (1 to 3 equiv).

(11) (a) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183. (b) Rathke, M. W.; Nowak, M. *J. Org. Chem.* **1985**, *50*, 2624. (c) Rosen, T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1985**, *107*, 3731. (d) Tsuge, O.; Kanemasa, S.; Nakagawa, N.; Suga, H. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2463.

(12) The use of dry THF is essential in the reaction of **1a** with methyl acrylate since the cycloadduct **2d** is contaminated by a Michael adduct when the same reaction is carried out in wet THF or dry acetonitrile.

Table II. LiBr/Amine-Induced Cycloaddition of Methyl 2-(Benzylideneamino)propanoate (1b) or Methyl 2-(Benzylideneamino)-3-methylbutanoate (1c) to Electron-Deficient Olefins[a]

entry	imine	olefin	LiBr (equiv)	amine (equiv)	time/h	product	EWG	R^1	R^2	R^3	yield,[b] %
1	**1b**	*N*-methylmaleimide	0.1	NEt_3 0.1	72	**3a**					86
2	**1b**	dimethyl fumarate	1.5	NEt_3 1.2	72	**3b**	COOMe	H	COOMe	H	87
3	**1b**	methyl acrylate	1.5	NEt_3 1.2	49	**3c**	COOMe	H	H	H	79
4	**1b**	methyl crotonate	1.5	NEt_3 1.2	23	**3d**	COOMe	H	Me	H	33 (66)[c]
5	**1b**	methyl crotonate	1.5[d]	NEt_3 1.2	23	**3d**					50 (45)[c]
6	**1b**	methyl crotonate	1.5	NEt_3 1.2	24[e]	**3d**					50 (30)[c]
7	**1b**	methyl crotonate	1.5	DBU 1.0	23	**3d**					82
8	**1b**	methyl methacrylate	1.5	NEt_3 1.2	24	**3e**	COOMe	Me	H	H	81
9	**1b**	acrylonitrile	1.5	NEt_3 1.2	72	**3f** + **3f′**					97[f]
10	**1c**	methyl crotonate	1.5	DBU 1.2	24						94% recovered
11	**1c**	methyl methacrylate	1.5	DBU 1.2	24	**4**					80

[a] All reactions were carried out in dry THF at room temperature. [b] Yields of isolated products. [c] Recovered **1b**. [d] Lithium iodide was used instead of lithium bromide. [e] Under reflux. [f] **3f**, 25%, **3f′**, 72%.

stereoselectivity, affording a mixture containing more than three isomeric cycloadducts from which three stereoisomers, **2d** (29%), **2d′** (15%), and **2d″** (4%), were isolated (Figure 1).[13] Since the pyrrolidine ring is the conformationally flexible and its stable conformation depends upon the size of the substituents on the ring, comparison of the ^1H NMR spectra of **2d**, **2d′**, and **2d″** is informative. The regiochemistry (2,4-dicarboxylate structure) and the 4,5-cis configuration of **2d** as well as **2d′** are easily confirmed since the 4-ester methyl is magnetically shielded by the adjacent 5-phenyl. The coupling pattern of 2-H (a doublet of doublets) and no shielding of the 4-ester methyl of **2d″** is consistent with the 4,5-trans 2,4-dicarboxylate structure. On the basis of vicinal couplings measured from molecular models, the structures were assigned as follows: **2d**, dimethyl *c*-5-phenylpyrroline-*r*-2,*c*-4-dicarboxylate (2,5-dipseudoequatorial); **2d′**, dimethyl *t*-5-phenylpyrrolidine-*r*-2,*t*-4-dicarboxylate (2-pseudoaxial, 5-pseudoequatorial); **2d″**, dimethyl *c*-5-phenylpyrrolidine-*r*-2,*t*-4-dicarboxylate (2,5-dipseudoequatorial).

Thus **2d** corresponds to an endo cycloadduct of the syn form of lithiated anionic intermediate A. Exclusive syn and endo selectivity presumably is a result of the lithium chelation[14] involved in the two possible approaches as illustrated in Figure 2: (1) the concerted cycloaddition of N-lithiated azomethine ylide A-1 via approach C-1 or (2) the tandem Michael–imine addition of lithium enolate A-2 via C-2 (Y = OMe, $R^1 = R^2 = R^3 = H$). Discrimination between A-1 and A-2, and hence C-1 and C-2, is not possible thus far.

High contribution of the lithium chelation is evidenced by the following two examples: (1) A similar reaction of **1a** with acrylonitrile is highly syn-selective but poor in endo selectivity so that it produces a mixture of two stereoisomeric cycloadducts **2m** + **2m′** (2:5, entry 15 in Table I). (2) Reaction of **1a** with methyl acrylate in the absence of lithium bromide was very poor in syn selectivity so that a mixture of two endo cycloadducts **2d** + **2d′** (1:1) is produced.[15] Although such chelation control is structurally impossible in the reaction with *N*-methylmaleimide, a high endo selection is still observed to give **2a**. The high

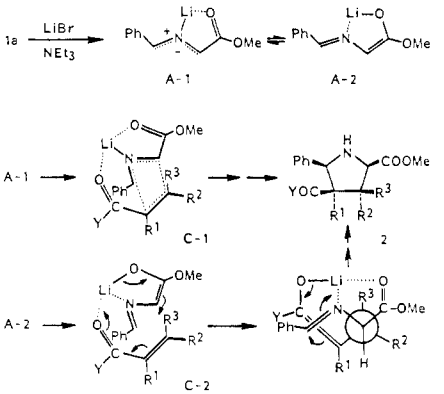


Figure 2. Two possible mechanisms for the lithium bromide/triethylamine induced cycloaddition of **1a**.

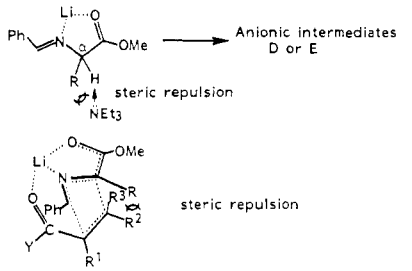


Figure 3. Steric congestion by the α-substitution of **1a**.

selectivity is the same as that observed in the reaction of N-protonated azomethine ylide B, shown in Figure 1, with the maleimide.[3d,e]

Other cycloadducts **2a–c** and **2e–l** were characterized on the basis of their spectroscopic data as well as the stereochemical mode of the aforementioned cycloadditions.

α-Substitution of the imine **1a** with an alkyl moiety (methyl or isopropyl) makes it difficult for the remaining α-hydrogen to be deprotonated with lithium bromide and triethylamine.[16] In addition, there presumably is some steric repulsion in the cycloaddition step of D or E between the methyl or isopropyl group and the olefin substituent R^2 which is trans to the electron-withdrawing group EWG (EWG = COY, Figure 3). Nonetheless, deprotonation of methyl 2-(benzylideneamino)propanoate (**1b**) with lithium bromide and triethylamine occurs readily at room temperature (Scheme II). The intermediate D is trapped by *N*-methylmaleimide, methyl acrylate, methacrylate (R^2 = H in all cases, so negligible steric congestion to the methyl),

(13) The reaction of **1a** with methyl acrylate has been previously reported to give four regioselective cycloadducts (1:0.5:2:0.75) (ref 4). Although this report points out that formation of the four isomers may arise from thermal isomerization, neither the cycloaddition conditions nor the spectroscopic data of each product is given therein.

(14) Maleimides are the olefins whose carbonyl moieties cannot make a stable lithium chelation. Their high endo selectivity may arise from the attractive secondary orbital interaction which has been observed from previous cases (ref 3d and 3e).

(15) In this case triethylamine presumably acted as a catalyst for the imine–azomethine ylide tautomerization of **1a** generating N-protonated azomethine ylide B (the combined yield of **2d** and **2d′** was 70%).

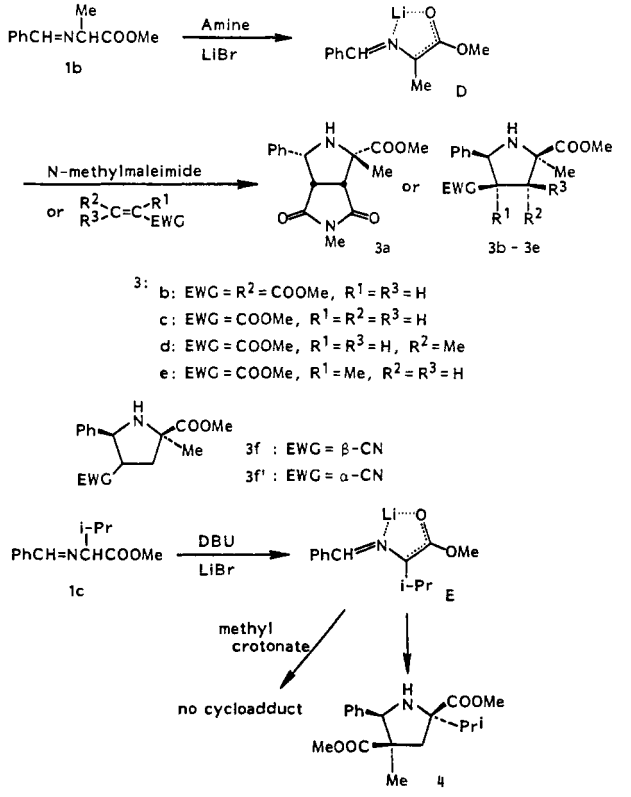
(16) Optically active imine **1b** completes its racemization in 20 h at room temperature in THF in the presence of lithium bromide (1.5 equiv) and triethylamine (1.2 equiv), while imine **1c** retains its full activity under identical conditions.

Table III. LiBr/NEt_3-Induced Reaction of *N,N*-Tetramethylene-2-(benzylideneamino)ethanamide (1d) or *N-tert*-Butyl-2-(benzylideneamino)ethanamide (1e) with Electron-Deficient Olefins[a]

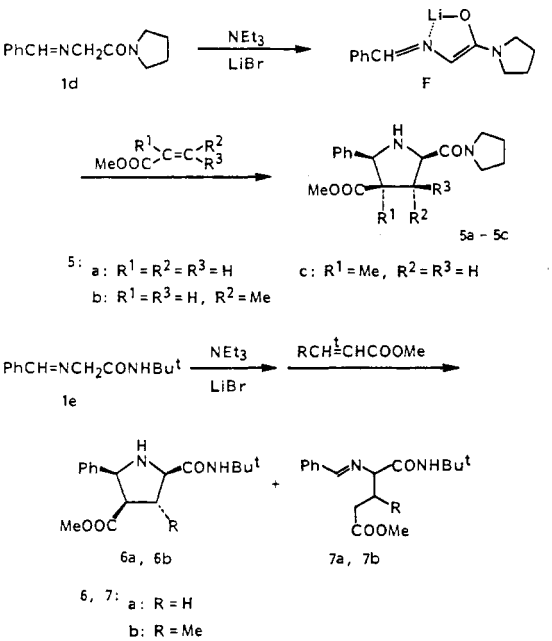
entry	imine	olefin	product	R^1	R^2	R^3	R	yield,[b] %
1	1d	methyl acrylate	5a	H	H	H		89
2	1d	methyl crotonate	5b	H	Me	H		95
3	1d	methyl methacrylate	5c	Me	H	H		98
4	1d	methyl acrylate	6a + 7a				H	97 (6a, 31%; 7a, 66%[c])
5	1e	methyl crotonate	6b + 7b				Me	66 (6b, 46%; 7b, 20%[c])[d]

[a] All reactions were carried out in THF at room temperature for 24 h in the presence of LiBr (1.5 equiv) + NEt_3 (1.2 equiv). [b] Yields of isolated products. [c] Determined by ^1H NMR of the crude reaction mixture. [d] Recovered 1e: 23% (^1H NMR).

Scheme II



Scheme III



and dimethyl fumarate (a highly activated dipolarophile) to give diastereoselective cycloadducts **3a–c** and **3e**, respectively (Table II). The generation of the intermediate is still rate-determining.

The endo-selective cycloaddition of anion D to methyl crotonate (R^2 = Me) would suffer from a serious steric repulsion between the two methyl moieties so that the cycloaddition step is expected to be extremely sluggish. This reaction is not complete under comparable conditions even using lithium iodide (entry 5) or under reflux in THF (entry 6). However, use of DBU instead of triethylamine gives a satisfactory yield of endo cycloadduct **3d** (entry 7), indicating that the cycloaddition is now the rate-determining step.

Deprotonation of the imine **1c** derived from valine ester with lithium bromide and triethylamine did not occur. When DBU was employed, the intermediate E was generated but failed to be trapped by methyl crotonate (Scheme II, Table II, entry 9). Only olefins bearing no α-substituent (R^2 = H) could be involved in the cycloaddition to E. For example cycloadduct **4** was obtained in 80% yield as a single isomer in the reaction with methyl methacrylate (entry 10).

The imine of glycine amide, *N,N*-tetramethylene-2-(benzylideneamino)ethanamide (**1d**), underwent similar syn- and endo-selective cycloadditions to methyl acrylate, methacrylate, and crotonate to give **5a–c** in excellent yields, respectively (Scheme III and Table III). On the other hand the imine **1e** derived from a secondary amide produced a mixture of cycloadducts **6a,b** and the Michael adducts **7a,b**. Lithium chelation presumably exists in the latter amide case also, but the structure of reacting species is not clear.

In conclusion, the imines of 2-amino esters and amides can be activated by simple treatment with lithium bromide and triethylamine in THF; the resulting species show high reactivity to a wide variety of carbonyl-activated olefin dipolarophiles; they undergo exclusive regioselective, endo-selective, and stereospecific cycloadditions to produce stereochemically defined pyrrolidines.

Experimental Section

General. Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with a JASCO IRA-1 or a JASCO A-702 spectrometer. ^1H and ^{13}C NMR spectra were recorded on Hitachi R-40 (^1H, 90 MHz), JEOL FX-100 (both ^1H and ^{13}C, 100 MHz), and JEOL Model JSX-270 spectrometers (both ^{13}C and ^1H, 270 MHz). Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Mass as well as high resolution mass spectra were measured with a JEOL-01SG-2 spectrometer. Elemental analyses were performed on a Hitachi 026 CHN analyzer. Thin-layer chromatography (TLC) was accomplished on 0.2-mm precoated plates of silica gel 60 F-254 (Merck). Visualization was made with ultraviolet light (254 and 365 nm), iodine, molybdophosphoric acid (5% in ethanol), or *p*-anisaldehyde (5% in ethanol containing 5% of sulfuric acid). For preparative column chromatography, Wakogel C-200, C-300 (Wako), and silica gel 60 (Merck) were employed. Flash chromatography was carried out on an EYELA EF-10 apparatus using a column (20 × 180 mm) packed with silica gel 60 (Merck, size 0.04–0.063 mm). Gas–liquid chromatography (GLC) was accom-

plished on a Yanaco G-2800 gas chromatograph (Yanagimoto) with an ionization flame detector using a glass column (SE-30, 3 × 2000 mm) or a glass capillary column (Silicone GE, SE-30, 0.25 × 50000 mm). Microvacuum distillation was carried out on a Sibata GTO-250R Kugelrohr distilling apparatus. Solvents were evaporated with a Tokyo Rikakikai rotary evaporator type-V at about 50 °C unless otherwise stated.

Materials and Solvents. The imines **1a–c** were all prepared by the condensation of the corresponding 2-amino ester hydrochlorides with benzaldehyde: An equimolar mixture of the salt, benzaldehyde, and triethylamine was heated under reflux in benzene for 1 h. The reaction mixture was washed with water, and the benzene was dried over magnesium sulfate and evaporated in vacuo. The residue was distilled on a Kugelrohr distilling apparatus to give pure imines **1a–c**. **1a**: ^{1}H NMR ($CDCl_3$) δ 3.70 (3 H, s, COOMe), 4.35 (2 H, s, NCH_2), 7.3–7.4, 7.7–7.8 (3 H + 2 H, m, Ph), and 8.21 (1 H, s, CH=N). **1b**: ^{1}H NMR ($CDCl_3$) δ 1.51 (3 H, d, J = 6.7 Hz, Me), 3.69 (3 H, s, COOMe), 4.13 (1 H, q, J = 6.7 Hz, CH), 7.3–7.4, 7.7–7.8 (3 H + 2 H, m, Ph), and 8.25 (1 H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ 19.41 (q, Me), 52.12 (q, COOMe), 67.95 (d, NCH), 128.65, 129.13, 131.24 (each d, Ph), 136.01 (s, Ph), 163.13 (d, CH=N), and 173.12 (s, COOMe). **1c**: ^{1}H NMR ($CDCl_3$) δ 0.93, 0.95 (each 3 H, d, J = 6.7 Hz, *i*-Pr), 2.39 (1 H, dq, J = 6.7 and 7.4 Hz, *i*-Pr), 3.65 (1 H, d, J = 7.4 Hz, NCH), 3.70 (3 H, s, COOMe), 7.3–7.4, 7.7–7.8 (3 H + 2 H, m, Ph), and 8.21 (1 H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ 18.71, 19.35 (each q, *i*-Pr), 31.77 (d, *i*-Pr), 51.95 (q, COOMe), 80.48 (d, NCH), 128.77, 131.24 (each d, Ph), 135.95 (s, Ph), 163.48 (d, CH=N), and 172.65 (s, COOMe); MS, m/z 219 (M^+). Imine **1d** was similarly prepared by the following sequence: the reaction of chloroacetyl chloride with pyrrolidine (NEt_3, in dichloromethane, room temperature) the amination of *N*-(chloroacetyl)pyrrolidine with liquid ammonia, and the final condensation of *N*-(aminoacetyl)pyrrolidine with benzaldehyde: ^{1}H NMR ($CDCl_3$) δ 1.8–2.0 (4 H, m, py), 3.4–3.7 (4 H, m, py), 4.36 (2 H, s, NCH_2), 7.3–7.4, 7.7–7.8 (3 H + 2 H, m, Ph), and 8.28 (1 H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ 24.24, 26.18 (each t, py), 46.00, 46.65 (each t, py), 64.24 (t, NCH_2), 128.54, 128.72, 131.07 (each d, Ph), 136.13 (s, Ph), 164.60 (d, CH=N), and 167.89 (s, CON); MS, m/z 216 (M^+). Imine **1e** was prepared according to the identical method by using *tert*-butylamine instead of pyrrolidine. **1e**: ^{1}H NMR ($CDCl_3$) δ 1.38 (9 H, s, *t*-Bu), 4.13 (2 H, s, NCH_2), 6.73 (1 H, br s, NH), 7.4–7.5, 7.7–7.8 (3 H + 2 H, m, Ph), and 8.20 (1 H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ 28.88 (q, *t*-Bu), 50.94 (s, *t*-Bu), 63.59 (t, NCH_2), 128.42, 128.95, 131.54 (each d, Ph), 135.71 (s, Ph), 163.31 (d, CH=N), and 169.48 (s, CON); MS, m/z 218 (M^+). Triethylamine (dried over KOH pellet) diazabicyclo[5.4.0]undec-7-ene (DBU, dried over molecular sieves 5A), lithium bromide, and lithium iodide were all commercially available and used without further purification. Tetrahydrofuran (THF) was distilled over lithium aluminum hydride immediately prior to its use.

General Procedures for the Reactions of 2-(Benzylideneamino) Esters 1a–c and Amides 1d,e with Electron-Deficient Olefins. As a typical example, the reaction of **1a** with methyl acrylate is described below: To a mixture of **1a** (0.177 g, 1 mmol) and methyl acrylate (0.095 g, 1.1 mmol) in dry THF (2.5 mL) was added lithium bromide (0.13 g, 1.5 mmol in THF (1.5 mL)) and then triethylamine (0.121 g, 1.2 mmol in THF (1 mL)) by the aid of a syringe. The mixture was stirred at room temperature for 21 h under nitrogen (checked by TLC) and poured into concentrated aqueous ammonium chloride (10 mL). The products were extracted with diethyl ether (15 mL × 2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using chloroform as an eluent to give **2d** (0.216 g, 82%).

Other reactions were performed according to the above procedure. The reaction conditions as well as the results are all listed in Tables I–III.

2a: colorless needles (column chromatography, chloroform; crystallization, chloroform–hexane); mp 216–218 °C; IR (KBr) 3335, 1737, and 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.10 (1 H, br s, NH), 2.84 (3 H, s, NMe), 3.3–3.6 (2 H, m, 3a- and 6a-H), 3.84 (3 H, s, COOMe), 4.03 (1 H, d, J_{4-3a} = 6.5 Hz, 4-H), 4.47 (1 H, d, J_{6-6a} = 8.2 Hz, 6-H), and 7.27 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 25.00 (NMe), 48.36, 49.65 (3a- and 6a-C), 52.36 (COOMe), 61.83 (4-C), 64.18 (6-C), 127.24, 128.60, 136.89 (Ph), 170.37, 174.89, and 176.13 (COOMe and CON); MS, m/z (rel intensity) 288 (M^+, 6), 229 (47), 177 (42), 144 (63), 117 (base peak), 115 (24), and 90 (20). Anal. Calcd for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.40; H, 5.60; N, 9.58.

2b: colorless needles (column chromatography, chloroform; crystallization, chloroform–hexane); mp 106–107 °C; IR (KBr) 3300, 1740, and 1707 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.70 (1 H, br s, NH), 3.20 (3 H, s, 4-COOMe), 3.5–3.7 (2 H, m, 3- and 4-H), 3.65, 3.78 (each 3 H, s, 2- and 3-COOMe), 4.15 (1 H, d, J_{2-3} = 8.5 Hz, 2-H), 4.47 (1 H, d, J_{5-4} = 6.3 Hz, 5-H), and 7.28 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 51.24, 52.59, 52.77 (each q, COOMe), 51.53, 52.30 (each d, 3- and 4-C), 62.42 (d, 2-C), 65.59 (d, 4-C), 127.01, 128.07, 128.65 (each d, Ph), 137.42 (s, Ph), 171.24, and 171.42 (each s, COOMe); MS, m/z (rel intensity) 321 (M^+, 14), 262 (85), 202 (31), 177 (base peak), 170 (20), 145 (22), 144 (31), 143 (24), 142 (79), 141 (23), 117 (83), 115 (27), 114 (29), and 59 (30). Anal. Calcd for $C_{16}H_{19}NO_6$: C, 59.80; H, 5.96; N, 4.36. Found: C, 60.03; H, 5.99; N, 4.45.

2c: colorless liquid (column chromatography, chloroform); IR (neat) 3350 and 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.65 (1 H, br s, NH), 3.16 (3 H, s, 4-COOMe), 3.5–3.7 (2 H, m, 3- and 4-H), 3.72, 3.79 (each 3 H, s, COOMe), 4.18 (1 H, d, J_{2-3} = 7.5 Hz, 2-H), 4.72 (1 H, d, J_{5-4} = 7.8 Hz, 5-H), and 7.24 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 50.83, 52.65, 53.95 (each q, COOMe), 51.65, 52.65 (each d, 3- and 4-C), 63.48, 65.53 (each d, 2- and 5-C), 127.07, 128.13, 128.48 (each d, Ph), 138.42 (s, Ph), 171.89, 172.36, and 172.89 (each s, COOMe); MS, m/z (rel intensity) 321 (M^+, 44), 262 (30), 230 (34), 202 (54), 177 (base peak), 117 (65), and 115 (22); HRMS calcd for $C_{16}H_{19}NO_6$ (M) 321.1211, found m/z 321.1211.

2d: pale yellow liquid (column chromatography, chloroform–diethyl ether (4:1 vol/vol)); IR (neat) 3370 and 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.38 (2 H, dd, J_{3-2} = 8.4 and J_{3-4} = 6.7 Hz, 3-H), 2.65 (1 H, s, NH), 3.17 (3 H, s, 4-COOMe), 3.28 (1 H, dt, J_{4-3} = 6.7, 6.7, and J_{4-5} = 7.9 Hz, 4-H), 3.77 (3 H, s, 2-COOMe), 3.95 (1 H, t, J_{2-3} = 8.4 Hz, 2-H), 4.49 (1 H, d, J_{5-4} = 7.9 Hz, 5-H), and 7.24 (5H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 33.36 (t, 3-C), 49.77 (d, 4-C), 51.30, 52.30 (each q, COOMe), 60.00 (d, 2-C), 65.95 (d, 5-C), 126.95, 127.77, 128.36 (each d, Ph), 139.36 (s, Ph), 173.30, and 174.01 (each s, COOMe); MS, m/z (rel intensity) 263 (M^+, 4), 204 (41), 177 (16), 145 (23), 144 (99), and 117 (base peak); HRMS calcd for $C_{14}H_{17}NO_4$ (M) 263.1157, found m/z 263.1153.

2e: colorless prisms (column chromatography, chloroform; crystallization, diethyl ether–hexane); mp 75–76 °C; IR (KBr) 3300, 1740, and 1707 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.99 (9 H, s, *t*-Bu), 2.3–3.0 (2 H, m, 3-H), 2.84 (1 H, br s, NH), 3.23 (1 H, ddd, J_{4-3} = 7.5, 6.8, and J_{4-5} = 7.9 Hz, 4-H), 3.76 (3 H, s, 2-COOMe), 3.91 (1 H, dd, J_{2-3} = 8.7 and 8.3 Hz), 4.42 (1 H, d, J_{5-4} = 7.9 Hz, 5-H), and 7.2–7.4 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 27.02 (*t*-Bu), 33.58 (3-C), 49.66 (4-C), 51.59 (COOMe), 59.32 (2-C), 65.05 (5-C), 79.91 (*t*-Bu), 126.83, 127.59, 139.04 (Ph), 171.35, and 173.16 (COOMe and COOBu-*t*); MS, m/z (rel intensity) 305 (M^+, 26), 249 (15), 248 (51), 246 (42), 232 (29), 190 (base peak), 177 (99), 172 (21), 146 (38), 145 (34), 144 (53), 117 (99), 91 (23), and 57 (37). Anal. Calcd for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.95; H, 7.58; N, 4.74.

2f: colorless liquid (column chromatography, chloroform); IR (neat) 3380 and 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.22 (3 H, d, J_{Me-3} = 6.7 Hz, 3-Me), 2.66 (1 H, br s, NH), 2.70 (1 H, ddq, J_{3-Me} = 6.7, J_{3-2} = 8.6, and J_{3-4} = 8.0 Hz, 3-H), 2.99 (1 H, dd, J_{4-3} = 8.0 and J_{4-5} = 8.3 Hz, 4-H), 3.18 (3 H, s, 4-COOMe), 3.51 (1 H, d, J_{2-3} = 8.6 Hz, 2-H), 3.77 (3 H, s, 2-COOMe), 4.58 (1 H, d, J_{5-4} = 8.3 Hz, 5-H), and 7.24 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 17.82 (q, 3-Me), 41.41 (d, 3-C), 51.24, 52.24 (each q, COOMe), 58.36 (d, 4-C), 64.42 (d, 2-C), 67.36 (d, 5-C), 127.13, 127.77, 128.36 (each d, Ph), 140.30 (s, Ph), 172.48, and 173.83 (each s, COOMe); MS, m/z (rel intensity) 277 (M^+, 16), 218 (base peak), 177 (70), 158 (64), 117 (87), and 91 (22); HRMS calcd for $C_{15}H_{19}NO_4$ (M) 277.1311, found m/z 277.1311.

2g: colorless needles (column chromatography, chloroform; crystallization, chloroform–hexane); mp 64–65 °C; IR (KBr) 3380 and 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.73 (1 H, br s, NH), 3.10 (3 H, s, 4-COOMe), 3.49 (1 H, dd, J_{4-3} = 7.3 and J_{4-5} = 8.8 Hz, 4-H), 3.65 (3 H, s, 2-COOMe), 3.86 (1 H, dd, J_{3-2} = 9.0 and J_{3-4} 7.3 Hz, 3-H), 4.03 (1 H, d, J_{2-3} = 9.0 Hz, 2-H), 4.81 (1 H, d, J_{5-4} = 8.8 Hz, 5-H), and 7.24 (10 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 51.36, 52.36 (each q, COOMe), 52.24 (d, 3-C), 59.00 (d, 4-C), 65.42 (d, 2-C),

67.89 (d, 5-C), 127.24, 127.36, 127.89, 128.42, 128.95 (each d, Ph), 139.36, 140.36 (each s, Ph), 172.18, and 173.30 (each s, COOMe); MS, m/z (rel intensity) 339 (M^+, 16), 280 (33), 220 (20), 177 (base peak), 117 (48), 85 (26), and 83 (40). Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.36; H, 6.33; N, 4.26.

2h: pale yellow liquid (column chromatography, chloroform); IR (neat) 3350 and 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (3 H, s, Me), 2.06 (1 H, dd, J_{gem} = 13.2 and J_{3-2} = 9.0 Hz, one of 3-H), 2.70 (1 H, dd, J_{gem} = 13.2 and J_{3-2} = 6.9 Hz, the other of 3-H), 2.93 (1 H, br s, NH), 3.17 (3 H, s, 4-COOMe), 3.75 (3 H, s, 2-COOMe), 3.99 (1 H, dd, J_{2-3} = 9.0 and 6.9 Hz, 2-H), 4.00 (1 H, s, 5-H), and 7.22 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 22.24 (q, Me), 41.18 (t, 3-C), 51.00, 51.89 (each q, COOMe), 54.42 (s, 4-C), 58.71 (d, 2-C), 73.71 (d, 5-C), 126.60, 127.71, 128.01 (each d, Ph), 138.72 (s, Ph), 174.13, and 174.60 (each s, COOMe); MS, m/z (rel intensity) 277 (M^+, 22), 218 (24), 177 (64), 158 (35), 118 (22), 117 (base peak), 91 (26), and 90 (30). Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.96; H, 6.91; N, 5.05. Found: C, 64.69; H, 6.85; N, 5.02.

2i: pale orange liquid (column chromatography, chloroform–diethyl ether (4:1 vol/vol)); IR (neat) 3360, 1740, and 1712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.53 (3 H, s, COMe), 2.2–2.4 (2 H, m, 3-H), 2.65 (1 H, br s, NH), 3.42 (1 H, ddd, J_{4-3} = 7.5, 5.7, and J_{4-5} = 7.9 Hz, 4-H), 3.79 (3 H, s, 2-COOMe), 3.94 (1 H, dd, J_{2-3} = 8.7 and 7.4 Hz, 2-H), 4.53 (1 H, d, J_{5-4} = 7.9 Hz, 5-H), and 7.24 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 30.94 (COMe), 33.00 (3-C), 52.30 (COOMe), 56.71 (4-C), 59.89 (2-C), 66.24 (5-C), 127.13, 128.07, 128.83, 138.95 (Ph), 174.07 (COOMe), and 207.84 (COMe); MS, m/z (rel intensity) 247 (M^+, 35), 204 (22), 188 (76), 177 (57), 161 (27), 146 (45), 145 (22), 144 (42), 129 (21), 117 (base peak), and 106 (36); HRMS calcd for $C_{14}H_{17}NO_3$ (M) 247.1207, found m/z 247.1190.

2j: colorless needles (column chromatography, chloroform–diethyl ether (5:1 vol/vol); crystallization, diethyl ether–hexane); mp 64–65 °C; IR (KBr) 3380, 1740, and 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (3 H, d, J_{Me-3} = 6.6 Hz, 3-Me), 1.59 (3 H, s, COMe), 2.71 (1 H, br s, NH), 2.73 (1 H, m, 3-H), 3.10 (1 H, dd, J_{4-3} = 7.7 and J_{4-5} = 8.5 Hz, 4-H), 3.48 (1 H, d, J_{2-3} = 8.3 Hz, 2-H), 3.76 (3 H, s, 2-COOMe), 4.61 (1 H, d, J_{5-4} = 8.5 Hz, 5-H), and 7.23 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 18.18 (q, 3-Me), 30.94 (q, COMe), 41.00 (d, 3-C), 52.18 (q, COOMe), 64.59, 65.65, 67.30 (each d, 2-, 4-, and 5-C), 127.36, 127.95, 128.72 (each d, Ph), 139.95 (s, Ph), 173.77 (s, COOMe), and 208.02 (s, COMe); MS, m/z (rel intensity) 202 (M^+ – 59, 15), 193 (17), 177 (16), 149 (26), 117 (66), 115 (28), 105 (19), 91 (53), 77 (27), 71 (22), 57 (48), 55 (22), 51 (21), and 43 (base peak). Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 69.00; H, 7.29; N, 5.46.

2k: pale yellow liquid (column chromatography, chloroform); IR (neat) 3370, 1735, and 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (3 H, s, COMe), 2.84 (1 H, br s, NH), 3.64 (3 H, s, 2-COOMe), 3.5–3.8, 3.8–4.1 (1 H + 2 H, m, 2-, 3-, and 4-H), 4.83 (1 H, d, J_{5-4} = 8.4 Hz, 5-H), and 7.1–7.4 (10 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 31.36 (q, COMe), 52.06 (q, COOMe), 52.30 (d, 3-C), 65.83 (d, 4-C), 66.00 (d, 2-C), 67.89 (d, 5-C), 127.36, 127.54, 127.89, 128.25, 128.89, 129.07 (each d, Ph), 139.30, 141.36 (each s, Ph), 173.36 (s, COOMe), and 207.78 (s, COMe); MS, m/z (rel intensity) 323 (M^+, 7), 264 (28), 178 (31), 177 (base peak), 118 (20), 117 (82), 116 (29), 91 (22), and 43 (37); HRMS calcd for $C_{20}H_{21}NO_3$ (M) 323.1520, found m/z 323.1509.

2l: colorless needles (column chromatography, chloroform; crystallization, chloroform–hexane); mp 140–141 °C; IR (KBr) 3330, 1735, and 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.26 (3 H, s, *p*-Me), 3.07 (1 H, br s, NH), 3.69 (3 H, s, 2-COOMe), 4.12 (1 H, dd, J_{3-2} = 8.8 and J_{3-4} = 7.3 Hz, 3-H), 4.18 (1 H, d, J_{2-3} = 8.8 Hz, 2-H), 4.50 (1 H, dd, J_{4-3} = 7.3 and J_{4-5} = 8.4 Hz, 4-H), 4.98 (1 H, d, J_{5-4} = 8.4 Hz, 5-H), and 7.0–7.5 (14 H, m, Ar); ^{13}C NMR ($CDCl_3$) δ 21.50 (*p*-Me), 52.11 (COOMe), 52.74 (3-C), 60.33 (4-C), 66.62 (2-C), 67.69 (5-C), 127.04, 127.40, 127.50, 127.63, 127.73, 128.04, 128.17, 128.74, 128.91, 129.24, 135.04, 139.28, 140.80, 143.52 (Ar), 173.37 (COOMe), and 198.15 (COAr); MS, m/z (rel intensity) 400 (M^+ + 1, 3), 340 (7), 177 (60), 119 (69), 117 (base peak), 115 (42), 91 (93), 90 (28), 77 (20), and 65 (33). Anal. Calcd for $C_{26}H_{25}NO_3$: C, 78.17; H, 6.31; N, 3.51. Found: C, 78.02; H, 6.27; N, 3.46.

2m + 2m′. One isomer (**2m′**) was crystallized from the crude reaction mixture on trituration with diethyl ether–hexane. The filtrate was chromatographed over silica gel by using chloroform–diethyl ether (5:1 vol/vol) as an eluent to give pure sample of the other isomer **2m**. **2m**: colorless liquid; IR (neat) 3340, 2230, and 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.3–2.9 (4 H, m, NH, 3- and 4-H), 3.72 (3 H, s, COOMe), 4.02 (1 H, dd, J_{2-3} = 8.0 and 6.0 Hz, 2-H), 4.31 (1 H, d, J_{5-4} = 8.9 Hz, 5-H), and 7.3–7.5 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 34.30 (t, 3-C), 36.47 (d, 4-C), 52.53 (q, COOMe), 58.59 (d, 2-C), 67.30 (d, 5-C), 119.95 (s, CN), 126.83, 128.83, 129.13 (each d, Ph), 139.13 (s, Ph), and 173.90 (s, COOMe); MS, m/z (rel intensity) 230 (M^+, 21), 177 (22), 171 (base peak), 117 (45), and 113 (21); HRMS calcd for $C_{13}H_{14}N_2O_2$ (M) 230.1054, found m/z 230.1061. **2m′**: colorless needles (benzene–hexane); mp 93–94 °C; IR (KBr) 3345, 2245, and 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.4–2.6 (3 H, m, NH and 3-H), 3.23 (1 H, ddd, J_{4-3} = 6.9, 5.7, and J_{4-5} = 6.5 Hz, 4-H), 3.75 (3 H, s, 2-COOMe), 3.92 (1 H, dd, J_{2-3} = 8.0 and 7.2 Hz, 2-H), 4.36 (1 H, d, J_{5-4} = 6.5 Hz, 5-H), and 7.2–7.5 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 34.12 (t, 3-C), 35.94 (d, 4-C), 52.59 (q, COOMe), 58.53 (d, 2-C), 64.71 (d, 5-C), 119.48 (s, CN), 127.19, 128.65, 128.77 (each d, Ph), 137.95 (s, Ph), and 173.19 (s, COOMe); MS, m/z (rel intensity) 230 (M^+, 17), 177 (28), 171 (base peak), 154 (25), 117 (69), and 86 (37). Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.70; H, 6.21; N, 11.97.

3a: colorless prisms (crystallization, benzene–hexane); mp 217–219 °C; IR (KBr) 3320, 1735, 1705, and 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (3 H, s, 2-Me), 2.52 (1 H, br s, NH), 2.77 (3 H, s, NMe), 3.24 (1 H, d, J_{3a-6a} = 7.6 Hz, 3a-H), 3.51 (1 H, dd, J_{6a-3a} = 7.6 and J_{6a-6} = 8.7 Hz, 6a-H), 3.84 (3 H, s, 2-COOMe), 4.72 (1 H, d, J_{6-6a} = 8.7 Hz, 6-H), and 7.26 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 23.83, 24.88 (each q, 2- and *p*-Me), 50.47 (d, 6a-C), 52.71 (q, COOMe), 55.83 (d, 3a-C), 62.24 (s, 4-C), 67.36 (d, 6-C), 127.19, 128.54, 128.65 (each d, Ph), 137.24 (s, Ph), 173.07, 174.89, and 176.07 (each s, COOMe and CON); MS, m/z (rel intensity) 302 (M^+, 7), 243 (base peak), 191 (59), 158 (29), 131 (57), and 57 (25). Anal. Calcd for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.83; H, 6.02; N, 9.17.

3b: colorless prisms (column chromatography, chloroform; crystallization, chloroform–hexane); mp 102–103 °C; IR (KBr) 3365, 1750, 1740, and 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (3 H, s, 2-Me), 2.70 (1 H, br s, NH), 3.13 (3 H, s, 4-COOMe), 3.68, 3.81 (each 3 H, s, 2- and 3-COOMe), 3.8–4.1 (2 H, m, 3- and 4-H), 4.79 (1 H, d, J_{5-4} = 8.7 Hz, 5-H), and 7.25 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 21.18 (q, 2-Me), 51.53, 52.24, 52.95 (each q, COOMe), 52.59 (d, 4-C), 53.95 (d, 3-C), 63.06 (d, 5-C), 67.30 (s, 2-C), 127.48, 128.07, 128.42 (each d, Ph), 139.95 (s, Ph), 171.36, 171.71, and 174.54 (each s, COOMe); MS, m/z (rel intensity) 335 (M^+, 1), 276 (72), 244 (52), 216 (base peak), 191 (33), 184 (37), 177 (41), 158 (23), 157 (21), and 131 (46). Anal. Calcd for $C_{17}H_{21}NO_6$: C, 60.88; H, 6.31; N, 4.18. Found: C, 60.94; H, 6.37; N, 4.18.

3c: colorless liquid (column chromatography, chloroform); IR (neat) 3360 and 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (3 H, s, 2-Me), 2.01 (1 H, dd, J_{gem} = 13.4 and J_{3-4} = 7.6 Hz, one of 3-H), 2.70 (1 H, dd, J_{gem} = 13.4 and J_{3-4} = 5.3 Hz, the other of 3-H), 2.98 (1 H, br s, NH), 3.16 (3 H, s, 4-COOMe), 3.32 (1 H, ddd, J_{4-3} = 7.6, 5.3, and J_{4-5} = 7.6 Hz, 4-H), 3.77 (3 H, s, 2-COOMe), 4.62 (1 H, d, J_{5-4} = 7.6 Hz, 5-H), and 7.23 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 27.65 (q, 2-Me), 40.41 (t, 3-C), 50.65 (d, 4-C), 51.24, 52.59 (each q, COOMe), 65.12 (d, 5-C), 65.95 (s, 2-C), 126.95, 127.42, 128.42 (each d, Ph), 139.30 (s, Ph), 173.30, and 176.89 (each s, COOMe); MS, m/z (rel intensity) 277 (M^+, 1), 218 (base peak), 158 (44), and 131 (44). Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.96; H, 6.91; N, 5.05. Found: C, 65.03; H, 6.96; N, 5.04.

3d: pale yellow liquid (column chromatography, chloroform); IR (neat) 3360 and 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (3 H, d, J_{Me-3} = 6.6 Hz, 3-Me), 1.31 (3 H, s, 2-Me), 2.76 (1 H, s, NH), 2.89 (1 H, dq, J_{3-Me} = 6.6 and J_{3-4} = 11.0 Hz, 3-H), 3.10 (1 H, dd, J_{4-3} = 11.0 and J_{4-5} = 9.2 Hz, 4-H), 3.12 (3 H, s, 4-COOMe), 3.75 (3 H, s, 2-COOMe), 4.64 (1 H, d, J_{5-4} = 9.2 Hz, 5-H), and 7.21 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 13.77 (q, 3-Me), 20.30 (q, 2-Me), 42.71 (d, 3-C), 51.18, 52.47 (each q, COOMe), 57.06 (d, 4-C), 62.42 (d, 5-C), 67.65 (s, 2-C), 127.54, 127.71, 128.25 (each d, Ph), 141.30 (s, Ph), 172.18, and 176.13 (each s, COOMe); MS, m/z (rel intensity) 232 (M^+ – 59, base peak), 172 (48), and 131 (41). Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 66.06; H, 7.29; N, 4.95.

3e: colorless prisms (column chromatography, chloroform; crystallization, chloroform–hexane); mp 52–53 °C; IR (KBr) 3340, 1728, and 1707 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3 H, s, 4-Me), 1.51

(3 H, s, 2-Me), 1.77 (1 H, d, J_{gem} = 13.8 Hz, one of 3-H), 3.04 (1 H, d, J_{gem} = 13.8 Hz, the other of 3-H), 3.21 (1 H, br s, NH), 3.24 (3 H, s, 4-COOMe), 3.79 (3 H, s, 2-COOMe), 4.10 (1 H, s, 5-H), and 7.23 (5 H, s, Ph); ^{13}C NMR ($CDCl_3$) δ 21.71 (q, 4-Me), 29.12 (q, 2-Me), 50.30 (t, 3-C), 51.24, 52.47 (each q, COOMe), 56.12 (s, 4-C), 65.06 (s, 2-C), 73.18 (d, 5-C), 126.65, 128.13, 128.36 (each d, Ph), 137.48 (s, Ph), 175.07, and 177.43 (each s, COOMe); MS, m/z (rel intensity) 291 (M^+, 9), 232 (46), 191 (83), 172 (31), 131 (base peak), 130 (24), and 90 (23). Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 65.71; H, 7.30; N, 4.86.

3f + 3f'. One isomer (**3f'**) was crystallized from the crude reaction mixture on trituration with diethyl ether–hexane. The filtrate was chromatographed over silica gel by using chloroform as an eluent to give the other isomer **3f**. **3f**: colorless liquid; IR (neat) 3380, 2250, and 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.52 (3 H, s, 2-Me), 2.11 (1 H, m, one of 3-H), 2.45 (1 H, br, NH), 2.7–3.0 (2 H, m, 4-H and the other of 3-H), 3.74 (3 H, s, 2-COOMe), 4.44 (1 H, d, J_{5-4} = 9.0 Hz, 5-H), and 7.36 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 26.35 (q, 2-Me), 37.65 (d, 4-C), 42.06 (t, 3-C), 52.89 (q, COOMe), 65.06 (s, 2-C), 66.59 (d, 5-C), 119.71 (s, CN), 126.77, 128.77, 129.13 (each d, Ph), 139.30 (s, Ph), and 176.25 (s, COOMe); MS, m/z (rel intensity) 244 (M^+, 4), 185 (base peak), 131 (72), 130 (27), 104 (26), 51 (22), and 31 (21); HRMS calcd for $C_{14}H_{16}N_2O_2$ (M) 244.1210, found m/z 244.1200. **3f'**: colorless prisms (benzene–hexane); mp 137–138 °C; IR (KBr) 3185, 2230, and 1723 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.45 (3 H, s, 2-Me), 2.15 (1 H, dd, J_{gem} = 13.7 and J_{3-4} = 7.6 Hz, one of 3-H), 2.81 (1 H, dd, J_{gem} = 13.7 and J_{3-4} = 3.2 Hz, the other of 3-H), 2.96 (1 H, br s, NH), 3.26 (1 H, ddd, J_{4-3} = 7.6, 3.2, and J_{4-5} = 5.9 Hz, 4-H), 3.76 (3 H, s, 2-COOMe), 4.49 (1 H, d, J_{4-5} = 5.9 Hz, 5-H), and 7.36 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 26.59 (q, 2-Me), 37.06 (d, 4-C), 41.20 (t, 3-C), 52.59 (q, COOMe), 63.59 (d, 5-C), 64.48 (s, 2-C), 119.07 (s, CN), 126.89, 128.30, 128.54 (each d, Ph), 137.83 (s, Ph), and 175.78 (s, COOMe); MS, m/z (rel intensity) 244 (M^+, 1) and 185 (base peak). Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 69.06; H, 6.68; N, 11.28.

4: pale yellow liquid (column chromatography, chloroform); IR (neat) 3360, 1730, and 1725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92, 1.01 (each 3 H, d, J = 6.7 Hz, i-Pr), 1.27 (3 H, s, 4-Me), 1.92 (1 H, m, i-Pr), 1.95, 2.93 (each 1 H, d, J_{gem} = 14.2 Hz, 3-H), 3.16 (1 H, br s, NH), 3.24 (3 H, s, 4-COOMe), 3.80 (3 H, s, 2-COOMe), 3.97 (1 H, s, 5-H), and 7.23 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 17.47, 18.24 (each q, i-Pr), 21.30 (q, 4-Me), 37.71 (d, i-Pr), 46.77 (t, 3-C), 51.12, 52.06 (each q, COOMe), 55.83 (s, 4-C), 72.53 (s, 2-C), 74.95 (d, 5-C), 126.54, 128.13, 128.42 (each d, Ph), 137.89 (s, Ph), 175.13, and 176.89 (each s, COOMe); MS, m/z (rel intensity) 319 (M^+, 14), 276 (88), 260 (base peak), 219 (61), 216 (20), 159 (82), 158 (21), 144 (26), 117 (24), 91 (25), and 41 (20); HRMS calcd for $C_{18}H_{25}NO_4$ (M) 319.1782, found m/z 319.1787.

5a: colorless needles (column chromatography, chloroform; crystallization, chloroform–hexane); mp 119–120 °C; IR (KBr) 3290, 1730, and 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.8–2.0 (4 H, m, py), 2.1–2.4 (2 H, m, 3-H), 3.19 (3 H, s, 4-COOMe), 3.33 (1 H, s, NH), 3.3–3.7 (5 H, m, py and 4-H), 3.97 (1 H, dd, J_{2-3} = 9.1 and 7.5 Hz, 2-H), 4.55 (1 H, d, J_{5-4} = 8.3 Hz, 5-H), and 7.1–7.3 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 24.06, 26.12, 46.06, 46.18 (each t, py), 33.06 (t, 3-C), 51.00 (d, 4-C), 51.24 (q, COOMe), 60.12 (d, 2-C), 65.77 (d, 5-C), 127.19, 127.66, 128.30 (each d, Ph), 139.66 (s, Ph), 170.66, and 172.95 (each s, COOMe and CON); MS, m/z (rel intensity) 302 (M^+, 2), 204 (73), 144 (base peak), 117 (43), 116 (23), 91 (26), 56 (29), and 41 (26). Anal. Calcd for $C_{17}H_{22}N_2O_3$: C, 67.53; H, 7.33; N, 9.27. Found: C, 67.34; H, 7.27; N, 9.09.

5b: colorless prisms (column chromatography, chloroform; crystallization, chloroform–hexane); mp 147–148 °C; IR (KBr) 3350, 1740, and 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.14 (3 H, d, J_{Me-3} = 6.2 Hz, 3-Me), 1.8–2.0 (4 H, m, py), 2.7–3.2 (3 H, m, NH, 3- and 4-H), 3.16 (3 H, s, 4-COOMe), 3.4–3.7 (5 H, m, py and 2-H), 4.60 (1 H, d, J_{5-4} = 8.8 Hz, 5-H), and 7.2–7.5 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 16.65 (q, 3-Me), 24.12, 26.12, 46.30, 46.83 (each t, py), 42.65 (d, 3-C), 51.18 (q, COOMe), 59.00 (d, 4-C), 65.00, 66.89 (each d, 2- and 5-C), 127.48, 127.71, 128.36 (each d, Ph), 140.60 (s, Ph), 170.71, and 172.31 (each s, COOMe and CON); MS, m/z (rel intensity) 316 (M^+, 4), 219 (16), 218 (base peak), 158 (14), 117 (14), 91 (11), and 56 (11). Anal. Calcd for $C_{18}H_{24}N_2O_3$: C, 68.33; H, 7.65; N, 8.85. Found: C, 68.15; H, 7.65; N, 8.98.

5c: colorless needles (column chromatography, chloroform; crystallization, chloroform–hexane); mp 151–152 °C; IR (KBr) 3360, 1725, and 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.48 (3 H, s, 4-Me), 1.8–2.0 (4 H, m, py), 2.00 (1 H, dd, J_{gem} = 12.7 and J_{3-2} = 7.7 Hz, one of 3-H), 2.57 (1 H, dd, J_{gem} = 12.7 and J_{3-2} = 9.3 Hz, the other of 3-H), 3.17 (3 H, s, 4-COOMe), 3.32 (1 H, s, NH), 3.4–3.6 (4 H, m, py), 4.02 (1 H, dd, J_{2-3} = 9.3 and 7.7 Hz, 2-H), 4.05 (1 H, s, 5-H), and 7.2–7.4 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 23.83 (q, 4-Me), 24.12, 26.12, 46.06, 46.18 (each t, py), 41.47 (t, 3-C), 51.36 (q, COOMe), 56.36 (s, 4-C), 59.24 (d, 2-C), 74.12 (d, 5-C), 127.13, 127.83, 128.25 (each d, Ph), 139.71 (s, Ph), 170.95, and 175.07 (each s, COOMe and CON); MS, m/z (rel intensity) 316 (M^+, 5), 219 (15), 218 (base peak), 216 (37), 158 (38), and 117 (21).

Separation of 6 and 7. The crude product which was obtained according to the above general procedure was first weighed and submitted to ^{1}H NMR measurement to determine the yield of **6** and **7**. Then the mixture was chromatographed over silica gel by using chloroform–diethyl ether (5:1 vol/vol) to give **6**. The Michael adduct **7** mostly decomposed during this chromatographic operation, only **7a** having been partly isolated.

6a: colorless needles (chloroform–hexane); mp 102–103 °C; IR (KBr) 3330, 3300, 1735, and 1655 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40 (9 H, s, t-Bu), 2.2–2.6 (3 H, m, NH and 3-H), 3.15 (3 H, s, 4-COOMe), 3.20 (1 H, m, 4-H), 3.73 (1 H, dd, J_{2-3} = 8.6 and 7.8 Hz, 2-H), 4.61 (1 H, d, J_{5-4} = 8.1 Hz, 5-H), 7.27 (5 H, s, Ph), and 7.33 (1 H, m, CONH); ^{13}C NMR ($CDCl_3$) δ 28.77 (q, t-Bu), 32.77 (t, 3-C), 49.30 (d, 4-C), 50.42 (s, t-Bu), 51.18 (q, COOMe), 60.77 (d, 2-C), 64.89 (d, 5-C), 127.19, 127.83, 128.25 (each d, Ph), 140.42 (s, Ph), 172.83, and 173.54 (each s, COOMe and CONH); MS, m/z (rel intensity) 304 (M^+, 6), 205 (14), 204 (base peak), 203 (26), 145 (11), 144 (50), 143 (12), 117 (16), 57 (31), 56 (14), and 43 (12). Anal. Calcd for $C_{17}H_{24}N_2O_3$: C, 67.08; H, 7.95; N, 9.20. Found: C, 67.27; H, 8.11; N, 9.13.

6b: colorless prisms (chloroform–hexane); mp 121–122 °C; IR (KBr) 3350, 3290, 1740, and 1655 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.25 (3 H, d, J_{Me-3} = 6.6 Hz, 3-Me), 1.38 (9 H, s, t-Bu), 2.50 (1 H, br s, NH), 2.56 (1 H, ddq, J_{3-Me} = 6.6, J_{3-2} = 8.0, and J_{3-4} = 7.5 Hz, 3-H), 2.88 (1 H, dd, J_{4-3} = 7.5 and J_{4-5} = 8.7 Hz, 4-H), 3.15 (3 H, s, 4-COOMe), 3.25 (1 H, d, J_{2-3} = 8.0 Hz, 2-H), 4.62 (1 H, d, J_{5-4} = 8.7 Hz, 5-H), and 7.25 (6 H, s, Ph and CONH); ^{13}C NMR ($CDCl_3$) δ 18.71 (q, 3-Me), 28.71 (q, t-Bu), 41.00 (d, 3-C), 50.30 (s, t-Bu), 51.06 (q, COOMe), 57.77 (d, 4-C), 62.89 (d, 2-C), 68.06 (d, 5-C), 127.24, 127.60, 128.07 (each d, Ph), 141.07 (s, Ph), 172.13, and 172.83 (each s, COOMe and CONH); MS, m/z (rel intensity) 318 (M^+, 3), 219 (15), 218 (base peak), and 158 (11). Anal. Calcd for $C_{18}H_{26}N_2O_3$: C, 67.89; H, 8.23; N, 8.80. Found: C, 67.81; H, 8.25; N, 8.82.

7a: colorless liquid; IR (neat) 3380, 1740, and 1670 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35 (9 H, s, t-Bu), 2.1–2.5 (4 H, m, CH_2), 3.56 (3 H, COOMe), 3.74 (1 H, m, CH), 6.62 (1 H, br s, NH), 7.4–7.5, 7.7–7.9 (3 H + 2 H, m, Ph), and 8.17 (1 H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ 28.83 (q, t-Bu), 30.18, 30.47 (each t, CH_2), 50.83 (s, t-Bu), 51.53 (q, COOMe), 73.06 (d, NCH), 128.54, 128.95, 131.66 (each d, Ph), 135.66 (s, Ph), 162.89 (d, CH=N), 171.54, and 173.48 (each s, COOMe and CONH); MS, m/z (rel intensity) 304 (M^+, 2), 273 (14), 205 (56), 204 (base peak), 201 (91), 144 (45), 132 (66), 128 (26), 104 (28), and 58 (21); HRMS calcd for $C_{17}H_{24}N_2O_3$ (M) 304.1786, found m/z 304.1790.

7b. Separation of pure **7b** by column chromatography was unsuccessful. Its formation as a mixture of two diastereomers was indicated stereoscopically. ^{1}H NMR ($CDCl_3$) δ 1.00, 1.04 (3 H, each d, Me), 1.37, 1.40 (9 H, each s, t-Bu), 1.8–2.8 (3 H, m, CH_2 and CH), 3.60 (3 H, s, COOMe), 3.6–3.7 (1 H, m, NCH), 6.53 (1 H, m, NH), 7.3–7.4, 7.6–7.7 (3 H + 2 H, m, Ph), 8.05, and 8.07 (1 H, each br s, CH=N); ^{13}C NMR ($CDCl_3$) δ 15.41, 16.41 (each Me), 28.88 (t-Bu), 35.18, 35.59 (each CH_2), 37.18, 38.47 (each CHMe), 51.00, 51.47 (COOMe and t-Bu), 77.30, 77.89 (each NCH), 128.42, 128.59, 129.01, 131.60, 135.78 (Ph), 163.01, 163.42 (each CH=N), 170.95, and 173.54 (COOMe and CON).

Thermal Cycloaddition of 1a to Methyl Acrylate Leading to 2d + 2d' + 2d'' + Others. A mixture of **1a** (0.72 g, 4 mmol) and methyl acrylate (1.92 g, 22 mmol) was heated under reflux for 24 h. The excess acrylate was removed in vacuo and the residue was chromatographed over silica gel with chloroform–diethyl ether (4:1 vol/vol) to give **2d'** (0.165 g, 16%), **2d''** (0.041 g, 4%), and then **2d** (0.311 g, 29%). Characterization of **2d** was already made above.

2d': pale yellow liquid; IR (neat) 3360 and 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.1–2.8 (2 H, m, 3-H), 2.34 (1 H, br s, NH), 3.18 (3 H, s, 4-COOMe), 3.33 (1 H, dd, J_{4-3} = 5.6 and J_{4-5} = 7.8 Hz, 4-H), 3.73 (3 H, s, 2-COOMe), 4.27 (1 H, dd, J_{2-3} = 8.7 and 4.4 Hz, 2-H), 4.70 (1 H, d, J_{5-4} = 7.8 Hz, 5-H), and 7.22 (5 H, br s, Ph); ^{13}C NMR ($CDCl_3$) δ 32.12 (t, 3-C), 49.42 (d, 4-C), 51.24, 52.30 (each q, COOMe), 59.30 (d, 2-C), 64.53 (d, 5-C), 127.07, 127.66, 128.18 (each d, Ph), 140.30 (s, Ph), 173.12, and 176.03 (each s, COOMe); MS, m/z (rel intensity) 263 (M^+, 36), 204 (base peak), 177 (32), 145 (13), 144 (50), and 117 (46); HRMS calcd for $C_{14}H_{17}NO_4$ (M) 263.1157, found m/z 263.1150.

2d'': pale yellow liquid; IR (neat) 3350 and 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.2–2.4 (2 H, m, 3-H), 2.38 (1 H, br s, NH), 2.91 (1 H, dt, J_{4-3} = 9.0, 8.3, J_{4-5} = 8.3 Hz, 4-H), 3.59 (3 H, s, 4-C), 3.73 (3 H, s, 2-COOMe), 4.01 (1 H, dd, J_{2-3} = 8.0 and 6.2 Hz, 2-H), 4.40 (1 H, d, J_{5-4} = 8.3 Hz, 5-H), and 7.2–7.5 (5 H, m, Ph); ^{13}C NMR ($CDCl_3$) δ 34.59 (t, 3-C), 51.36 (d, 4-C), 52.00, 52.36 (each q, COOMe), 59.42 (d, 2-C), 66.83 (d, 5-C), 127.07, 128.01, 128.83 (each d, Ph), 141.42 (s, Ph), 174.07, and 174.84 (each s, COOMe); MS, m/z (rel intensity) 263 (M^+, 29), 204 (base peak), 177 (49), 145 (12), 144 (49), and 117 (40); HRMS calcd for $C_{14}H_{17}NO_4$ (M) 263.1157, found m/z 263.1157.

Chiral Synthesis via Organoboranes. 17. Preparation of α-Chiral α'-Alkynyl Ketones of High Enantiomeric Excess from Optically Pure Organyl(1-alkynyl)borinic Esters

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Optically pure alkynylborinic esters R*BC≡CR''(OR') are cleanly obtained at low temperatures from optically pure boronic esters R*B(OR')$_2$ and a lithium acetylide followed by treatment of the "ate" complex LiR*BC≡CR''(OR')$_2$ with ethereal hydrogen chloride. These borinic esters react with α,α-dichloromethyl methyl ether, DCME, in the presence of a hindered base to yield, after hydrogen peroxide oxidation, α-chiral α'-alkynyl ketones R*COC≡CR'' which exhibit the same high enantio- and stereoselectivity of the chiral boronic esters. β-Heterosubstituted (1-alkynyl)borinic esters, such as $\overline{CH_2OCH_2CH_2}CBC{\equiv}CR''(OR')$, despite their sensitivity to elimination reactions, can be similarly converted into the corresponding ketones in excellent yields. This development considerably expands the range of applicability of the "DCME" reaction.

Alkynyl ketones in general and optically active alkynyl ketones in particular are potentially interesting intermediates for the synthesis of natural products.[1] α-Chiral α'-alkynyl ketones have been prepared from optically active acyl halides and alkynes in the presence of cuprous iodide and $Pd(PPh_3)_2Cl_2$.[2] α-Chiral-amino α'-alkynyl ketones have been similarly obtained from α-amino acid derivatives and metalloacetylides.[3] However, these methods, in addition to involving considerable racemization in certain cases, are not general and are seriously restricted by the availability of the starting carboxylic acid unit. Organoborane routes to 1-alkynyl ketones include reaction of a lithium acetylide with a carboxylic acid anhydride in the presence of boron trifluoride etherate,[4a] hydroboration sequences with thexylborane,[4b] selective hydroboration of conjugated diynes with dialkylboranes,[4c] and reaction of iodine with "ate" complexes obtained from lithium organylacetylides and triorganylboranes.[4d] These methods, however, do not lend themselves readily to the synthesis of optically active 1-alkynyl ketones. Our approach to the preparation of these ketones is based on chiral organoboron chemistry.

Chiral organoboranes have emerged as an important class of asymmetric reagents for the preparation of a variety of compounds, usually with very high enantiomeric excess.[5] Among chiral organoboranes, optically pure boronic esters[6] are particularly suited for carbon–carbon bond-forming reactions[7] with elaboration into useful organic compounds.[8] Recently we have used optically pure boronic esters in a general synthesis of enantiomerically pure α-chiral acyclic ketones.[9] We have now extended our studies and report our results on the preparation of the title compounds via the "DCME" reaction of chiral (1-alkynyl)borinic esters.[10]

Results and Discussion

We have previously demonstrated that lithium acetylides react with boronic esters in a reversible manner, low temperatures favoring the formation of the ate complex (eq 1).[10]

$$R^*B(OR')_2 + LiC{\equiv}CR'' \underset{\text{room temperature}}{\overset{-78\ ^\circ C}{\rightleftharpoons}} LiR^*BC{\equiv}CR''(OR')_2 \quad (1)$$

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