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Michael Addition and Alkylation of 2-Azaallyl Anions Derived from *N*-(1-Cyanoalkyl)imines, and Stereoselective Cyclization of Imine Esters or Ketones Leading to 1-Pyrrolines

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The 2-azaallyl anions derived from *N*-(1-cyanoalkyl)imines and DBU undergo Michael addition or alkylation to produce *N*-(1-alkylated 1-cyanoalkyl)imines. The Michael addition of some aryl-substituted imines are highly diastereoselective. The alkylated Michael adducts are converted into lactams through a hydrolysis and recyclization sequence. Base-induced cyclization furnishes 1-pyrrolines through a cyclization and HCN elimination sequence. In the latter reaction, 4,5-*cis*-1-pyrrolines are selectively produced when the adducts are treated with LDA in the presence of lithium iodide.

Deprotonation of imines adjacent to the nitrogen generates 2-azaallyl anions, while prior *N*-protonation or *N*-alkylation leads to azomethine ylides. These two anionic species are conplementary in organic synthesis: 2-Azaallyl anions undergo either nucleophilic addition to electrophilic multiple bonds or cycloaddition with nonactivated olefins,[1] while azomethine ylides react only with electron-poor activated olefins affording cycloadducts.[2] Recently both azomethine ylide and 2-azaallyl anion species have been generated by a separated procedure using a common precursor and their reactions with electron-poor olefins showed reverse regioselectivity, synthetic value of the precursor being increased.[3]

Deprotonation of the imines of 2-amino esters occurs readily to generate ester-stabilized 2-azaallyl anions. Reaction of the anions with Michael acceptors or alkylating agents followed by hydrolysis is one of the most important preparation method of 2-alkylated 2-amino acids.[4] Compared to the broad applications of the imines of 2-amino esters, synthetic utilization of the imines of 2-amino nitriles is quite limited.[5]

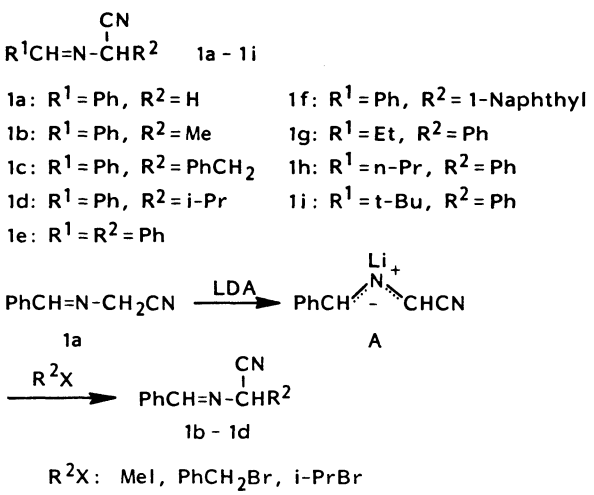
We have continued to study on the synthetic utility of the imines of 2-amino nitriles. The most important reaction on these imines must be its thermal tautomerization generating *N*-protonated azomethine ylides of cyano-stabilized types.[6] These ylides are found to be useful synthetic equivalents of non-stabilized nitrile ylides through a cycloaddition and HCN elimination sequence.

The present article deals with the chemistry of 2-azaallyl anions which can be generated by deprotonation of *N*-(1-cyanoalkyl)imines. Michael additions as well as alkylation reactions using these anions are investigated. Cyclization reactions of the Michael adducts and alkylated products lead to a variety of nitrogen heterocycles. Some of these conversions can be carried out in a stereoselective fashion.

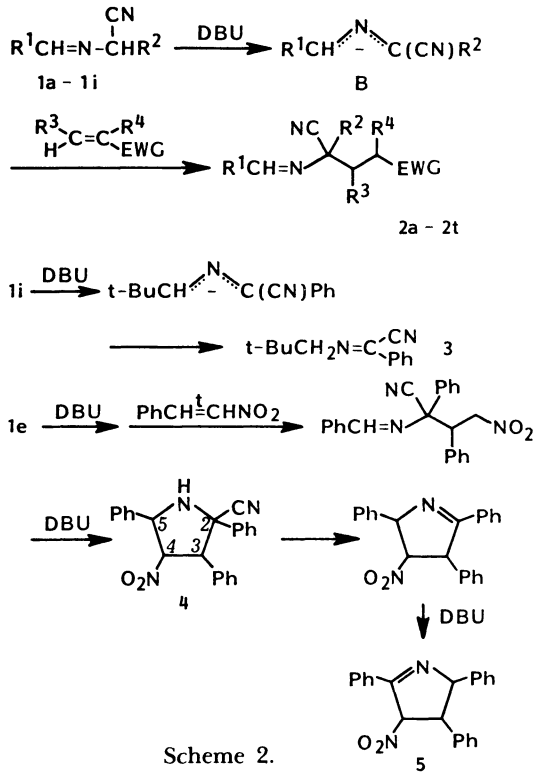
Results and Discussion

Michael Addition and Alkylation of *N*-(1-Cyanoalkyl)imines. *N*-(1-Cyanoalkyl)imines **1** are available by condensation of 2-amino nitriles with carbonyl compounds (Scheme 1). Among these imines **1a** is most easily accessible from aminoacetonitrile and benzaldehyde. Treating **1a** with LDA in THF at −78 °C forms the anion **A** and it can be smoothly alkylated with methyl iodide, benzyl bromide, or isopropyl bromide all in excellent yields. Accordingly the alkylation of **1a** is the most easy access to the alkylated derivatives **1b—1d**. Other imines **1e—1i** were prepared by the reactions of α-aminophenylacetonitrile or α-amino-(1-naphthyl)acetonitrile with the corresponding aldehydes.

N-(1-Cyanoalkyl)imines **1a—1i** generate the corresponding 2-azaallyl anions **B** when treated with DBU in THF at −78 °C and undergo Michael additions to a variety of electron-deficient olefins such



Scheme 1.



Scheme 2.

as methyl and *t*-butyl acrylates, 3-buten-2-one, acrylonitrile, methyl crotonate, and methyl α-silylacrylate, and (*E*)-β-nitrostyrene (Scheme 2 and Table 1). Acrylates, 3-buten-2-one, and acrylonitrile which carry a sterically less hindered β-carbon smoothly reacted with the anions **B** (R^1=Ph, R^2=$PhCH_2$ or *i*-Pr) derived from imines **1c** and **1d** bearing a bulky alkyl moiety on the carbon. However, these anions showed only decreased reactivity toward methyl crotonate even under harder conditions probably due to a steric hindrance.

The anion **B** (R^1=Ph, R^2=H) from **1a** is very reactive to methyl acrylate to furnish a Michael adduct. This adduct can be again deprotonated to form the anion **B** (R^2=CH_2CH_2COOMe) which can react with the second molecule of the acrylate, frequently yielding a mixture of 1:1 and 1:2 Michael adducts.

Though 2-azaallyl anions **B** have two nucleophilic sites, all the Michael additions took place regioselectively at the carbon substituted by CN. These high selectivity presumably resulted from the anion-stabilizing ability of sterically small CN group.

The anion **B** (R^1=*t*-Bu, R^2=Ph) from **1i** was found

Table 1. Michael Addition of *N*-(1-Cyanoalkyl)imines **1a**—**1i** to Electron-Deficient Olefins Leading to **2a**—**2t** and **3**—**5**[a]

Acceptor	Donor	DBU (equiv)	Time/h (−78 °C→rt)	Product	R^1	R^2	R^3	R^4	EWG	Yield/%[b]	Isomer ratio[c]
CH_2=CHCOOMe	**1b**	0.5	0.5→1	**2a**	Ph	Me	H	H	COOMe	100	—
	1c	0.5	0.5→15	**2b**	Ph	$PhCH_2$	H	H	COOMe	71	—
	1d	0.5	0.5→17	**2c**	Ph	*i*-Pr	H	H	COOMe	74	—
	1e	0.5	0.5→1	**2d**	Ph	Ph	H	H	COOMe	92	—
	1g	1.1	0.2→0.5	**2e**	Et	Ph	H	H	COOMe	100	—
CH_2=CHCOOBu^t	**1b**	1.1	0.2→3	**2f**	Ph	Me	H	H	COOBu^t	95	—
CH_2=CHCOMe	**1c**	0.5	0.5→15	**2g**	Ph	$PhCH_2$	H	H	COMe	88	—
	1e	0.5	0.5→1	**2h**	Ph	Ph	H	H	COMe	90	—
	1g	1.1	0.2→0.7	**2i**	Et	Ph	H	H	COMe	100	—
CH_2=CHCN	**1e**	0.5	0.5→1	**2j**	Ph	Ph	H	H	CN	73	—
	1g	1.1	1→3	**2k**	Et	Ph	H	H	CN	95	—
MeCH=^{t}CHCOOMe	**1a**	0.5	0.5→22	**2l**	Ph	H	Me	H	COOMe	78	1:1
	1b	0.5	2→0	**2m**	Ph	Me	Me	H	COOMe	95	3:2
	1b	1.1	1→14	**2m**						82	3:1
	1c	0.5	0.5→15	No reaction[d]							
	1c	0.5	8 (reflux)	**2n**	Ph	$PhCH_2$	Me	H	COOMe	92	1:1
	1d	0.5	10 (reflux)	No reaction[d]							
	1e	0.5	1→8	**2o**	Ph	Ph	Me	H	COOMe	81	single
	1f	0.5	1→8	**2p**	Ph	1-Nph	Me	H	COOMe	81	single
	1g	0.5	2.5→0	**2q**	Et	Ph	Me	H	COOMe	95	single
	1h	0.8	2.5→0	**2r**	*n*-Pr	Ph	Me	H	COOMe	91	single
	1i	0.5	2.5→0	**3**						100	—
CH_2=C(TMS)COOMe	**1e**	0.1	0.5→1	**2s**	Ph	Ph	H	TMS	COOMe	97	single
	1g	0.1	1→1.5	**2t**	Et	Ph	H	TMS	COOMe	100	mixture
PhCH=^{t}CHNO$_2$	**1e**	1.0	0→3	**4**+**5**						**4**:11	
										5:83	

a) All reactions were carried out in THF by using each one equivalent amount of **1** and an olefin. b) Yield of isolated products. c) Isomer ratio was determined by ^{1}H NMR spectrum. d) The starting imine was recovered intact.

inactive. It was quenched to form quantitatively a double bond-migrated imine **3** (Scheme 2). Cyclization products **4** and **5** of the Michael adducts were produced (**4**: 11%, **5**: 83%), both as single stereoisomers, in the reaction of the anion **B** (R^1=R^2=Ph) derived from **1e** with (*E*)-β-nitrostyrene. Elimination of HCN and subsequent double bond migration of pyrrolidine **4** would be a route leading to 1-pyrroline **5**. Strong electron-withdrawing property of the nitro group should be responsible for the instability of the Michael adduct.

It was surprising that the anions **B** bearing an aryl group as R^2 underwent stereoselective Michael additions to methyl crotonate to produce single diastereomers **2o—2r**, while reactions of other anions bearing an aliphatic R^2 are nonregioselective (Table 1).

These stereoselective adducts **2o**, **2q**, and **2r** were converted into the same 2-pyrrolidinone **6** as a single stereoisomer through hydrolytic cyclization (Scheme 3). This compound **6** was assigned to be an isomer in which 4-Me and 5-Ph are cis to each other on the basis of spectral data. For instance irradiation at the 4-Me (δ=1.24) resulted in a 13% of NOE enhancement of the 5-Ph. A similar hydrolytic cyclocondensation of **2p** produced **7** also as a single isomer.

On the other hand diastereomeric mixtures **21** (1:1) and **2m** (3:1) gave stereoisomeric mixtures of 2-pyrrolines **8** (1:1) and **9** (2.8:1), respectively. The major isomer of **9** was assigned to be cis, and minor one trans, on the basis of the ^{1}H chemical shifts of 4-Me and 5-Me (cis: δ=1.13 and 1.51; trans: 1.30 and 1.63) as well as the ^{13}C chemical shifts of 4-Me, 5-Me, 4-C, 5-C, and CN (cis: δ=14.30q, 21.24q, 38.94d, 55.89s, and 121.54s; trans: 15.00q, 24.76q, 41.36d, 59.06s, and 119.36s).

Stereoselectivity in the Michael addition of 2-azaallyl anions **B** is most likely to depend upon the electronic nature of R^2 substituent; Steric effect of R^2 is not important. We believe that there exists an attractive interaction between the aryl of 2-azaallyl anions **B** and the ester of methyl crotonate in the transition state.[7] As shown in Fig. 1, there are two possible approaches **C** and **C'** in which the ester is effectively overlapping with the aryl plane. The approach **C'** is more crowded between the methyl and the imine part so that the approach **C** leading to **2o—2r** becomes more favored. When R^2 is alkyl group no such attractive interaction exists. Neither of the two

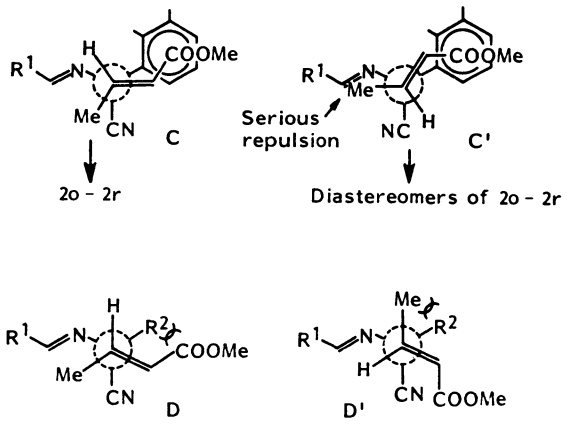
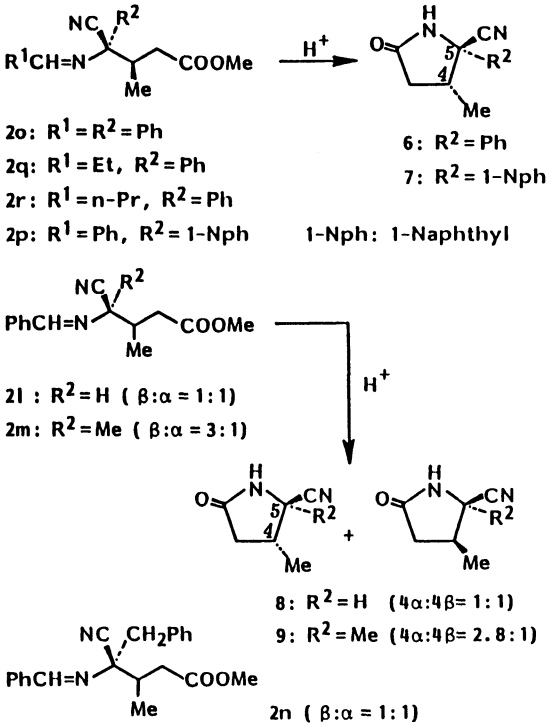
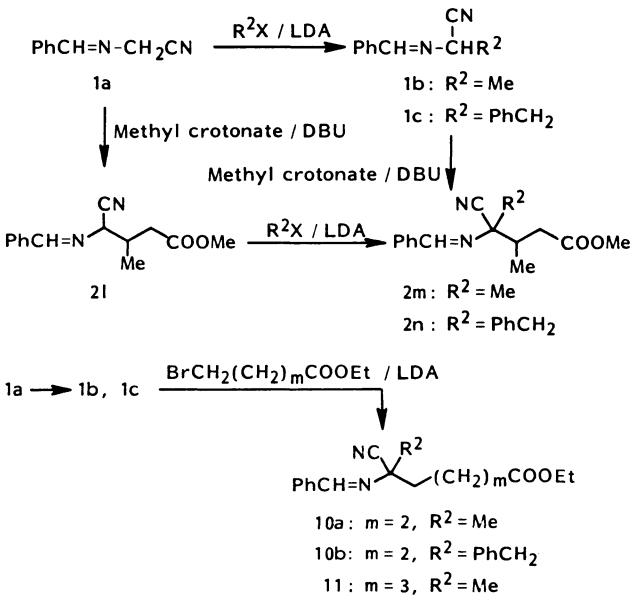


Fig. 1. Stereoselective Michael additions of aryl-substituted imines **1e—1g** with methyl crotonate.



Scheme 3.



Scheme 4.

most likely approaches **D** and **D'** can find sterical predominance over the other. Accordingly the Michael additions become non-stereoselective, two diastereomers of Michael adducts being formed.

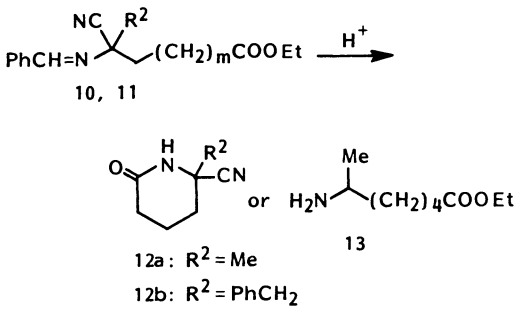
As described above two alkyl substituents can be introduced to α-(benzylideneamino)acetonitrile (**1a**) by two sequential alkylations using an alkyl halide/LDA and then a Michael acceptor/DBU (Scheme 4, **1a**, **1b**, **1c**, **2m**, **2n**). On the other hand the Michael addition of **1a** can be followed by the alkylation with an alkyl halide. For example **1a** was first allowed to react with methyl crotonate to afford a Michael adduct **21** which was then alkylated with methyl iodide or benzyl bromide to give the same dialkylated products **2m** and **2n** (Table 2).

Alkylation of **1** by the Michael addition route using α,β-unsaturated esters leads to 4-amino esters **2**. 6-Amino as well as 5-amino esters are also available when imines **1** are alkylated with ω-halo esters as alkylating agents (Scheme 4). Thus **1a** was first methylated or benzylated into **1b** or **1c**, and then alkylated with ethyl 4-bromobutanoate or 5-bromopentanoate to produce **10a**, **10b**, or **11**.

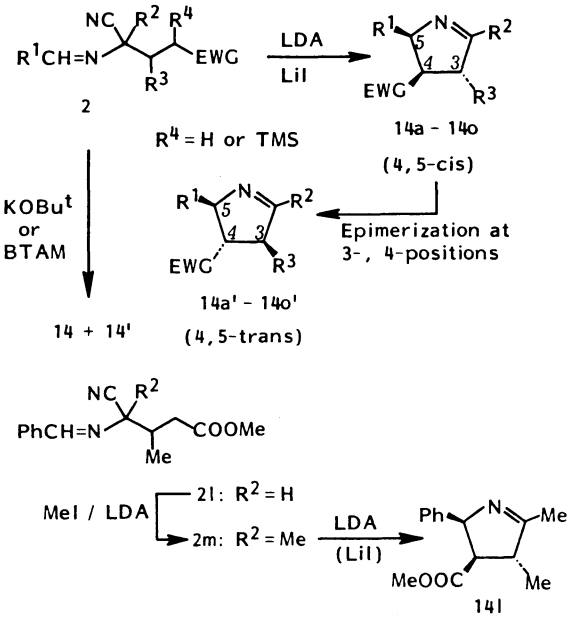
A quantitative conversion of the Michael adducts **21**—**2m** into γ-lactams **6**—**9** through a hydrolytic cyclization process was above mentioned in Scheme 3. The imine **10** bearing a longer framework by one carbon could undergo a similar hydrolytic cyclization to produce δ-lactams, 2-piperidinones **12a** and **12b** (Scheme 5). However the hydrolysis of **11** under comparable conditions gave methyl 6-aminoheptanoate **13**, no further cyclization being observed.

Base-Induced Cyclization of 2-(Alkylideneamino) Esters Leading to 1-Pyrrolines. Grigg and his coworkers have demonstrated the base-induced Michael additions between the imines of 2-amino esters and α,β-unsaturated esters.[8] These Michael adducts were converted into pyrrolidines by treatment with potassium *t*-butoxide or benzyltrimethylammonium methoxide in benzene. Stereoselectivity of these cyclizations was not high.

We first employed his cyclization procedure to *N*-(1-cyanoalkyl)imines **2** (Scheme 6 and Table 3). The cyclization of imines **2** was exclusively accompanied by a spontaneous elimination of CN group giving 1-pyrrolines **14** and/or **14'**. As shown with Entries 1, 6, 8, 13, 14, 24 (KOBu-*t*) and Entries 11 and 23 (BTAM) in Table 3, the cyclization of **2** under these conditions



Scheme 5.



Scheme 6.

Table 2. Consecutive Alkylation of α-(Benzylideneamino)acetonitrine (**1a**)

Reaction sequence	1st Alkylation[a]				2nd Alkylation[a]				Total yield
	Alkylating agent	Temp	Time	Yield[b]	Alkylating agent	Temp	Time	Yield[b]	
1a→1b→2m	MeI/LDA	−78 °C	0.5 h	85%	$MeCH^{t}$=CHCOOMe/DBU	c)		95%	**2m**: 81%
1a→1c→2n	$PhCH_2Br$/LDA	−78 °C	0.5 h	88%	$MeCH^{t}$=CHCOOMe/DBU	c)		92%	**2n** : 81%
1a→21→2m	$MeCH^{t}$=CHCOOMe/DBU	c)		78%	MeI/LDA	−78 °C	1 h	100%	**2m**: 78%[d]
1a→21→2n	$MeCH^{t}$=CHCOOMe/DBU	c)		78%	$PhCH_2Br$/LDA	−78 °C	1 h	82%	**2n** : 64%[e]
1a→1b→10a	MeI/LDA	f)		85%	$Br(CH_2)_3COOEt$/LDA	rt	2 h	96%	**10a** : 82%
1a→1c→10b	$PhCH_2Br$/LDA	f)		88%	$Br(CH_2)_3COOEt$/LDA	rt	1.5 h	63%	**10b** : 55%
1a→1b→11	MeI/LDA	f)		85%	$Br(CH_2)_4COOEt$/LDA	rt	2 h	67%	**11** : 57%

a) Carried out in THF in the presence of LDA or DBU (1 equiv). b) Yield of isolated products. c) The reaction conditions are listed in Table 1. d) Isomer ratio : 4:1 (^{1}H NMR). e) Isomer ratio : 1.5:1 (^{1}H NMR).

is very poor in stereoselectivity. Either mixtures of two 4,5-stereoisomers **14**+**14′** were obtained or the only isomers were 4,5-*trans*-1-pyrrolines **14′** when the cyclization was stereoselective (Entries 11 and 13). Stereochemistry at the 3-position is not important since this position is known to isomerize into a thermodynamically more stable 3,4-trans configuration through an imine/enamine tautomerization.[9]

To our great surprise methylation of the Michael adduct **21** with LDA and methyl iodide provided 4,5-*cis*-1-pyrroline **141** as a single isomer (Scheme 6 and Entry 17 in Table 3). Although it was easily understood that **21** was first methylated leading to **2m**, why the cyclization of **2m** under the methylation conditions was so fast and cis-selective? Both **21** and **2m** were completely recovered intact on treatment with LDA at −78 °C (Entries 16 and 18), but a 1:1 stereoisometric mixture of cyclized products **141**+**141′** was obtained at an elevated temperature (Entry 19). In the presence of methyl iodide the cyclization was again cis-selective to give **141** as a single product (Entry 20). In the end we noticed that lithium iodide would play an important role in the cis-selective cyclization reactions. Actually only cis isomer **141** was given in an excellent yield in the reaction of **2m** with LDA in the presence of lithium iodide (Entry 21).

Thus cyclizations of other imines **2** were carried out under the cyclization conditions using LDA and lithium iodide, and 4,5-*cis*-1-pyrrolines **14** were the only products in most cases (Table 3). Lithium iodide probably worked as a Lewis acid to activate the C=N bond of imines **2** so that the intramolecular cyclization was considerablly facilitated. The high stereoselectivity would be discussed later.

Cyclization of imines **2g**—**2i** which bear an acetyl moiety as EWG was found also stereoselective but 4,5-*trans*-1-pyrrolines **14′** were the only or major products (Entries 10—13). As 4,5-*cis*-1-pyrroline **14i** readily epimerizes into 4,5-trans isomer **14i′** under the cyclization conditions, the predominant formation of **14g′**—**14i′** would be a result of facile epimerization at the carbon which is substituted with EWG (Scheme 6).

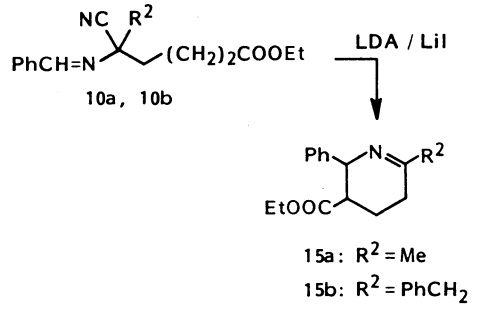
Table 3. Base-Induced Cyclization of Alkylated Imines **2**

Entry	Imine	Condition[a]	Time/h −78 °C	Time/h rt	Product	R^1	R^2	R^3	EWG	Yield/%[b]	Isomer ratio
1	**2a**	A	0.5	18	No reaction (recovered **2a**:96%)					0	
2	**2a**	B	6	0	**14a**	Ph	Me	H	COOMe	65	
3	**2a**	C	2	1	**14a**					82	
4	**2b**	C	0.5	2	**14b**	Ph	$PhCH_2$	H	COOMe	80	
5	**2c**	C	0.5	1.5	**14c**+**14c′**	Ph	*i*-Pr	H	COOMe	61[c]	**14c**:**14c′**=2:1[d]
6	**2d**	A	0.5	15	**14d**+**14d′**	Ph	Ph	H	COOMe	65[e]	**14d**:**14d′**=1:1[d]
7	**2e**	C	0.7	1.5	**14e**	Et	Ph	H	COOMe	57	
8	**2e**	A	0.5	19	**14e**+**14e′**					82	**14e**:**14e′**=4:1[d]
9	**2f**	B	6	0	**14f**+**14f′**	Ph	Me	H	$COOBu^t$	60	**14f**:**14f′**=3:2[d]
10	**2g**	C	0.5	1.5	**14g′**	Ph	$PhCH_2$	H	COMe	82	
11	**2h**	D	0	22	**14h′**	Ph	Ph	H	COMe	84	
12	**2i**	C	0.8	0.5	**14i**+**14i′**	Et	Ph	H	COMe	81	**14i**:**14i′**=1:2[d]
13	**2i**	A	1	20	**14i′**					93	
14	**2k**	A	1	19	**14j**+**14j′**	Et	Ph	H	CN	80	**14j**:**14j′**=10:1[d]
15	**21**	C	0.5	1.5	**14k**	Ph	H	Me	COOMe	25	
16	**21**	B	9	0	No reaction (recovered **21**:100%)					0	
17	**21**	B (MeI)	0.5	1	**141**	Ph	Me	Me	COOMe	77	
18	**2m**	B	7	0	No reaction (recovered **2m**:95%)					0	
19	**2m**	B	0.5	2	**141**+**141′**					70	**141**:**141′**=1:1[d]
20	**2m**	B (MeI)	0.5	1	**141**					66	
21	**2m**	C	0.5	2	**141**					84	
22	**2n**	C	0.2	3	**14m**	Ph	$PhCH_2$	Me	COOMe	81	
23	**2o**	D	0	16	**14n**+**14n′**	Ph	Ph	Me	COOMe	60[f]	**14n**:**14n′**=1:3[d]
24	**2q**	A	1	27	**14o**+**14o′**	Et	Ph	Me	COOMe	80	**14o**:**14o′**=3:2[d]
25	**2t**	E	1	17	**14e**+**14e′**					40[g]	h)
26	**2t**	F	1 (0° C)	2	**14e**+**14e′**					71	h)

a) A: $KOBu^t$ (1.1 equiv) in THF. B: LDA (1 equiv) in THF. B (MeI): LDA (2 equiv) and then MeI (1.1 equiv) in THF. C: LDA + LiI (each 1 equiv) in THF. D: Benzyltrimethylammonium methoxide in THF. E: TBAF (0.1 equiv) in THF. F: TBAF (0.1 equiv) in HMPA. b) Yield of isolated products. c) Recovered **2c**: 31%. d) Inseparable mixture. Isomer ratio was determined by ^1H NMR or ^{13}C NMR spectrum. e) Recovered **2d**: 14%. f) Recovered **2o**: 11%. g) Yield determined by ^1H NMR spectrum (recovered **2t**: 60%). h) Isomer ratio is uncertain.

When 4-H of 4,5-cis isomers **14** is highly acidic, this position epimerizes presumably via an enol intermediate to lead to thermodynamically more stable 4,5-trans relationship. Quick isomerization at the 3-position is followed through an imine/enamine tautomerization to give **14'**.[9]

In other base-induced cyclizations of imines **2**, 4,5-*cis*-1-pyrrolines **14** would be formed exclusively or predominantly as the initial products. They undergo a similar epimerization both at the 3- and 4-positions leading to 4,5-*trans*-1-pyrrolines **14'**. It is apparent that isomer ratios **14**:**14'** depend upon the cyclization conditions (base, temperature, time etc.). As LDA/LiI-induced cyclization occurs more rapidly than the other cyclizations, one can conduct this reaction at a low temperature in a short period. As a result the subsequent epimerization is suppressed.



Scheme 7.

The alkylated imines **10a** and **10b** with one more carbon also underwent a similar cyclization under the influence of LDA and lithium iodide to give tetrahydropyridines **15a** and **15b** both as mixtures of two stereoisomers, respectively (Scheme 7). Contrary to this the cyclization of **11** under comparable conditions was entirely unsuccessful, **11** being quantitatively recovered.

The above 4,5-*cis*-selective cyclizations of Michael adducts **2** is explained with an example of cyclization of **2m** (Fig. 2). One possible transition model is called Cyclic Model which implies a seven-menbered ring of lithium chelate **F** and **F'** The other one called Open Chain Model involves a chair-like enolate geometry **G** and **G'**. The LDA/LiI-induced cyclization of **2m** which is a 1:1 mixture of two diastereomers (*ul*-**2m** and *lk*-**2m**) at −78 °C allowed the selective consumption of one isomer *ul*-**2m** forming **14 l**. The other isomer *lk*-**2m** was recovered intact. In the both models the enolate intermediates **F** and **G** derived from *ul*-**2m** are sterically more favored than their isomeric intermediates **F'** and **G'** making possible the kinetical separation.

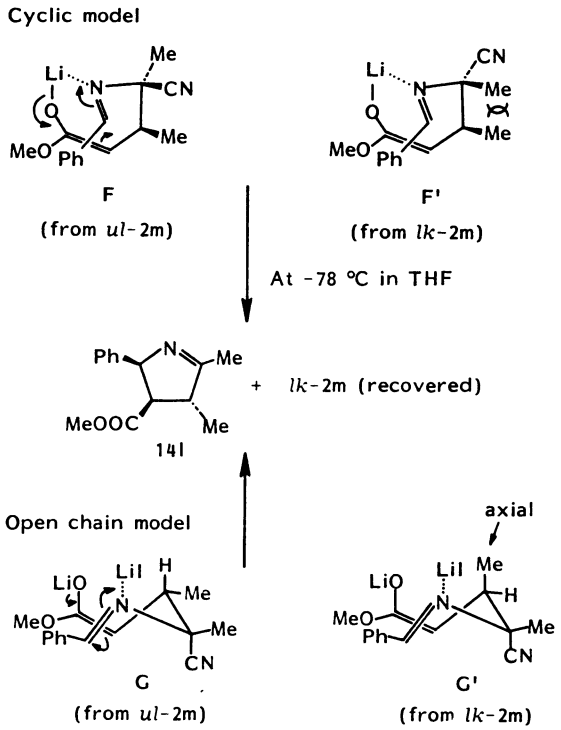


Fig. 2. Two possible transition models for the stereoselective cyclization of **2m** leading to **14l**.

Experimental

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. ^{1}H NMR spectra were recorded on a Hitachi R-40 (90 MHz) or a JEOL FX-100 instrument (100 MHz) and ^{13}C NMR on a JEOL FX-100 spectrometer at 25.05 MHz. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Mass spectra as well as high resolution mass spectra were measured with a JEOL-01SG-2 spectrometer at 70 eV of ionization energy. 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). For preparative column chromatography Wakogel C-200, C-300 (Wako), and Silicagel 60 (Merck) were employed. Flash chromatography was carried out on an EYELA EF-10 apparatus using a column (20×180 mm) packed with Silicagel 60 (Merck, size: 0.04—0.063 mm). Micro vacuum distillation was made on a Sibata GTO-250R Kugelrohr distilling apparatus. Solvents were evaporated with a Tokyo Rikakikai rotary evaporator type-V.

General Procedure for Preparation of *N*-(1-Cyanoalkyl)-imines 1a—1i. Imines **1a** and **1e—1i** were prepared by the condensation of 2-aminoalkanenitriles with carbonyl compounds: Equimolar mixture of a 2-aminoalkanenitrile and a carbonyl compound was heated under reflux in the solvent described below (2—5 ml for 1 mmol of the substrate). The solution was dried over anhydrous magnesium sulfate and evaporated in vacuo to give imines **1** in an almost quantitative yield. Imines **1a**, **1e**, and **1g** are known.[6d] The reaction solvent and time are as follows: **1f**: In benzene for 1 h; **1h**: in chloroform for 2 h; **1i**: in benzene for 2 h. Imines **1b—1d** were prepared by the alkylations of **1a**: To a solution

of LDA (3 mmol in THF (3 ml)) freshly prepared from butyllithium and diisopropylamine was added imine **1a** (0.43 g, 3 mmol in THF (5 ml)) at −78 °C. After 5 min an alkylating agent (methyl iodide, benzyl bromide, or isopropyl bromide, each 3.3 mmol in THF (2—3 ml)) was added. The mixture was stirred under the following conditions: **1b**: at −78 °C for 2 h; **1c** and **1d**: at −78 °C for 1 h and then at room temperature for 1 h. The reaction was quenched by treating with ice water and the products were extracted with diethyl ether (30 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using chloroform to give **1b** (0.4 g, 85%), **1c** (0.614 g, 88%), or **1d** (0.48 g, 52%).

1b: Pale yellow liquid; bp 150 °C (133 Pa, bulb-to-bulb); IR (neat) 2225 and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.63 (3H, d, J=6.0 Hz, Me), 4.64 (1H, dq, J=6.0 and 2.0 Hz, CH), 7.2—7.6 (3H, m, Ph), 7.7—7.9 (2H, m, Ph), and 8.42 (1H, d, J=2.0 Hz, CH=N); ^{13}C NMR ($CDCl_3$) δ=21.06 (q, Me), 53.24 (d, CH), 118.89 (s, CN), 128.89, 131.83 (each d), 135.07 (s), and 162.66 (d, CH=N); MS m/z (rel intensity, %) 158 (M^+, 62), 143 (64), 131 (19), 130 (14), 117 (base peak), 105 (26), 104 (49), 103 (17), 90 (16), 89 (33), and 77 (88). HRMS Found: m/z 158.0840. Calcd for $C_{10}H_{10}N_2$: M, 158.0839.

1c: Pale yellow liquid; IR (neat) 2250, 1740, and 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.17, 3.22 (each 1H, dd, J=13.0 and 8.0 Hz, CH_2Ph), 4.77 (1H, dt, J=8.0 and 2.0 Hz, NCH), 7.2—7.9 (10H, m, Ph), and 8.20 (1H, d, J=2.0 Hz, CH=N); MS m/z (rel intensity, %) 234 (M^+, 37), 143 (54), 118 (17), 117 (18), 116 (29), 107 (43), 91 (base peak), and 77 (30). HRMS Found: m/z 234.1165. Calcd for $C_{16}H_{14}N_2$: M, 234.1157.

1d: Pale yellow liquid; IR (neat) 2240 and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.05, 1.13 (3H, d, J=8.0 Hz, i-Pr), 2.23 (1H, m, i-Pr), 4.44 (1H, dd, J=6.0 and 2.0 Hz, NCH), 7.3—7.5 (3H, m, Ph), 7.70 (2H, m Ph), and 8.35 (1H, d, J=2.0 Hz, CH=N); ^{13}C NMR ($CDCl_3$) δ=17.94, 19.18 (each q, i-Pr), 32.88 (d, i-Pr), 65.06 (d, NCH), 117.24 (s, CN), 128.95, 129.19, 131.83, 134.66, and 163.00 (d, CH=N); MS m/z (rel intensity, %) 186 (M^+, 11), 144 (50), 143 (68), 116 (base peak), 104 (16), 91 (12), 90 (36), and 89 (54). HRMS Found: m/z 186.1158. Calcd for $C_{12}H_{14}N_2$: M, 186.1157.

1f: Yellow liquid; IR (neat) 2240 and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.33 (1H, d, J=2.0 Hz, CH), 7.2—8.2 (12H, m, Ar), and 8.52 (1H, d, J=2.0 Hz, CH=N); MS m/z (rel intensity, %) 270 (M^+, 45), 166 (base peak), 140 (11), and 127 (4). HRMS Found: m/z 270.1168. Calcd for $C_{19}H_{14}N_2$: M, 270.1168.

1h: Pale yellow liquid; bp 150 °C (133 Pa, bulb-to-bulb); IR (neat) 2430 and 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.95 (3H, t, J=7.0 Hz, n-Pr), 1.60 (2H, m, n-Pr), 2.34 (2H, m, n-Pr), 5.46 (1H, s, CH), 7.36 (5H, s, Ph), and 8.00 (1H, t, CH=N); ^{13}C NMR ($CDCl_3$) δ=13.69 (t, n-Pr), 19.01, 37.79 (each t, n-Pr), 61.90 (d, CH), 117.20 (s, CN), 127.30, 129.00, 129.12 (each d), 134.97 (s), and 168.55 (d, CH=N); MS m/z (rel intensity, %) 186 (M^+, 8), 181 (16), 158 (39), 157 (18), 132 (22), 118 (22), 116 (base peak), 89 (21), and 58 (11). HRMS Found: m/z 186.1160. Calcd for $C_{12}H_{14}N_2$: M, 186.1157.

1i: Pale yellow liquid; bp 130 °C (133 Pa, bulb-to-bulb); IR (neat) 2250 and 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.10 (9H, s, t-Bu), 5.46 (1H, d, J=2.0 Hz, CH), 7.30 (5H, s, Ph), and 7.85 (1H, d, J=2.0 Hz, CH=N); ^{13}C NMR ($CDCl_3$) δ=26.65 (q, t-Bu), 36.94 (s, t-Bu), 61.36 (d, CH), 117.30 (s, CN), 127.24, 128.48, 129.01 (each d), 135.19 (s), and 175.19 (d, CH=N); MS m/z (rel intensity, %) 200 (M^+, 26), 185 (33), 117 (39), 116 (base peak), 89 (18), and 58 (39). HRMS Found: m/z 200.1310. Calcd for $C_{13}H_{16}N_2$: M, 200.1991.

General Procedure for Michael Additions of *N*-(1-Cyanoalkyl)imines 1a—1i to Olefins Leading to 2a—2t. To a solution of imine **1** (1 mmol) in dry THF (5 ml) was added at −78 °C DBU (0.167 to 0.015 g, 1.1 to 0.1 mmol in 1 ml of THF). After 5 min, an olefin (1.1 mmol in 1 ml of THF) was added to the resulting red solution. This mixture was allowed to react under the conditions listed in Table 1 in an atmosphere of nitrogen, poured into ice water, and then extracted with diethyl ether (25 ml×2). The combined extracts were dried over anhydrous magnesium sulfate and evaporated in vacuo. The residue was chromatographed through a short column packed with silica gel by using chloroform as an eluent. The results are listed in Table 1.

2a: Pale yellow liquid; IR (neat) 2225, 1740, and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.62 (3H, s, Me), 2.2—2.4 (4H, m, 2×CH_2), 3.56 (3H, s, COOMe), 7.2—7.6 (3H, m, Ph), 7.7—7.9 (2H, m, Ph), and 8.46 (1H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ=27.65 (q, Me), 29.41, 36.18 (each t, CH_2), 51.59 (q, COOMe), 62.59 (s, q-C), 119.36 (s, CN), 128.83, 131.77 (each d), 135.07 (s), 160.36 (d, CH=N), and 172.42 (s, COOMe); MS m/z (rel intensity, %) 244 (M^+, 2), 213 (38), 158 (39), 157 (base peak), 141 (82), and 104 (34). HRMS Found: m/z 244.1209. Calcd for $C_{14}H_{16}N_2O_2$: M, 244.1209.

2b: Pale yellow liquid; IR (neat) 2240, 1740, and 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.37 (4H, m, 2×CH_2), 3.12 (2H, s, CH_2Ph), 3.52 (3H, s, COOMe), 7.1—7.4 (8H, s and m, Ph), 7.60 (2H, m, Ph), and 7.97 (1H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ=29.47, 35.12, 46.18 (each t, CH_2), 51.65 (q, COOMe), 68.06 (s, q-C), 118.07 (s, CN), 127.60, 128.30, 128.83, 131.00, 131.77, 134.07, 134.83, 161.66 (d, CH=N), and 172.65 (s, COOMe); MS m/z (rel intensity, %) 320 (M^+, 15), 230 (16), 229 (base peak), 197 (12), 169 (56), and 104 (17). HRMS Found: m/z 320.1546. Calcd for $C_{20}H_{20}N_2O_2$: M, 320.1567.

2c: Pale yellow liquid; IR (neat) 2250, 1740, and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.95, 1.15 (each 3H, d, J=7.0 Hz, i-Pr), 2.0—2.4 (4H, m, CH_2), 3.55 (3H, s, COOMe), 7.3—7.5 (3H, m, Ph), 7.78 (2H, m, Ph), and 8.42 (1H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ=17.53, 17.71 (each q, i-Pr), 29.53, 32.59 (each t, CH_2), 36.65 (d, i-Pr), 51.77 (q, COOMe), 61.06 (s, q-C), 117.89 (s, CN), 128.95, 131.80 (each d), 135.00 (s), 160.89 (d, CH=N), and 173.07 (s, COOMe); MS m/z (rel intensity, %) 272 (M^+, 14), 241 (26), 230 (32), 229 (93), 186 (32), 185 (36), 144 (67), and 143 (base peak). HRMS Found: m/z 272.1533. Calcd for $C_{16}H_{20}N_2O_2$: M, 272.1541.

2d: Colorless liquid; IR (neat) 2220, 1715, and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.3—2.7 (4H, m, CH_2), 3.50 (3H, s, COOMe), 7.2—7.8 (10H, m, Ph), and 8.50 (1H, s, CH=N); MS m/z (rel intensity, %), 306 (M^+, 26), 220 (22), 219 (base peak), 142 (60), and 115 (39). HRMS Found: m/z 306.1363. Calcd for $C_{19}H_{18}N_2O_2$: M, 306.1360.

2e: Pale yellow liquid; IR (neat) 2220, 1740, and 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.15 (3H, t, J=7.0 Hz, Et), 1.7—2.0 (2H, m, Et), 2.2—2.6 (4H, m, CH_2), 3.60 (3H, s, COOMe), 7.2—7.7 (5H, m, Ph), and 8.07 (1H, t, J=5.0 Hz, CH=N); ^{13}C NMR ($CDCl_3$) δ=9.59 (q, Et), 29.12, 29.41 (each t, Et and CH_2), 38.77 (t, CH_2), 51.65 (q, COOMe), 70.01 (s,

q-C), 118.36 (s, CN), 126.07, 128.83, 129.01 (each d), 139.66 (s), 166.66 (d, CH=N), and 172.42 (s, COOMe); MS *m/z* (rel intensity, %) 258 (M^+, 4), 203 (16), 171 (24), 143 (23), 142 (base peak), 116 (39), 115 (57), 104 (36), 91 (29), 77 (32), and 41 (31). HRMS Found: *m/z* 258.1361. Calcd for $C_{15}H_{18}N_2O_2$: M, 258.1367.

2f: Yellow liquid; IR (neat) 2240, 1725, and 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.40 (9H, s, *t*-Bu), 1.63 (3H, s, Me), 2.1—2.5 (4H, m, CH_2), 7.3—7.5 (3H, m, Ph), 7.6—7.8 (2H, m, Ph), and 8.41 (1H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ=27.77 (q, Me), 28.00 (q, *t*-Bu), 30.77, 36.24 (each t, CH_2), 62.65 (s, *t*-Bu), 80.48 (s, q-C), 119.36 (s, CN), 128.83, 128.95, 131.77 (each d), 135.07 (s), 160.18 (d, CH=N), and 171.24 (s, COOBu-*t*); MS *m/z* (rel intensity, %) 286 (M^+, 1), 230 (15), 213 (98), 203 (28), 183 (34), 158 (42), 127 (65), 104 (52), and 57 (base peak). HRMS Found: *m/z* 286.1680. Calcd for $C_{17}H_{22}N_2O_2$: M, 286.1680.

2g: Pale yellow liquid; IR (neat) 2200, 1720, and 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.04 (3H, s, COMe), 2.2—2.6 (4H, m, CH_2), 3.10 (2H, s, CH_2Ph), 7.07 (5H, s, Ph), 7.20 (3H, m, Ph), 7.60 (2H, m, Ph), and 7.93 (1H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ=25.94 (q, COMe), 30.06, 34.06, 38.77 (each t, CH_2), 68.12 (s, q-C) 118.12 (s, CN), 127.66, 128.36, 128.89, 131.13, 131.89, 134.13, 134.89, 161.66 (d, CH=N), and 206.72 (s, COMe); MS *m/z* (rel intensity, %) 304 (M^+, 19), 213 (58), 198 (16), 171 (23), 105 (27), 91 (base peak), and 77 (28). HRMS Found: *m/z* 304.1596. Calcd for $C_{20}H_{20}N_2O$: M, 304.1616.

2h: Colorless liquid; IR (neat) 2220, 1715, and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.03 (3H, s, COMe), 2.50 (4H, m, CH_2), 7.2—7.9 (10H, m, Ph), and 8.49 (1H, s, CH=N); MS *m/z* (rel intensity, %) 290 (M^+, 46), 220 (25), 219 (base peak), 186 (25), 116 (16), and 89 (16). HRMS Found: *m/z* 290.1417. Calcd for $C_{19}H_{18}N_2O_2$: M, 290.1417.

2i: Pale yellow liquid; IR (neat) 2220, 1715, and 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.15 (3H, t, *J*=7.0 Hz, Et), 1.7—1.9 (2H, m, Et), 2.10 (3H, s, COMe), 2.2—2.6 (4H, m, CH_2), 7.2—7.7 (5H, m, Ph), and 8.08 (1H, t, *J*=5.0 Hz, CH=N); ^{13}C NMR ($CDCl_3$) δ=9.65 (q, Et), 29.06 (t, Et), 29.88 (q, COMe), 37.53, 38.47 (each t, CH_2), 69.83 (s, q-C), 118.54 (s, CN), 126.01, 128.72, 128.95 (each d), 139.71 (s), 166.37 (d, CH=N), and 206.30 (s, COMe); MS *m/z* (rel intensity, %) 242 (M^+, 36), 187 (24), 186 (98), 171 (50), 168 (30), 144 (69), 115 (30), and 43 (base peak). HRMS Found: *m/z* 242.1424. Calcd for $C_{15}H_{18}N_2O$: M, 242.1418.

2j: Colorless liquid; IR (neat) 2450, 2390, and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.3—2.7 (4H, m, CH_2), 7.3—7.6 (8H, m, Ph), 7.85 (2H, m, Ph), and 8.60 (1H, s, CH=N); MS *m/z* (rel intensity, %) 273 (M^+, 2), 219 (17), 169 (12), 142 (26), 129 (34), 116 (25), 115 (33), 105 (36), and 77 (base peak). HRMS Found: *m/z* 273.1266. Calcd for $C_{18}H_{15}N_3$: M, 273.1266.

2k: Colorless liquid; IR (neat) 2240, 2190, and 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.14 (3H, t, *J*=7.0 Hz, Et), 1.6—2.1 (2H, m, Et), 2.2—2.5 (4H, m, CH_2), 7.2—7.6 (5H, m, Ph), and 8.07 (1H, t, *J*=5.0 Hz, CH=N); MS *m/z* (rel intensity, %) 225 (M^+, 1), 210 (3), 198 (59), 172 (28), 169 (69), 145 (93), 144 (36), 143 (41), 132 (27), 131 (48), 130 (base peak), 116 (44), 104 (66), 103 (23), 96 (24), 91 (28), 77 (37), and 52 (21). HRMS Found: *m/z* 225.1263. Calcd for $C_{14}H_{15}N_3$: M, 225.1263.

2l (a 1:1 mixture of diastereomers): Yellow liquid; IR (neat) 2240, 2200, 1740, and 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.15 (3H, d, J=7.0 Hz, Me), 2.2—2.8 (3H, m, CH_2 and CH), 3.63, 3.66 (each 1/2×3H, s, COOMe), 4.72 (1H, m, CHN), 7.2—7.5 (3H, m, Ph), 7.6—7.8 (2H, m, Ph), and 8.40 (1H, d, *J*=2.0 Hz, CH=N); ^{13}C NMR ($CDCl_3$) δ=16.06, 16.30 (each q, Me), 34.59, 34.88 (each d, CH), 36.77, 37.71 (each t, CH_2), 51.77 (q, COOMe), 62.36, 62.95 (each d, CHN), 116.95 (s, CN), 129.01, 132.01 (each d), 135.07 (s), 163.65, 163.89 (each d, CH=N), 172.36, and 172.60 (each s, COOMe); MS *m/z* (rel intensity, %) 244 (M^+, 37), 213 (25), 171 (base peak), 144 (20), 143 (36), 117 (16), 116 (41), 89 (20), and 76 (15). HRMS Found: *m/z* 244.1204. Calcd for $C_{14}H_{16}N_2O_2$: M, 244.1209.

2m (a 3:2 mixture of diastereomers): Pale yellow liquid; IR (neat) 2225, 1735, and 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.0—1.3 (3H, m, Me), 1.60 (3H, s, Me), 2.0—2.8 (3H, m, CH_2 and CH), 3.53 (2/5×3H, s, COOMe), 3.62 (3/5×3H, s, COOMe), 7.2—7.6 (3H, m, Ph), 7.7—7.9 (2H, m, Ph), and 8.48 (1H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ=15.30, 15.71 (each q, Me), 24.77, 26.24 (each q, Me), 36.77 (t, CH_2), 39.53 (d, CH), 51.71, 51.83 (each q, COOMe), 67.00, 67.59 (each s, q-C), 118.89, 119.42 (each s, CN), 125.66, 128.95, 129.95, 131.83 (each d), 135.24 (s), 160.13, 160.54 (each d, CH=N), and 172.72 (s, COOMe); MS *m/z* (rel intensity, %) 258 (M^+, 2), 158 (77), 157 (base peak), 155 (26), 143 (48), 131 (23), 121 (23), 116 (49), 105 (37), 104 (36), 77 (52), and 52 (28). HRMS Found: *m/z* 258.1368. Calcd for $C_{15}H_{18}N_2O_2$: M, 258.1368.

2n (a 1:1 mixture of diastereomers): Pale yellow liquid; IR (neat) 2210, 1730, and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.18, 1.27 (each 1/2×3H, d, *J*=7.0 Hz, Me), 2.2—3.0 (3H, m, CH_2 and CH), 3.12 (2H, s, CH_2Ph), 3.52, 3.62 (each 1/2×3H, s, COOMe), 7.04 (5H, s, Ph), 7.30 (3H, m, Ph), 7.55 (2H, m, Ph), 7.76, and 7.79 (each 1/2H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ=15.30, 16.00 (each q, Me), 37.18, 39.06 (each t, CH_2), 39.24 (d, CH), 42.53, 43.77 (each t, CH_2Ph), 51.65, 51.89 (each q, COOMe), 72.36, 72.95 (each s, q-C), 117.42, 117.95 (each s, CN), 127.54, 128.18, 128.83, 131.24, 131.71, 134.30, 134.95 135.07, 141.83, 161.48 (d, CH=N), 161.89 (d, CH=N), 172.65, and 172.78 (each s, COOMe); MS *m/z* (rel intensity, %) 334 (M^+, 9), 244 (10), 243 (61), 183 (base peak), 116 (18), 104 (24), and 91 (86). HRMS Found: *m/z* 334.1983. Calcd for $C_{21}H_{22}N_2O_2$: M, 334.1683.

2o: Colorless liquid; IR (neat) 2220, 1740, and 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.02 (3H, d, *J*=7.0 Hz, Me), 2.23 (1H, dd, *J*=15.0 and 9.0 Hz, one of CH_2), 2.55 (1H, dd, *J*=15.0 and 5.0 Hz, the other of CH_2), 3.00 (1H, m, CH), 3.50 (3H, s, COOMe), 7.2—7.8 (10H, m, Ph), and 8.54 (1H, s, CH=N); MS *m/z* (rel intensity, %) 320 (M^+, 6), 219 (base peak), 115 (55), 91 (26), 90 (22), 89 (54), and 77 (46). HRMS Found: *m/z* 320.1516. Calcd for $C_{20}H_{20}N_2O_2$: M, 320.1510.

2p: Pale yellow liquid; IR (neat) 2235, 1740, and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.00 (3H, d, *J*=7.0 Hz, Me), 2.36 (1H, dd, *J*=16.0 and 9.0 Hz, one of CH_2), 2.75 (1H, dd, *J*=16.0 and 6.0 Hz, the other of CH_2), 3.46 (3H, s, COOMe), 3.76 (1H, ddq, *J*=9.0, 6.0, and 7.0 Hz, CH), 7.2—7.9 (11H, m, Ar), 8.55 (1H, s, CH=N), and 8.82 (1H, d, ArH); ^{13}C NMR ($CDCl_3$) δ=16.47 (q, Me), 37.30 (t, CH_2), 38.53 (d, CH), 51.53 (q, COOMe), 77.47 (s, q-C), 117.77 (s, CN), 124.72, 126.13, 126.24 126.48, 126.60, 126.89, 128.13, 128.95, 129.19, 129.42, 129.60, 130.53, 132.07, 134.18, 135.19, 162.71 (d, CH=N), and 172.83 (s, COOMe); MS *m/z* (rel intensity, %) 370 (M^+, 20), 270 (25), 269 (base peak), 192 (10), and 191 (18). HRMS Found: *m/z* 370.1684. Calcd for $C_{24}H_{22}N_2O_2$: M, 370.1684.

2q: Pale yellow liquid; IR (neat) 2230, 1740, and

1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.9—1.3 (6H, m, Et and Me), 1.6—2.0 (2H, m, Et), 2.1—3.0 (3H, m, CH_2 and CH), 3.56 (3H, s, COOMe), 7.2—7.6 (5H, m, Ph), and 7.96 (1H, t, J=5.0 Hz, CH=N); ^{13}C NMR ($CDCl_3$) δ=9.18 (q, Et), 15.00 (q, Me), 28.77 (t, Et), 35.88 (t, CH_2), 41.00 (d, CH), 51.18 (q, COOMe), 74.71 (s), 117.19 (CN), 126.13, 128.48 (each d), 138.89 (s), 166.66 (d, CH=N), and 172.18 (COOMe). MS m/z (rel intensity, %) 272 (M^+, 11), 172 (59), 171 (base peak), 144 (50), 143 (87), 104 (36), 91 (49), 77 (22), 59 (20), 41 (31), and 39 (23). HRMS Found: m/z 272.1525. Calcd for $C_{16}H_{20}N_2O_2$: M, 272.1525.

2r: Colorless liquid; IR (neat) 2230, 1740, and 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.8—1.0 (6H, m, Me and *n*-Pr), 1.3—1.7 (2H, m, *n*-Pr), 2.0—2.6 (4H, m, CH_2 and *n*-Pr), 2.80 (1H, m, CH), 3.60 (3H, s, COOMe), 7.2—7.6 (5H, m, Ph), and 8.00 (1H, t, J=5.0 Hz, CH=N); ^{13}C NMR ($CDCl_3$) δ=13.82, 15.47 (each q, Me and *n*-Pr), 18.94 (t, *n*-Pr), 36.36, 37.82 (each t, CH_2 and *n*-Pr), 41.36 (d, CH), 51.71 (q, COOMe), 75.24 (s, q-C), 117.71 (s, CN), 126.60, 128.83, 129.53 (each d), 139.24 (s), 166.60 (d, CH=N), and 172.83 (s, COOMe); MS m/z (rel intensity, %) 286 (M^+, 1), 258 (16), 255 (7), 186 (30), 185 (58), 158 (22), 144 (23), 143 (63), 116 (51), 104 (55), 103 (31), 91 (base peak), and 76 (41). Elemental analysis by HRMS could not be achieved because of the weak parent ion peak.

2s: Colorless liquid; IR (neat) 2200, 1740, 1645, 1250, and 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.85 (9H, s, Me_3Si), 1.92 (1H, d, J=12.0 Hz, one of CH_2), 2.08 (1H, d, J=15.0 Hz, the other of CH_2), 2.81 (1H, dd, J=15.0 and 12.0 Hz, CH), 3.31 (3H, s, COOMe), 7.1—7.7 (10H, m, Ph), and 8.43 (1H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ=−3.12 (q, Me_3Si), 32.94 (d, CH), 41.83 (t, CH_2), 51.24 (q, COOMe), 71.06 (s, q-C), 118.65 (s, CN), 126.48, 128.83, 128.95, 129.19, 131.95, 135.24, 139.54, 160.95 (d, CH=N), and 174.71 (s, COOMe); MS m/z (rel intensity, %) 378 (M^+, 12), 363 (3), 306 (26), 219 (base peak), and 159 (40). HRMS Found: m/z 378.1779. Calcd for $C_{22}H_{26}N_2O_2Si$: M, 378.1795.

2t (mixture of two diastereomers): Pale yellow liquid; IR (neat) 2220, 1715, 1250, and 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.00 (9H, s, Me_3Si), 1.15 (3H, t, J=7.0 Hz, Et), 1.7—3.0 (5H, m, Et, CH_2, and CH), 3.50 (3H, s, COOMe), 7.2—7.6 (5H, m, Ph), and 8.08 (1H, t, J=5.0 Hz, CH=N); ^{13}C NMR ($CDCl_3$) δ=0.00 (q, Me_3Si), 9.47 (q, Et), 29.12 (t, Et), 32.77 (d, CH), 41.41 (t, CH_2), 51.06, 51.65 (each q, COOMe), 70.89 (s, q-C), 118.30, 118.54 (each s, CN), 125.95, 126.13, 126.36, 127.36, 128.65, 128.89 (each d), 139.24, 139.54 (each s), 165.30, 166.42 (each d, CH=N), and 174.60 (s, COOMe); MS m/z (rel intensity, %) 330 (M^+, 1), 115 (42), 104 (33), 89 (33), 73 (base peak), 59 (29), 55 (40), and 44 (32). Elemental analysis based on HRMS was unsuccessful because of the parent ion peak with a low intensity.

3: Pale yellow liquid; IR (neat) 2250 and 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.00 (9H, s, *t*-Bu), 3.65 (2H, s, CH_2), 7.39 (3H, m, Ph), and 7.90 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=27.88 (q, *t*-Bu), 33.30 (s, *t*-Bu), 70.53 (t, CH_2), 109.71 (s, CN), 127.60, 128.95 (each d), 132.07 (s). The imine carbon can not be observed.

4: Pale yellow needles (chloroform–hexane); mp 190—192 °C; IR (KBr) 3340, 2430, and 1550 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.96 (1H, br, NH), 4.40 (1H, d, J=8.0 Hz, 3-H), 5.36 (1H, d, J=8.0 Hz, 5-H), 5.78 (1H, t, J=8.0 Hz, 4-H), and 7.0—7.7 (15H, m, Ph); MS m/z (rel intensity, %) 369 (M^+, 1), 296 (2), 220 (8), 193 (base peak), 178 (18), 116 (17), and 115 (79). Found: C, 74.69; H, 5.27; N, 11.36%. Calcd for $C_{23}H_{19}N_3O_2$: C, 74.78; H, 5.18; N, 11.38%.

5: Yellow liquid; IR (neat) 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.95 (1H, t, J=8.0 Hz, 4-H), 5.37 (1H, dd, J=8.0 and 2.0 Hz, 5-H), 6.22 (1H, dd, J=8.0 and 2.0 Hz, 3-H), 7.0—7.5 (8H, m, Ph), and 7.85 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=61.06 (d, 4-C), 78.42 (d, 5-C), 99.36 (d, 3-C), 126.89, 127.54, 127.83, 128.06, 128.30, 128.48, 128.95, 129.19, 129.54, 131.30, 131.54, 132.07, 138.42, 141.01, and 164.89 (s, 2-C); MS m/z (rel intensity, %) 296 (M^+−46, 2), 218 (10), 165 (19), 115 (26), 105 (12), 104 (66), and 77 (base peak). Elemental analysis based on HRMS failed because of the absence of the parent ion peak.

General Procedure for Hydrolytic Cyclization of Michael Adducts 2 Leading to 2-Pyrrolidinones 6—9. A solution of the Michael adduct **2** in MeOH (5 ml for 1 mmol of **2**) was heated under reflux in the presence of *p*-toluenesulfonic acid (PTSA, 30 mg) or concentrated hydrochloric acid (HCl, a few drops). The mixture was poured into ice water and extracted with dichloromethane (25 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using chloroform to give **6—9**.

6: Obtained in 96% from **2o**, 79% from **2q**, and 95% from **2r** in the reactions with PTSA for 2h each as a single isomer: Colorless prisms (chloroform–hexane); mp 126—127 °C; IR (KBr) 3380, 2250, 1755 and 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.24 (3H, d, J=7.0 Hz, 4-Me), 2.3—2.7 (3H, m, 3- and 4-H), 6.84 (1H, s, NH), and 7.3—7.6 (6H, m, Ph and NH); ^{13}C NMR ($CDCl_3$) δ=14.18 (q, 4-Me), 37.77 (t, 3-C), 45.54 (d, 4-C), 66.77 (s, 5-C), 117.95 (s, CN), 125.24, 129.48, 129.77 (each d), 136.54 (s), and 176.89 (s, 2-C). Found: C, 72.04; H, 6.08; N, 13.84%. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99%.

7: Obtained as a single isomer in 89% yield in the reaction with HCl for 3 h: Colorless prisms (chloroform–hexane); mp 205—206 °C; IR (KBr) 3200—2800, 2240, and 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.42 (3H, d, J=7.0 Hz, 4-Me), 2.05 (1H, dd, J=17.0 and 6.0 Hz, one of 3-H), 2.46 (1H, dd, J=17.0 and 8.0 Hz, the other of 3-H), 3.00 (1H, ddq, J=8.0, 6.0, 3×7.0 Hz, 4-H), 7.4—8.2 (7H, m, Ar), and 9.40 (1H, s, NH); ^{13}C NMR ($CDCl_3$+DMSO-d_6) δ=17.59 (q, 4-Me), 36.65 (t, 3-C), 39.83 (d, 4-C), 65.18 (s, 5-C), 118.89 (s, CN), 123.83, 124.42 125.00, 126.24, 126.89, 129.00, 129.91, 130.65, 132.13, 134.66, and 175.42 (s, 2-C); Found: C, 76.63; H, 5.59; N, 10.97%. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19%.

8: Obtained in 79% yield as a 1:1 mixture of 4,5-trans and 4,5-cis isomers (^1H NMR) in the reaction with PTSA for 2 h. These isomers were separated from each other through column chromatography over silica gel by using chloroform (4,5-trans: 36%, 4,5-cis: 32%). 4,5-trans-**8:** Pale yellow liquid; IR (neat) 3200, 2250, and 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.26 (3H, d, J=7.0 Hz, 4-Me), 1.9—3.0 (3H, m, 3- and 4-H), 3.98 (1H, d, J=5.0 Hz, 5-H), and 7.35 (1H, br, NH); ^{13}C NMR ($CDCl_3$) δ=18.94 (q, 4-Me), 35.59 (d, 4-C), 37.12 (t, 3-C), 50.42 (d, 5-C), 118.48 (s, CN), and 177.50 (s, 2-C); MS m/z (rel intensity, %) 124 (M^+, 50), 70 (12), 55 (26), and 42 (base peak). HRMS Found: m/z 124.0629. Calcd for $C_6H_8N_2O$: M, 124.0624. 4,5-cis-**8:** Colorless prisms (diethyl ether–hexane); mp 92—94 °C; IR (KBr) 3200, 2440, and 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.25 (3H, d, J=7.0Hz, 4-Me),

2.14 (1H, dd, J=16.0 and 10.0 Hz, one of 3-H), 2.20 (1H, dd, J=16.0 and 8.0 Hz, the other of 3-H), 2.80 (1H, m, 4-H), 4.44 (1H, d, J=8.0 Hz, 5-H), and 6.80 (1H, br, NH). Found: C, 58.19; H, 6.54; N, 22.47%. Calcd for $C_6H_8N_2O$: C, 58.05; H, 6.50; N, 22.57%.

9: Obtained in 95% yield as an inseparable mixture of 4,5-cis and 4,5-trans isomers (2.8:1) in the reaction with PTSA for 2 h: Colorless solid; IR (KBr) 2250 and 1670 cm^{-1}, ^1H NMR ($CDCl_3$) 4,5-cis: δ=1.13 (3H, d, J=7.0 Hz, 4-Me), 1.51 (3H, s, 5-Me), 2.0—3.0 (3H, m, 3- and 4-H), and 7.75 (1H, br, NH); 4,5-trans: δ=1.30 (3H, d, J=7.0 Hz, 4-Me), 1.63 (3H, s, 5-Me), 2.0—3.0 (3H, m, 3- and 4-H), and 7.75 (1H, br, NH); ^{13}C NMR ($CDCl_3$) 4,5-cis: δ=14.30 (q, 4-Me), 21.24 (q, 5-Me), 37.30 (t, 3-C), 38.94 (d, 4-C), 55.89 (s, 5-C), 121.54 (s, CN), and 176.85 (s, 2-C); 4,5-trans: δ=15.00 (q, 4-Me), 24.76 (q, 5-Me), 38.00 (t, 3-C), 41.36 (d, 4-C), 59.06 (s, 5-C), 119.36 (s, CN), and 177.01 (s, 2-C). Found: C, 60.70; H, 7.27; N, 20.00%. Calcd for $C_7H_{10}N_2O$: C, 60.85; H, 7.30; N, 20.28%.

General Procedure for Alkylation of 2 l Leading to 2m—2n and of 1b—1c Leading to 10 and 11. An imine **2 l**, **1b**, or **1c** (1 mmol in THF (1 ml)) was added to a solution of LDA (1.1 mmol in THF (2 ml)) at −78 °C. After 5 min, methyl iodide or benzyl bromide (1 mmol) was added and the mixture was allowed to stir under the conditions listed in Table 2. The mixture was poured into ice water and extracted with diethyl ether (20 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. The results are summarized in Table 2.

10a: Colorless liquid; bp 180 °C (133 Pa, bulb-to-bulb); IR (neat) 2200, 1730 and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.25 (3H, t, J=7.0 Hz, Et), 1.5—2.5 (6H, m, CH_2), 1.64 (3H, s, Me), 4.07 (2H, q, J=7.0 Hz, Et), 7.3—7.4 (3H, m, Ph), 7.7 (2H, m, Ph), and 8.40 (1H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ=14.24 (q, Et), 20.18 (q, Me), 27.94, 33.71, 40.59 (each t, CH_2), 60.42 (t, Et), 63.36 (s, q-C), 119.83 (s, CN), 128.89, 131.71 (each d), 135.24 (s), 159.94 (d, CH=N), and 172.95 (s, COOEt); MS m/z (rel intensity, %) 272 (M^+, 21), 227 (54), 169 (90), 158 (83), 157 (base peak), 123 (36), and 104 (26). HRMS Found: m/z 272.1522. Calcd for $C_{16}H_{20}N_2O_2$: M, 272.1522.

10b: Colorless liquid; IR (neat) 2240, 1725, and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.20 (3H, t, J=7.0 Hz, Et), 1.5—2.4 (6H, m, CH_2), 3.12 (2H, s, CH_2Ph), 4.05 (2H, q, J=7.0 Hz, Et), 7.1—7.6 (10H, m, Ph), and 7.97 (1H, s, CH=N); ^{13}C NMR ($CDCl_3$) δ=14.30 (q, Et), 20.18, 33.88, 39.53, 46.47 (each t, CH_2), 60.53 (t, Et), 68.83 (s, q-C), 118.65 (s, CN), 127.66, 128.36, 128.95, 131.19, 131.71 (each d), 134.42, 135.19 (each s), 161.30 (d, CH=N), and 173.07 (s, COOEt); MS m/z (rel intensity, %) 254 (M^+−94, 11), 253 (62), 233 (50), 143 (68), 116 (30), 91 (base peak), 88 (17), 85 (30), 83 (43), and 77 (16). Elemental analysis based on HRMS could not be performed because of the absence of the parent ion peak.

11: Colorless liquid; IR (neat) 2260, 1735, and 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.20 (3H, t, J=7.0 Hz, Et), 1.3—2.3 (8H, m, CH_2), 1.60 (3H, s, Me), 4.03 (2H, q, J=7.0 Hz, Et), 7.2—7.4 (3H, m, Ph), 7.30 (2H, m, Ph), and 8.40 (1H, s, CH=N); MS m/z (rel intensity, %) 286 (M^+, 6), 172 (17), 158 (59), 157 (base peak), 143 (57), 130 (29), 116 (70), and 77 (88). HRMS Found: m/z 286.1686. Calcd for $C_{17}H_{22}N_2O_2$: M, 286.1681.

General Procedure for Hydrolytic Cyclization of 10 Leading to 12 and Hydrolysis of 11 into 13. A solution of **10a**, **10b**, or **11** (1 mmol) in methanol (3 ml) was heated under reflux in the presence of a catalytic amount of concentrated hydrochloric acid. The mixture was poured into water and extracted with dichloromethane (15 ml×2). The combined extracts were washed with water, dried over magnesium sulfate, and evaporated in vacuo. Evaporation of the solvent gave solid of **12** which was purified by crystallization. The residue containing **13** was purified by column chromatography over silica gel by using chloroform as an eluent. The reaction time and yield were as follows: **12a**: 7.5 h, 78%; **12b**: 6 h, 58%; **13**: 6 h, 78%.

12a: Colorless prisms (chloroform–hexane); mp 175—176 °C; IR (KBr) 3220, 2460, and 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.66 (3H, s, Me), 1.8—2.6 (6H, m, CH_2), and 7.65 (1H, br, NH); MS m/z (rel intensity, %) 138 (M^+, 42), 123 (89), 82 (10), 70 (35), 55 (base peak), and 43 (74). Found: C, 60.95; H, 7.32; N, 20.08%. Calcd for $C_7H_{10}N_2O$: C, 60.85; H, 7.30; N, 20.28%.

12b: Colorless prisms (chloroform–hexane); mp 215—216 °C; IR (KBr) 3200 2430, and 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.8—2.5 (6H, m, CH_2), 2.95, 3.15 (each 1H, d, J=15.0 Hz, CH_2Ph), 6.40 (1H, br, NH), and 7.25 (5H, s, Ph); ^{13}C NMR ($CDCl_3$) δ=18.30, 30.88, 33.24, 46.77 (each t, CH_2), 56.30 (s, q-C), 120.36 (s, CN), 128.60, 129.30, 130.65 (each d), 132.18 (s), and 171.36 (s, CO); MS m/z (rel intensity, %) 214 (M^+, 12), 123 (28), 91 (base peak), 65 (46), 55 (43), and 43 (26). Found: C, 72.69; H, 6.49; N, 12.79%. Calcd for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59; N, 13.08%.

13: Colorless liquid; IR (neat) 3500, 3400, 3200, 2250, and 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.22 (3H, t, J=7.0 Hz, Et), 1.5—1.7 (4H, m, CH_2), 2.10 (3H, s, Me), 2.2—2.5 (4H, m, CH_2), 4.05 (2H, q, J=7.0 Hz, Et), and 7.35 (2H, br, NH_2); MS m/z (rel intensity, %) 172 (M^+−26, 17), 127 (31), 126 (17), 116 (27), 112 (11), 101 (22), 87 (11), 84 (14), 81 (23), 73 (14), and 43 (base peak). Elemental analysis by HRMS was not available because of the absence of the parent ion.

General Procedure for Base-Induced Cyclization of Alkylated Imines 2 Leading to 14. To a solution of appropriate base was added an imine **2** (1 mmol) at −78 °C: Method A: Imine **2** (in 2 ml of THF) was added to *t*-BuOK (1.1 mmol in THF (2 ml)); Method B: Imine **2** (in 2 ml of THF) was added to LDA (1 mmol) freshly prepared in THF (3 ml); Method B (MeI): Imine **2** (in 4 ml of THF) and then MeI (1.1 mmol in THF (0.6 ml)) were added to LDA (1.5 mmol in 7 ml); Method C: Lithium iodide (1 mmol) and then imine **2** (in 2 ml of THF) was added to LDA (1 mmol in THF (3 ml)); Method D: Imine **2** (in 5 ml of THF) was added to benzyltrimethylammonium methoxide (BTAM, 1 mmol in THF (1 ml)); Method E: Tetrabutylammonium fluoride (TBAF, 1M† solution in THF, 0.1 ml, 0.1 mmol) was added to imine **2** (in 5 ml of THF); Method F: TBAF (0.1 ml, 0.1 mmol) was added at 0 °C to imine **2** (in 5 ml of HMPA). The resulting mixture was stirred under the conditions listed in Table 3 and poured into ice water. The products were collected in dichloromethane (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 or chloroform–diethyl

† 1 M=1 mol dm^{-3}.

ether as an eluent to give **14**. Pyrrolines **14a**, **14d**, **14d'**, **14e**, **14k**, **14l**, **14n**, and **14o** are all known.[10]

14b: Pale yellow liquid; IR (neat) 1735 and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.55 (1H, dd, J=18.0 and 9.0 Hz, one of 3-H), 3.03 (3H, s, COOMe), 3.3—3.7 (2H, m, 4-H and the other of 3-H), 3.80 (2H, s, CH_2Ph), 5.43 (1H, d, J=9.0 Hz, 5-H), and 6.9—7.3 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=39.23, 40.65 (each t, 3-C and CH_2Ph), 48.18 (d, 4-C), 51.18 (q, COOMe), 78.24 (d, 5-C), 127.07, 127.65, 128.13, 128.95, 129.30 (each d), 136.54, 138.77 (each s), 172.59 (s, 2-C), and 177.48 (s, COOMe); MS m/z (rel intensity, %) 293 (M^+, 51), 234 (57), 207 (36), 206 (22), 115 (18), 105 (23), and 91 (base peak). HRMS Found: m/z 293.1391. Calcd for $C_{19}H_{19}NO$: M, 293.1413.

14c+14c' (a 2:1 mixture): Yellow liquid; IR (neat) 1730 and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.20 (1/3×6H, d, J=7.0 Hz, *i*-Pr), 1.25 (2/3×6H, d, J=7.0 Hz, *i*-Pr), 2.5—3.0 (3H, m, *i*-Pr and 3-H), 3.07 (2/3×3H, s, COOMe), 3.2—3.6 (1H, m, 4-H), 3.66 (1/3×3H, s, COOMe), 5.22 (1/3H, t, J=3.0 Hz, 5-H), 5.40 (2/3H, d, J=9.0 Hz, 5-H), and 6.9—7.4 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=20.24 (q, *i*-Pr), 32.65 (d, *i*-Pr), 38.01, 39.30 (each t, 2:1, 3-C), 48.06, 50.94 (each d, 2:1, 4-C), 51.24, 52.18 (each q, 2:1, COOMe), 77.82, 78.95 (each d, 2:1, 5-C), 126.48, 127.54, 128.07, 128.65 (each d), 138.89, 143.31 (each s), 172.83, 174.89 (each s, 2:1, COOMe), 181.95, and 183.60 (each s, 1:2, 2-C); MS m/z (rel intensity, %) 245 (M^+, 63), 214 (15), 186 (57), 159 (base peak), 117 (79), 91 (19), and 90 (34). HRMS Found: m/z 245.1368. Calcd for $C_{15}H_{19}NO_2$: M, 245.1413.

14e+14e' (a 4:1 mixture): Pale yellow liquid; IR (neat) 1735 and 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.10 (3H, m, Et), 1.4—1.9 (2H, m, Et), 2.5—3.7 (3H, m, 3- and 4-H), 3.70 (3H, s, COOMe), 4.45 (1H, m, 5-H), 7.2—7.6 (3H, m, Ph), and 7.7—7.9 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) **14e**: δ=11.59 (q, Et), 25.41 (t, Et), 38.06 (t, 3-C), 45.83 (d, 4-C), 51.65 (q, COOMe), 75.65 (d, 5-C), 127.89, 128.60, 130.77 (each d), 134.30 (s), 171.01 (s, 2-C), and 173.72 (s, COOMe); **14e'**: δ=10.41 (q, Et), 25.41 (t, Et), 38.06 (t, 3-C), 45.83 (d, 4-C), 51.65 (q, COOMe), 75.95 (d, 5-C), 127.89, 128.60, 130.77 (each d), 134.30 (s), 171.01 (s, 2-C), and 173.72 (s, COOMe); MS m/z (rel intensity, %) 231 (M^+, 33), 216 (24), 202 (36), 172 (72), 145 (42), 144 (42), 143 (38), 130 (base peak), 117 (24), 115 (41), 104 (70), and 77 (45). HRMS Found: m/z 231.1262. Calcd for $C_{14}H_{17}NO_2$: M, 231.1258.

14f+14f' (a 3:2 mixture): Pale yellow liquid; IR (neat) 1725 and 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.00 (3/5×9H, s *t*-BuOOC), 1.46 (2/5×9H, s, *t*-BuOOC), 2.17 (6H, d, J=2.0 Hz, Me), 2.5—3.7 (3H, m, 3- and 4-H), 5.25 (2/5H, br s, 5-H), 5.45 (3/5H, d, J=10.0 Hz, 5-H), and 7.1—7.4 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=19.60 (q, *t*-Bu), 27.44, 28.08 (each q, 2-Me), 42.36, 42.94 (each t, 3-C), 49.73, 52.36 (each d, 4-C), 78.34 (s, *t*-Bu), 79.62, 80.44 (each d, 5-C), 126.37, 127.13, 128.00, 128.47 (each d), 139.12, 143.27 (each s), 171.18, 173.23, 173.93, and 174.98 (each s, 2-C and COOBu-*t*); MS m/z (rel intensity, %) 259 (M^+, 7), 227 (15), 222 (18), 204 (22), 203 (base peak), 201 (53), 158 (53), and 157 (40). HRMS Found: m/z 259.0771. Calcd for $C_{21}H_{16}NO_2$: M, 259.0774.

14g': Colorless liquid; IR (neat) 1710 and 1640 cm^{-1}: ^1H NMR ($CDCl_3$) δ=2.10 (3H, s, COMe), 2.6—3.3 (3H, m, 3- and 4-H), 3.80 (2H, br s, $PhCH_2$), 5.25 (1H, br d, J=6.0 Hz, 5-H), and 7.2—7.4 (10H, m, Ph); MS m/z (rel intensity, %) 277 (M^+, 1), 249 (5), 248 (22), 234 (26), 186 (32), and 105 (base peak). Elemental analysis by HRMS could not be achieved because of the weak parent ion peak.

14h': Yellow liquid; IR (neat) 1710 and 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.10 (3H, s, COMe), 3.28 (3H, m, 3- and 4-H), 5.33 (1H, ddd, J=5.0, 3.2, and 2.0 Hz, 5-H), 7.1—7.5 (8H, m, Ph), and 7.85 (2H, m, Ph); MS m/z (rel intensity, %) 263 (M^+, 14), 221 (17), 220 (base peak), 193 (41), 117 (11), and 115 (16). HRMS Found: m/z 263.1303. Calcd for $C_{18}H_{17}NO$: M, 263.1308.

14i': Pale yellow liquid; IR (neat) 1710 and 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.04 (3H, t, J=7.0 Hz, Et), 1.5—2.0 (2H, m, Et), 2.16 (3H, s, COMe), 2.9—3.4 (3H, m, 3- and 4-H), 4.29 (1H, m, 5-H), 7.2—7.6 (3H, m Ph), and 7.7—7.9 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=10.35 (q, Et), 28.65 (q, COMe), 29.47 (t, Et), 37.30 (t, 3-C), 54.42 (d, 4-C), 77.30 (d, 5-C), 127.71, 128.42, 130.60 (each d), 133.95 (s), 170.19 (s, 2-C), and 207.89 (s, COMe); MS m/z (rel intensity, %) 215 (M^+, 4), 172 (22), 144 (43), 143 (61), 130 (42), 117 (24), 116 (33), 115 (base peak), 104 (73), 103 (41), 89 (24), 77 (50), 76 (24), 63 (22), and 55 (32). HRMS Found: m/z 215.1331. Calcd for $C_{14}H_{17}NO$: M, 215.1309.

14i+14i': This mixture (1:2) was identified on the basis of ^1H NMR in $CDCl_3$: δ=1.04 (3H, J=7.0 Hz, Et), 1.60 (1/3×2H, q, J=7.0 Hz, Et), 1.80 (2/3×2H, q, J=7.0 Hz, Et), 2.10 (3H, s, MeCO), 2.8—3.6 (3H, m, 3- and 4-H), 4.30 (2/3H, m, 5-H), 4.56 (1/3H, m, 5-H), 7.3—7.4 (3H, m, Ph), and 7.8—7.9 (2H, m, Ph). The signal at 4.30 ppm (5-H of **14i'**) showed a 15% of NOE enhancement when the acetyl signal at 2.10 ppm was irradiated, confirming the 4,5-trans structure of **14i'**.

14j+14j' (a 10:1 mixture): Pale yellow liquid; IR (neat) 2240 and 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.13 (3H, t, J=7.0 Hz, Et), 1.7—2.2 (2H, m, Et), 2.6—2.9 (2H, m, 3-H), 3.40 (1H, m, 4-H), 4.30 (1H, m, 5-H), 7.3—7.6 (3H, m, Ph), and 7.7—7.9 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=11.29 (q, Et), 26.71 (t, Et), 31.00 (d, 4-C), 40.30 (t, 3-C), 74.77 (d, 5-C), 116.77 (s, CN), 127.95, 128.89, 129.07, 129.42 (each d), 131.42, 133.36 (each s), and 169.77 (s, 2-C); MS m/z (rel intensity, %) 198 (M^+, 3), 130 (60), 115 (25), 105 (26), 104 (58), 103 (44), 77 (base peak), 76 (30), and 63 (24). HRMS Found: m/z 198.1161. Calcd for $C_{13}H_{14}N_2$: M, 198.1159.

14l+14l': All data of **14l** were presented in Ref. 10. Formation of **14l'** was deduced on the basis of ^1H NMR ($CDCl_3$) of the mixture with **14l**: δ=1.30 (3H, d, J=7.0 Hz, 3-Me), 2.05 (3H, d, J=2.0 Hz, 2-Me), 3.65 (3H, s, COOMe) and 5.10 (1H, m, 5-H). The other signals are overlapping with those of **14l**.

14m: Pale yellow liquid; IR (neat) 1735 and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.16 (3H, d, J=7.0 Hz, Me), 3.0—4.0 (4H, m, CH_2Ph, 3-H, and 4-H), 3.07 (3H, s, COOMe), 5.45 (1H, d, J=9.0 Hz, 5-H), and 7.0—7.4 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=16.53 (q, Me), 38.36 (t, CH_2Ph), 46.27 (d, 3-C), 51.18 (q, COOMe), 57.04 (d, 4-C), 75.71 (d, 5-C), 126.60, 128.13, 128.65, 128.89, 129.36, 131.30 (each d), 136.36, 138.21 (each s), 172.18 (s, COOMe), and 180.60 (s, 2-C); MS m/z (rel intensity, %) 307 (M^+, 15), 248 (20), 207 (29), 206 (19), 131 (19), 130 (16), 115 (14), 105 (32), 91 (base peak), and 76 (31). HRMS Found: m/z 307.1569. Calcd for $C_{20}H_{21}NO_2$: M, 307.1570.

14n+14n' (a 1:3 mixture): All data of **14n** were presented in Ref. 10. ^1H NMR ($CDCl_3$) of **14n'** was abstracted from that of the mixture with **14n**: δ=1.30 (3H, d, J=7.0 Hz, Me),

2.80 (1H, t, J=6.2 Hz, 4-H), 3.76 (3H, s, COOMe), 3.85 (1H, m, 3-H), 5.53 (1H, dd, J=6.2 and 1.5 Hz, 5-H), 7.2—7.5 (8H, m, Ph), and 7.85 (2H, m, Ph).

14o+14o' (a 3:2 mixture): Pale yellow liquid; IR (neat) 1730 and 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.9—1.4 (6H, m, Et and Me), 1.5—2.0 (2H, m, Et), 2.50 (2/5H, t, J=6.0 Hz, 4-H), 2.96 (3/5H, dd, J=8.0 and 4.2 Hz, 4-H), 3.63 (2/5×3H, s, COOMe), 3.68 (3/5×3H, s, COOMe), 3.6—4.0 (1H, m, 3-H), 4.27 (1H, m, 5-H), 7.2—7.6 (3H, m, Ph), and 7.7—7.9 (2H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=10.71, 11.88 (each q, 2:3, Et), 17.53, 19.71 (each q, 3:2, Me), 25.41, 29.94 (each t, 3:2, Et), 45.89, 47.06 (each d, 2:3, 3-C), 51.59, 52.12 (each q, 3:2 COOMe), 54.89, 55.89 (each d, 3:2, 4-C), 74.12, 76.77 (each d, 2:3 5-C), 128.25, 128.65, 130.48 (each d), 133.71, 133.95 (each s), 173.83, 174.60, and 175.66 (each s, 2-C and COOMe); MS m/z (rel intensity, %) 245 (M^+, 77), 216 (22), 186 (94), 158 (21), 145 (base peak), 131 (24), 130 (95), 127 (24), and 104 (41). HRMS Found: m/z 245.1414. Calcd for $C_{15}H_{19}NO_2$: M, 245.1415.

General Procedure for LDA-Induced Cyclization of 10 Leading to 15. To a solution of LDA (in THF 3 ml) freshly prepared from butyllithium and diisopropylamine (each 1 mmol) was added at −78 °C **10a** or **10b** (1 mmol) in THF (2 ml). After 30 min at −78 °C the mixture was stirred under nitrogen at room temperature for 6 h. The reaction was quenched with saturated aqueous ammonium chloride and extracted with diethyl ether (20 ml×2). The combined extracts were dried over anhydrous magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel to give **15a** or **15b** (**15a**: 37%; **15b**: 25%).

15a (a 2:1 mixture of stereoisomers): Yellow liquid; IR (neat) 1730, 1660, and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.04 (3H, t, J=7.0 Hz, Et), 1.5—3.0 (5H, m, CH_2 and 5-H), 2.02 (1/3×3H, d, J=2.0 Hz, Me), 2.06 (2/3×3H, d, J=2.0 Hz, Me), 3.90 (2H, m, Et), 4.67 (1/3H, br d, J=9.0 Hz, 6-H), 5.10 (2/3H, br d, J=5.0 Hz, 6-H), and 6.9—7.5 (5H, m, Ph); MS m/z (rel intensity, %) 245 (M^+, 96), 172 (60), 145 (40), 144 (28), and 104 (base peak). HRMS Found: m/z 245.1406. Calcd for $C_{15}H_{19}NO_2$: M, 245.1413.

15b Yellow liquid; IR (neat) 1725 and 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.03 (3H, t, J=7.0 Hz, Et), 1.6—3.0 (5H, m, CH_2 and 5-H), 3.60 (2H, br s, CH_2Ph), 4.80 (1H, br d, J=10.0 Hz, 6-H), and 7.25 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=14.00 (q, Et), 22.29 (d, 4-C), 27.12 (d, CH_2Ph), 46.89 (t, 3-C), 48.06 (d, 5-C), 60.53 (t, Et), 64.06 (d, 6-C), 126.95, 127.36, 127.60, 128.30, 128.60, 128.89, 129.24, 131.13, 137.71, 143.07, 170.30 (s, 2-C), and 174.42 (s, COOEt); MS m/z (rel intensity, %) 321 (M^+, 46), 248 (56), 220 (19), 130 (35), 116 (29), 91 (base peak), and 77 (32). HRMS Found: m/z 321.1724. Calcd for $C_{21}H_{23}NO_2$: M, 321.1727.

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