JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Chemoselective Intramolecular Alkylation of the Blaise Reaction Intermediates: Tandem One-Pot Synthesis of *exo*-Cyclic Enaminoesters and Their Applications toward the Synthesis of *N*-Heterocyclic Compounds

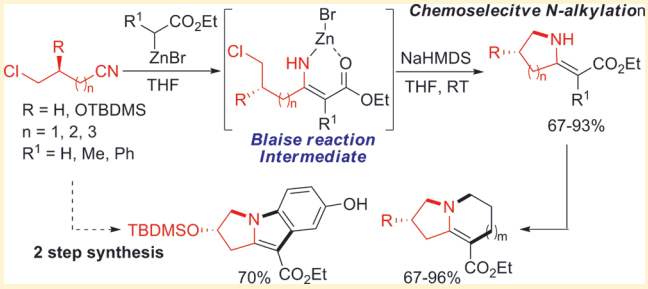
Ju Hyun Kim,[†] Hyunik Shin,*[,‡] and Sang-gi Lee*[,†]

[†]Department of Chemistry and Nano Science (BK21), Ewha Womans University, 125-750 Seoul, Korea

[‡]Chemical Development Division, LG Life Sciences, Ltd. R&D, Daejeon 305-380, Korea

Supporting Information

ABSTRACT: The intramolecular alkylative reactivity and N/C selectivity of the various Blaise reaction intermediates, which are formed from the reaction of the Reformatsky reagents with ω-chloroalkyl nitriles, did not reach the synthetic potential as an entry to *exo*-cyclic enaminoesters. To circumvent this issue, various additives were investigated, among which the addition of NaHMDS dramatically enhanced the reactivity and N/C selectivity. This modification provided a highly efficient route for the synthesis of various *N*-fused heterocyclic compounds, as it requires only two steps from nitriles.



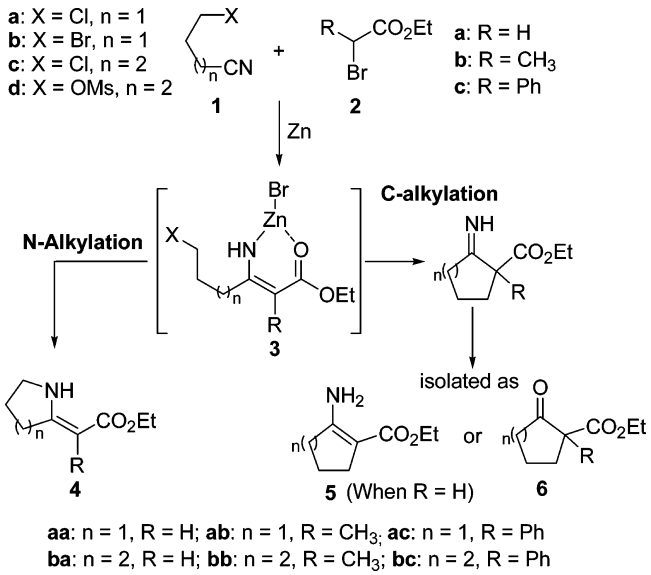
The *exo*-cyclic enaminoesters are highly versatile intermediates in the synthesis of *N*-heterocyclic fragments that are embedded in many useful pharmaceuticals and natural products.[1] Synthetic approaches to *exo*-cyclic enaminoesters mainly rely either on the use of existing *N*-heterocycles or on construction of the *N*-heterocyclic moiety via intramolecular ring closure reactions. Reaction of a thiolactam with a bromo methyl ketone or ester followed by sulfur extrusion in the presence of triphenylphosphine (Eschenmoser sulfide contraction)[2] or condensation of organometallic reagents with lactams or thiolactames are the most frequently employed approach for the synthesis of *exo*-cyclic enaminoesters.[3] Condensation reactions of lactim ethers with active methylene compounds have also been developed.[4] In contrast to the former methods, synthesis of *exo*-cyclic enaminoesters using ring closure reactions has been reported in only a few cases. Carrie and co-workers[5a] reported an approach utilizing the intramolecular aza-Wittig reaction of ω-azido β-dicarbonyls, which were prepared through lengthy steps of the γ-alkylation of β-dicarbonyl dianions with α,ω-dihaloalkane compounds followed by a nucleophilic substitution by sodium azide.[5] Other syntheses include, for example, intramolecular dehydrative cyclization of ω-amino β-dicarbonyls, which are accessible from the aziridine ring-opening with 1,3-dicarbonyl dianions,[6a] reaction of *N*-Boc-protected γ-lactam with lithium enolate of acetate or ketones,[6b] or lactone ring transformations.[6c] However, these ring-closing strategies generally require multistep syntheses of the cyclization precursors, and thus, the development of a new efficient method to construct *exo*-cyclic enaminoester moiety from readily available compounds remains a subject of significant interest. Herein, we report a general one-pot synthesis of *exo*-cyclic enaminoesters from the readily available chloroalkylnitriles through the chemoselective intramolecular *N*-alkylation of the Blaise reaction intermediate.

We recently envisioned that the Blaise reaction intermediates (the enaminozincate intermediates),[7] which are formed from the reaction of a Reformatsky reagent with a nitrile, could be a reactive aza-analogues of the zinc enolate of β-ketoesters, and we were intrigued by the possible use of the intermediate as a modular platform for tandem carbon−carbon and/or carbon−nitrogen bond-forming reactions via chemoselective electrophilic trapping reactions.[8] In this respect, we anticipated that chemoselective intramolecular *N*-alkylative trapping of the Blaise reaction intermediates, formed from ω-haloalkylnitriles and Reformatsky reagents, could be an efficient route for the construction of the *exo*-cyclic enaminoester moiety. In this regard, Kishi's work is the only precedent, in which it has been stated that "in situ alkylation of the initial adduct offers an additional synthetic application for the Blaise reaction".[9] Although the intramolecular alkylative trapping concept has been addressed, the reported successful results were on the alkylation of zinc salt-free enaminoesters. Therefore, a more detailed study on the intramolecular *C*- vs *N*-alkylation selectivity of the divalent Blaise reaction intermediate and on its reactivity has yet to be performed (Scheme 1). Herein, we describe intramolecular alkylative reactivity profile of the Blaise reaction intermediate and its modification, which led to highly valuable chemoselective intramolecular *N*-alkylative trapping

Received: September 27, 2011
Published: January 9, 2012

 © 2012 American Chemical Society dx.doi.org/10.1021/jo201964a | *J. Org. Chem.* 2012, 77, 1560−1565

Scheme 1. Intramolecular Alkylative Trapping Reactions of the Blaise Reaction Intermediate

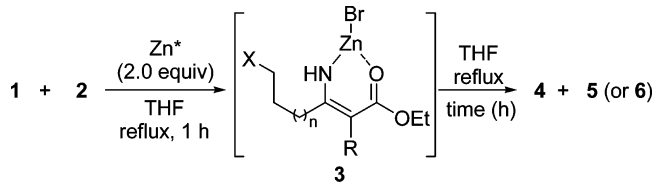


reactions affording *exo*-cyclic enaminoesters, which can be used toward the synthesis of *N*-heterocyclic compounds.

To investigate the reactivity and chemoselectivity of the intramolecular alkylative trapping reactions, the Blaise reaction intermediates **3** having different tether lengths and leaving groups were prepared by reaction of nitrile **1** with a Reformatsky reagent, generated in situ from α-bromoesters **2** (Table 1). The intrinsic reactivity of the Blaise reaction intermediate toward intramolecular alkylations (entries 1−8, Table 1) was investigated first, and we found that chemoselectivity was dependent on both tether length and the α-substituent R. Thus, the Blaise reaction intermediates with no α-substituents, **3aa** (n = 1, R = H, X = Cl), **3ba** (n = 1, R = H, X = Br), **3ca** (n = 2, R = H, X = Cl), and **3da** (n = 2, R = H, X = OMs), provided the corresponding *C*-cyclized cyclic enaminoesters **5aa** or **5ba** as a major product (entries 1−4, Table 1). In contrast, the Blaise intermediates **3ab** (X = Cl, n = 1, R = Me) having α-Me substituent afforded the *N*-cyclized five-membered *exo*-enaminoesters **4ab** in 46% yield as a mixture of the (*E*)/(*Z*)-isomers, which could be separated by silica column chromatography (entry 5, Table 1). Similarly, from the tandem reaction with α-Ph substituted **3ac** (n = 1, X = Cl, R = Ph), the *N*-alkylated (*Z*)-**4ac** was formed as a major product in 42% yield (entry 6, Table 1). However, alkylation of the Blaise reaction intermediate **3cb** (X = Cl, n = 2, R = Me) with the α-Me substituent and the C_4-tether length (n = 2) still afforded the *C*-alkylated product. Thus, the cyclohexanone **6bb** (the initially formed imine was hydrolyzed during the workup) was isolated in 45% yield along with small amount of *N*-cyclized product **4bb** (entry 7, Table 1). When the Blaise reaction intermediate **3cc** (X = Cl, n = 2, R = Ph) was used, the *N*-cyclized **4bc** and *C*-cyclized **6bc** were formed in almost a 1:1 ratio (entry 8, Table 1). In general, the reactivity of the unmodified Blaise reaction intermediate toward alkylation was insufficiently high to efficiently accomplish the intramolecular S_N2 alkylation; in fact, it took prolonged reaction time at reflux.

To increase reactivity and chemoselectivity, we next investigated the additive effect on this transformation. We found that addition of sodium hexamethyldisilazide (NaHMDS) dramatically increased not only the reactivity, but also the chemoselectivity. After varying the amount of NaHMDS (entries 1−4, Table 2), we found that addition of 3.5 equiv of NaHMDS to the Blaise reaction intermediate **3aa** at 0 °C followed by reaction for 5 h at room temperature afforded a 93% yield of the *N*-cyclized *exo*-enaminoester **4aa** (entry 4, Table 2). Although the reason for the excess amounts (3.5 equiv) of NaHMDS and its exact role are not yet clear, it may be associated with the proton exchange of its conjugate acid, HMDS, with the deprotonated Blaise reaction intermediate, which may have dianionic properties, and is probably more basic than NaHMDS. Thus, shifting the equilibrium to the deprotonated Blaise intermediate could be one of the limiting factors of efficient intramolecular alkylations.[10] The use of LiHMDS did not change the chemoselectivity, but decreased the yield of **4aa** to 55% (entry 5, Table 2). Other organolithium, inorganic, and organic bases such as ^{t}BuLi, nBuLi, K_2CO_3, Na_2CO_3, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), diisopropylethylamine (DIEA), and triethylamine were not as effective as NaHMDS (entries 6−12, Table 2).

Table 1. Chemoselectivity in Intramolecular *N*-Alkylation of the Blaise Reaction Intermediate 3[a]

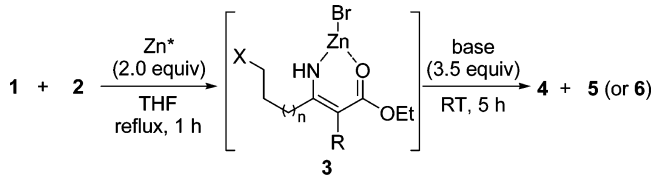


entry	1	2	3	time (h)[b]	*N*-alkylation **4** (%)[c]	*C*-alkylation **5** (or **6**) (%)[c]
1	**1a**	**2a**	**3aa**	14	**4aa** (6)	**5aa** (29)
2	**1b**	**2a**	**3ba**	8	**4aa** (−)	**5aa** (40)
3	**1c**	**2a**	**3ca**	6	**4ba** (−)	**5ba** (37)
4	**1d**	**2a**	**3da**	4	**4ba** (−)	**5ba** (62)
5	**1a**	**2b**	**3ab**	9	**4ab** (46)[d]	**6ab** (<5)
6	**1a**	**2c**	**3ac**	8	**4ac** (42)	**6ac** (<5)
7	**1c**	**2b**	**3cb**	7	**4bb** (<5)	**6bb** (45)
8	**1c**	**2c**	**3cc**	8	**4bc** (20)	**6bc** (25)

[a]Reaction conditions: **1** (3.82 mmol), **2** (4.97 mmol), Zn (7.65 mmol, preactivated with 6.5 mol % of methanesulfonic acid) in THF (1.5 mL) at reflux temperature. [b]Time for disappearance of the Blaise reaction intermediate, determined by GC after treatment the sample with saturated aqueous NH_4Cl solution. [c]Isolated yield after chromatographic purification. [d]A mixture of (*E*)- and (*Z*)-isomers.

dx.doi.org/10.1021/jo201964a | *J. Org. Chem.* 2012, 77, 1560−1565

Table 2. Intramolecular Alkylation of the Blaise Reaction Intermediate 3 in the Presence of Base[a]



entry	1	2	3	base	*N*-alkylation **4** (%)[b]	*C*-alkylation **5** (or **6**) (%)[b]
1[c]	**1a**	**2a**	**3aa**	NaHMDS	**4aa** (−)	**5aa** (−)
2[c,d]	**1a**	**2a**	**3aa**	NaHMDS	**4aa** (12)	**5aa** (17)
3[e]	**1a**	**2a**	**3aa**	NaHMDS	**4aa** (24)	**5aa** (−)
4	**1a**	**2a**	**3aa**	NaHMDS	**4aa** (93)	**5aa** (−)
5	**1a**	**2a**	**3aa**	LiHMDS	**4aa** (55)	**5aa** (−)
6	**1a**	**2a**	**3aa**	^{t}BuLi	**4aa** (14)	**5aa** (>5)
7	**1a**	**2a**	**3aa**	*n*BuLi	**4aa** (28)	**5aa** (>5)
8	**1a**	**2a**	**3aa**	K_2CO_3	**4aa** (−)	**5aa** (−)
9	**1a**	**2a**	**3aa**	Na_2CO_3	**4aa** (−)	**5aa** (−)
10	**1a**	**2a**	**3aa**	DBU	**4aa** (23)	**5aa** (>5)
11	**1a**	**2a**	**3aa**	DIEA	**4aa** (>5)	**5aa** (>5)
12	**1a**	**2a**	**3aa**	Et_3N	**4aa** (7)	**5aa** (−)
13	**1a**	**2a**	**3aa**	*t*-BuOK	**4aa** (68)	**5aa** (13)
14	**1a**	**2b**	**3ab**	NaHMDS	**4ab** (74)	**6ab** (>5)
15	**1a**	**2c**	**3ac**	NaHMDS	**4ac** (71)	**6ac** (>5)
16	**1c**	**2a**	**3ca**	NaHMDS	**4ba** (10)	**5ba** (42)
17	**1c**	**2b**	**3cb**	NaHMDS	**4bb** (72)	**6bb** (−)
18	**1c**	**2c**	**3cc**	NaHMDS	**4bc** (67)	**6bc** (−)

[a]Unless otherwise noted, the Blaise reaction intermediate **3** was prepared by reaction with **1** (3.82 mmol), **2** (4.97 mmol), Zn (7.65 mmol, preactivated with 6.5 mol % of methanesulfonic acid) in THF (1.5 mL), and after addition of 3.5 equiv of base at 0 °C, the reaction was continued for 5 h at room temperature. [b]Isolated yield after chromatographic purification. [c]Reaction with 1.0 equiv of base. [d]Reaction was carried out at THF reflux. [e]Reaction with 2.0 equiv of base.

Under these reaction conditions, the unreacted Blaise reaction intermediate **3aa** could be isolated as ethyl 2-amino-6-chloro-2-hexenoate. As we observed in Pd-catalyzed arylative intramolecular trapping of the Blaise reaction intermediate,[11] *t*-BuOK is reasonably effective for chemoslective intramolecular alkylation of the Blaise reaction intermediate (entry 13, Table 2). In the same manner, the yields of **4ab** and **4ac** formation also increased significantly in the presence of NaHMDS (entries 14 and 15, Table 2). However, in the case of the α-unsubstituted Blaise reaction intermediate **3ca** (X = Cl, *n* = 2, R = H) with a four-carbon tether length, although the *N*-selectivity was slightly improved, the *C*-alkylated compound **5ba** was still formed as a major product (entry 16, Table 2). In contrast, the α-substituted Blaise reaction intermediates **3cb** (X = Cl, *n* = 2, R = Me) and **3cc** (X = Cl, *n* = 2, R = Ph) were cyclized with high *N*-selectivity to afford the corresponding six-membered *exo*-enaminoesters **4bb** with 67% (entry 17, Table 1) and **4bc** with 72% yields (entry 18, Table 1). Noteworthy is that in the presence of NaHMDS, all *N*-cyclized products have (*Z*)-geometry, suggesting that the zinc bromide complex persists during the cyclization process.

The chemoselectivity observed from the intramolecular alkylation of the unmodified Blaise reaction intermediate may have originated from stereoelectronic factors. For the α-unsubstituted intermediates **3aa** and **3ba** (*n* = 1, R = H), the intramolecular S_N2 alkylation reaction may proceed via conformation **A** (Figure 1), which is stereoelectronically favorable for *C*-cyclization and affords **5aa** as a major product. In contrast, when R = Me or Ph, there is steric repulsion between R and X in conformation **A**, and the *N*-cyclization would be dominant via conformation **B**. The *C*-cyclization

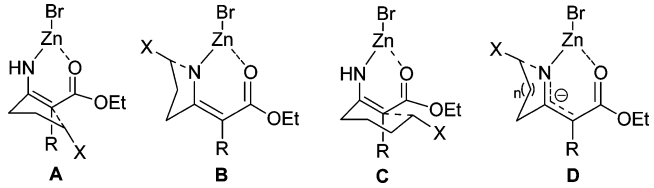


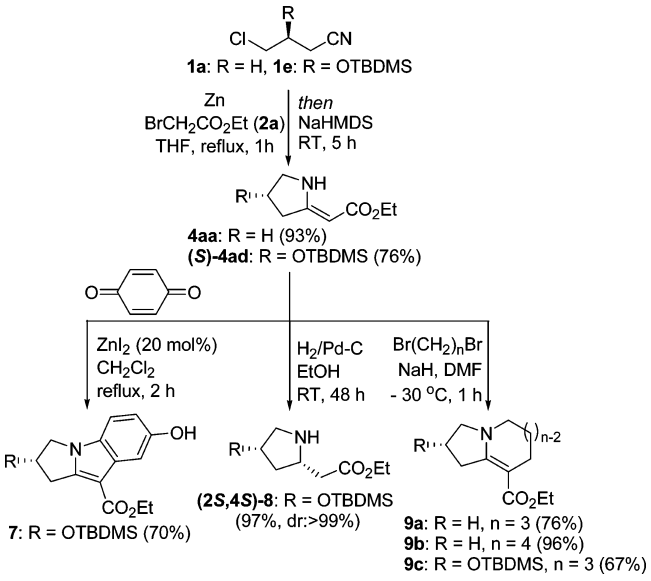
Figure 1. Plausible transition state conformations for the observed chemoselectivity in intramolecular alkylation of the Blaise reaction intermediates.

remained dominant when the tether length is *n* = 2, contributing to the formation of stable chair conformation **C**. In contrast, the observed *N*-alkylative chemoselectivity in the presence of NaHMDS could be attributed to the fact that deprotonation of acidic N−H could generate the enamino anion **D**, in which the anion may be placed dominantly at carbon atom to minimize the electronic repulsion with the N−zinc bonding electrons generating an appropriate S_N2 reaction trajectory to afford the *N*-cyclized products **4aa**−**ac** and **4bb**,**bc**. In the case of α-unsubstituted **3ca** (X = Cl, *n* = 2, R = H) with a four-carbon tether length, the stable chair conformation remains dominant, affording the *C*-cyclized product **5ba** as a major product.

The synthetic utility of the chemoselective intramolecular *N*-alkylative trapping reactions of the modified Blaise reaction intermediate has been demonstrated by two-step synthesis of a variety of *N*-heterocyclic compounds from nitriles (Scheme 2). The chiral *exo*-cyclic enaminoester **4ad** was synthesized in 76% yield through the intramolecular alkylative trapping of the Blaise reaction intermediate **3ea**, formed from chiral *O*-

dx.doi.org/10.1021/jo201964a | J. Org. Chem. 2012, 77, 1560−1565

Scheme 2. Two-Step Syntheses of *N*-Hetrocyclic Compounds via the *N*-Alkylative Trapping Reactions of the Blaise Reaction Intermediates



TBDMS-protected (3*S*)-4-chloro-3-hydroxybutyronitrile (**1e**), which was prepared using commercial epichlorohydrin.[12] The Nenitzescu reaction of **4ad** with 1,4-benzoquinone in the presence of 20 mol % of ZnI_2 afforded the *N*-fused indole **7** in 70% yield.[13] Hydrogenation of the *exo*-double bond of (*S*)-**4ad** in the presence of Pd−C catalyst provided (2*S*,4*S*)-**8** in 97% yield with >99% diastereoselectivity. The absolute stereochemistry was determined, after conversion to *N*-Cbz-protected pyrrolidine (*N*-CBz-**8**), by comparing the optical rotation with the reported (2*R*,4*R*)-*N*-Cbz-**8** {$[\alpha]_D^{20}$ = +13 (*c* = 1.02, EtOAc)}.[14] Optical rotation of the synthesized *N*-Cbz-**8** exhibited levorotatory {$[\alpha]_D^{24}$ = −11.8 (*c* = 10.0, EtOAc)}, indicating that the absolute stereochemistry of **8** is to be (2*S*,4*S*)-configuration, which suggests that the hydrogenation was proceeded *anti*-selectively as observed in the diastereoselective hydrogenation of ethyl (4-methoxypyrrolidin-2-ylidene)-acetate.[15] The 4-hydroxy homoprolines were used as the key intermediates for the synthesis of sequence-selective DNA-binding agents as potential antitumor drugs and antibiotics.[16] Compared to the reported four-step synthesis of **8** starting from 4-hydroxy-2-pyrrolidinone, which was reportedly the shortest synthetic procedure,[17] our protocol is highly step-economical. Biologically important indolizidine moiety[18] could also be synthesized from 4-chlorobutyronitriles **1a** and **1e** in an only two-step procedure. Thus, the *N*-/*C*-bisalkylations of **4aa** or **4ad** with 1,3-dibromopropane or 1,4-dibromobutane afforded the *N*-fused bicyclic compounds **9a**−**c** with yields ranging from 67 to 96%.

In conclusion, we have first disclosed the intramolecular alkylative reactivity profile of the Blaise reaction intermediate with a tethered leaving group, where the N/C cyclization was determined mainly by the tethered length and substituent at the C-2 position. To overcome its low reactivity and poor N/C selectivity, we manipulated the Blaise reaction intermediate by adding NaHMDS, which led to significant enhancement of reactivity and N/C selectivity. This modification is sufficient enough to use the current protocol as a general method for the construction of *N*-heterocyclic *exo*-cyclic enaminoesters that are embedded in many useful molecular structures.

EXPERIMENTAL SECTION

All reactions and manipulations were performed in a nitrogen atmosphere using standard Schlenk techniques. Flasks were flame-dried under a stream of nitrogen. Anhydrous solvents were distilled prior to use (THF was distilled from sodium benzophenone ketyl). All purchased reagents were used as received without further purification. Anhydrous solvents were transferred by oven-dried syringe. The chemical shifts were relative to TMS (as an internal reference) for ^{1}H NMR. Optical rotations data were reported as follows: $[\alpha]_D^{24}$ (concentration *c* = g/100 mL, solvent).

General Procedure for Intramolecular Alkylation of the Blaise Reaction Intermediate. To a suspension of zinc dust (500 mg, 7.65 mmol) was added 6.5 mol % of methanesulfonic acid in THF (1.5 mL), and the mixture was refluxed for 10 min. While maintaining reflux, nitrile **1** (3.82 mmol) was added all at once, followed by ethyl 2-bromoalkanoate **2** (4.97 mmol) added over 1 h using a syringe pump. The reaction was continued until all of the Blaise reaction intermediate had disappeared by GC, and then it was quenched by addition of saturated aqueous NH_4Cl and extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Then, the corresponding *N*-cyclized **4** and *C*-cyclized **5** (or **6**) products were separated using silica column chromatography to give the results in Table 1. For the reactions in the presence of base additive: after generation of the Blaise reaction intermediate as described above, the reaction mixture was cooled to 0 °C. To this reaction mixture was added a solution of sodium bis(trimethylsilyl)amide (1.0 M solution, 13.37 mmol) in THF. The reaction mixture was stirred for 5 h at room temperature, quenched by the addition of saturated aqueous NH_4Cl, and extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was then purified by column chromatography on silica gel to afford the corresponding *N*-cyclized product **4** with the yields given in Table 2.

*Ethyl 2-(Pyrrolidin-2-ylidene)acetate (**4aa**).* [$C_8H_{13}NO_2$: 35150−22−2]. Yield: 93% (552 mg, isolated from the reaction of entry 4 in Table 2). Eluents: *n*-hexane/EtOAc = 7/1. White solid: mp = 60−61 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.1 Hz, 3H), 1.97 (tt *J* = 7.3, 7.3 Hz, 2H), 2.58 (t, *J* = 7.7 Hz, 2H), 3.52 (t, *J* = 6.9 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H); 4.52 (s, 1H), 7.93 (brs, 1H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.4, 21.7, 31.9, 46.7, 58.0, 76.2, 166.1, 170.3 ppm.

*Ethyl 2-(Pyrrolidin-2-ylidene)propanoate (**4ab**).* [$C_9H_{15}NO_2$: 96319−44−7]. Yield: 74% (479 mg, isolated from the reaction of entry 14 in Table 2). Eluents: *n*-hexane/EtOAc = 7/1 to 3/1. (*E*)-Isomer, pale yellowish liquid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.30 (t, *J* = 7.1 Hz, 3H), 1.62 (s, 3H), 2.00 (tt, *J* = 7.5, 7.5 Hz, 2H), 2.49−2.75 (m, 2H), 3.89 (tt, *J* = 7.4, 2.0 Hz, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.45 (brs, 1H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.2, 23.5, 23.5, 33.5, 60.4, 62.1, 75.6, 173.1, 177.9e ppm. (*Z*)-Isomer (isolated from the reaction of entry 5 in Table 1), white solid: mp = 62 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.27 (t, *J* = 7.1 Hz, 3H), 1.73 (s, 3H), 1.97 (tt, *J* = 7.4, 7.4 Hz, 2H), 2.59 (t, *J* = 7.7 Hz, 2H), 3.50 (t, *J* = 6.9 Hz, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 8.02 (brs, 1H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 12.8, 14.7, 22.0, 31.2, 47.1, 58.6, 83.3, 163.9, 170.7 ppm.

*Ethyl 2-Phenyl(pyrrolidin-2-ylidene)ethanoate (**4ac**).* Yield: 71% (628 mg, isolated from the reaction of entry 15 in Table 2). Eluents: *n*-hexane/EtOAc = 10/1 to 7/1. Colorless liquid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.16 (t, *J* = 7.1 Hz, 3H), 1.89 (tt, *J* = 7.3, 7.3 Hz, 2H), 2.43 (t, *J* = 7.6 Hz, 2H), 3.57 (td, *J* = 6.9, 0.6 Hz, 2H), 4.10 (q, *J* = 7.1 Hz, 2H), 7.15−7.20 (m, 3H), 7.24−7.31 (m, 2H), 8.50 (brs, 1H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.7, 23.4, 32.4, 47.4, 59.0, 93.0, 125.7, 127.7, 131.7, 138.6, 165.5, 169.8 ppm. HRMS Calcd *m*/*z* for $C_{14}H_{18}NO_2$ [M + H]$^+$: 232.1338. Found: 232.1334.

*Ethyl 2-[4-(S)-tert-Butyl-dimethylsilanyloxypyrrolidin-2-ylidene]-acetate (**4ad**).* Yield: 76% (830 mg isolated from the reaction in scheme 2). Eluents: *n*-hexane/EtOAc = 7/1. Colorless liquid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.86 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H), 2.49 (dd, *J* = 16.6, 3.9 Hz, 1H), 2.74 (dd, *J* = 16.6, 6.3 Hz,

dx.doi.org/10.1021/jo201964a | J. Org. Chem. 2012, 77, 1560−1565

1H), 3.36 (dd, J = 10.4, 3.2 Hz, 1H), 3.65 (dd, J = 10.4, 5.6 Hz, 1H), 4.09 (q, J = 7.1 Hz, 2H), 4.45−4.49 (m, 1H), 4.51 (s, 1H), 7.78 (brs, 1H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ −4.8, −4.7, 14.8, 18.1, 25.8, 42.0, 55.6, 58.5, 69.2, 77.7, 164.4, 170.7 ppm. HRMS Calcd m/z for $C_{14}H_{27}NO_3Si$ $[M + H]^+$: 286.1838. Found: 286.1837.

*Ethyl 2-(Piperidin-2-ylidene)acetate (**4ba**).* [$C_9H_{15}NO_2$: 25654−24−4]. Yield: 10% (65 mg, isolated from the reaction of entry 16 in Table 2). Eluents: n-hexane/EtOAc = 7/1. Pale yellow liquid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.25 (t, J = 7.1 Hz, 3H), 1.64−1.83 (m, 4H), 2.35 (t, J = 6.4 Hz, 2H), 3.29 (td, J = 5.8, 2.3 Hz, 2H), 4.08 (q, J = 7.1 Hz, 2H), 4.36 (s, 1H), 8.73 (brs, 1H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.8, 20.1, 23.0, 29.3, 41.4. 58.3, 80.3, 162.9, 170.8 ppm.

*Ethyl 2-(Piperidin-2-ylidene)propanoate (**4bb**).* [$C_{10}H_{17}NO_2$: (*Z*)-96333−47−0]. Yield: 67% (470 mg, isolated from the reaction of entry 17 in Table 2). Eluents: n-hexane/EtOAc = 7/1. Pale yellowish liquid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.27(t, J = 7.1 Hz, 3H), 1.71 (s, 3H), 1.65−1.78 (m, 4H), 2.37−2.45 (m, 2H), 3.24−3.32 (m, 2H), 4.11 (q, J = 7.1 Hz, 2H), 9.52 (brs, 1H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 11.4, 14.8, 20.4, 22.4, 26.7, 41.6, 58.55, 84.5, 160.0, 171.0 ppm.

*Ethyl 2-Phenyl(piperidin-2-ylidene)ethanoate (**4bc**).* [$C_{15}H_{19}NO_2$: 21743−54−3]. Yield: 72% (675 mg, isolated from the reaction of entry 18 in Table 2). Eluents: n-hexane/diethylether = 6/1; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.11 (t, J = 7.1 Hz, 3H), 1.55−1.61 (m, 2H), 1.70−1.76 (m, 2H), 2.12 (t, J = 6.5 Hz, 2H), 3.34−3.38 (m, 2H), 4.04 (q, J = 7.1 Hz, 2H), 7.11−7.13 (m, 2H), 7.17−7.22(m, 1H), 7.26−7.31 (m, 2H), 9.72 (brs, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.7, 20.0, 22.4, 27.9, 41.4, 58.7, 95.0, 125.8, 127.8, 132.4, 138.4, 161.2, 170.1 ppm.

*Ethyl 2-Amino-1-cyclopentene-1-carboxylate (**5aa**).* [$C_8H_{13}NO_2$: 7149−18−0]. Yield: 29% (172 mg, isolated from the reaction of entry 1 in Table 1). Eluents: n-hexane/EtOAc = 7/1. White solid: mp = 48−49 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (t, J = 7.0 Hz, 3H), 1.81 (tt, J = 7.5, 7.5 Hz, 2H), 2.48 (t, J = 7.5 Hz, 2H), 2.52 (t, J = 7.5 Hz, 2H), 4.15 (q, J = 7.0 Hz, 2H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.55, 20.7, 29.4, 34.9, 58.5, 94.7, 162.0, 168.0 ppm.

*Ethyl 2-Amino-1-cyclohexene-1-carboxylate (**5ba**).* [$C_9H_{15}NO_2$: 1128−00−3]. Yield: 46% (478 mg, isolated from the reaction of entry 16 in Table 2). Eluents: n-hexane/EtOAc = 7/1. Pale yellow solid: mp = 60−62 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (t, J = 7.0 Hz, 3H), 1.59−1.64 (m, 4H), 2.20 (t, J = 6.0 Hz, 2H), 2.25 (t, J = 6.0 Hz, 2H), 4.13 (q, J = 7.0 Hz, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.6, 22.2, 23.2, 23.4, 30.5. 58.8, 92.1, 156.6, 170.5 ppm.

*Ethyl 1-Methyl-2-oxocyclopentanecarboxylate (**6ab**).* [$C_9H_{14}O_3$: 5453−88−3]. Yield: <5% (<10 mg, isolated from the reaction of entry 5 in Table 1). Eluents: n-hexane/EtOAc = 10/1. Colorless liquid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.25 (t, J = 7.1 Hz, 3H), 1.31 (s, 3H), 1.81−2.14 (m, 3H), 2.23−2.54 (m, 3H), 4.16 (q, J = 7.1 Hz, 2H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.0, 19.3, 19.5, 36.1, 37.6. 55.8, 61.2, 172.3, 215.9 ppm.

*Ethyl 1-Methyl-2-oxocyclohexanecarboxylate (**6bb**).* [$C_{10}H_{16}O_3$: 5453−94−1]. Yield: 45% (317 mg, isolated from the reaction of entry 7 in Table 1). Eluents: n-hexane/EtOAc = 10/1. Colorless liquid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 3H), 1.29 (s, 3H), 1.38−1.50 (m, 1H), 1.61−1.76 (m, 3H), 1.94−2.05 (m, 1H), 2.45−2.55 (m, 3H), 4.20 (qd, J = 7.1 Hz, 1.3, 2H), 9.52 (brs, 1H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1, 21.3, 22.7, 27.6, 38.3, 40.7, 57.2, 61.3, 173.1, 208.4 ppm.

*Ethyl 2-Oxo-1-phenylcyclohexanecarboxylate (**6bc**).* [$C_{15}H_{18}O_3$: 55285−81−9]. Yield: 25% (236 mg, isolated from the reaction of entry 8 in Table 1). Eluents: n-hexane/EtOAc = 7/1. Colorless liquid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.23 (t, J = 7.1 Hz, 3H), 1.76−1.85 (m, 3H), 1.91−2.03 (m, 1H), 2.32−2.40 (m, 1H), 2.48−2.62 (m, 2H), 2.73−2.80 (m, 1H), 4.20 (qd, J = 7.1, 1.8 Hz, 2H), 7.21−7.25 (m, 2H), 7.28−7.29 (m, 3H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1, 22.3, 27.8, 35.4, 40.9, 61.7, 66.5, 136.9, 171.3, 206.7 ppm.

Synthesis of Ethyl 7-Hydroxy-2-*tert*-butyl-dimethyl-silanyloxy-2,3-dihydro-1*H*-pyrrolo[1,2-a]indole-9-carboxylate 7. To a solution of 1,4-benzoquinone (116 mg, 1.05 mmol) in CH_2Cl_2 (5 mL) was added ZnI_2 (67 mg, 0.21 mmol). The reaction mixture was heated to reflux, and then a solution of *exo*-cyclic enaminoester **4ad** (300 mg, 1.05 mmol) in CH_2Cl_2 (2 mL) was added dropwise over 10 min. The mixture was stirred at reflux for an additional 2 h. The reaction was quenched at room temperature by addition of saturated aqueous NH_4Cl and extracted with ethyl acetate (20 mL × 3). The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification by silica column chromatography (n-hexane/EtOAc = 3/1) afforded **7** as a white solid (277 mg, 70% yield). White solid: mp = 180−182 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.11 (s, 6H), 0.90 (s, 9H), 1.40 (t, J = 7.1 Hz, 3H), 3.11 (dd, J = 17.8, 3.8 Hz, 1H), 3.48 (dd, J = 17.9, 6.9 Hz, 1H), 3.84 (dd, J = 10.7, 3.7 Hz, 1H), 4.18 (dd, J = 10.7, 6.3 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 5.02−5.05 (m, 1H), 6.81 (dd, J = 8.6, 2.2 Hz, 1H), 7.02 (d, J = 8.6 Hz, 1H), 7.59 (brs, 1H), 7.88 (d, J = 2.0 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.8, −4.7, 14.6, 18.1, 25.8, 37.7, 53.8, 59.9, 74.1, 98.9, 106.3, 110.6, 111.4, 127.8, 131.7, 150.6, 152.6, 166.3 ppm. HRMS Calcd m/z for $C_{20}H_{30}NO_4Si$ $[M + H]^+$: 376.1944. Found: 376.1941.

Synthesis of Ethyl (2*S*,4*S*)-[4-*tert*-Butyldimethylsilanyloxy-pyrrolidine-2-yl]acetate 8. [$C_{14}H_{29}NO_3Si$: 612843−60−4]. To a suspension of Pd/C (0.5 equiv, 10% Pd on charcoal) in ethanol (5 mL) was added *exo*-cyclic enaminoester **4ad** (285.5 mg, 1.0 mmol). The mixture was hydrogenated under H_2 atmosphere (1 atm, balloon) at room temperature for 48 h. The reaction mixture was filtered through Celite and washed with ethanol, and then the filtrate was concentrated in a vacuum to afford (2*S*,4*S*)-**8** (285 mg, 97% yield) as pale yellow liquid: $[\alpha]_D^{24}$ = +9.9 (c = 5.0, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 6H), 0.86 (s, 9H), 1.24 (t, J = 7.1 Hz, 3H), 1.34−1.43 (m, 1H), 2.12−2.21 (m, 1H), 2.51 (dd, J = 15.6, 6.3 Hz, 1H), 2.60 (dd, J = 15.6, 7.6 Hz, 1H), 2.68(brs, 1H), 2.84−2.95 (m, 2H), 3.45 (tt, J = 7.3, 7.0, 1H), 4.12(q, J = 7.1 Hz, 2H), 4.29−4.35 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.8, −4.7, 14.3, 18.1, 25.9, 41.1, 41.7, 54.5, 55.7, 60.4, 73.1, 172.1 ppm. The absolute stereochemistry was determined, after conversion to the *N*-Cbz-**8**, by comparison the optical rotation with the reported the reported (2*R*,4*R*)-*N*-Cbz-**8**.[14] (2*S*,4*S*)-N-Cbz-**8**, colorless liquid: $[\alpha]_D^{24}$ = −11.8 (c = 10.0, EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$, 50 °C) δ 0.06 (s, 6H), 0.88 (s, 9H), 1.22 (t, J = 7.1 Hz, 3H), 1.87 (d, J = 13.5 Hz, 1H), 2.12−2.21 (m, 1H), 2.77−3.07 (m, 2H), 3.35 (d, J = 11.3 Hz, 1H), 3.50−3.60 (m, 1H), 4.07−4.12 (m, 2H), 4.24−4.39 (m, 2H), 5.14(s, 2H), 7.25−7.37 (m, 5H) ppm.

General Procedure for the Synthesis of *N*-Fused Bicyclic Compounds 9a−9c. To a solution of *exo*-cyclic enaminoester **4aa** (310.4 mg, 2.0 mmol) in DMF (5 mL) was added NaH (120 mg, 3.5 mmol) at −30 °C. After stirring for 10 min, 1,3-dibromopropane (0.36 mL, 3.5 mmol) was added, and the reaction mixture was stirred at same temperature for an additional 30 min. The reaction was quenched by the addition of H_2O and extracted with ethyl acetate (20 mL × 3), and the combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by silica column chromatography (n-hexane/EtOAc = 5/1 to 3/1) to afford **9a** as a viscous colorless liquid (297 mg, 76% yield).

*Ethyl 1,2,3,5,6,7-Hexahydroindolizine-8-carboxylate (**9a**).* [$C_{11}H_{17}NO_2$: 90407−59−3]. Spectral data: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.21 (t, J = 7.1 Hz, 3H), 1.74−1.93 (m, 4H), 2.31 (t, J = 6.3 Hz, 2H), 3.01 (t, J = 7.6 Hz, 2H), 3.11 (t, J = 5.7 Hz, 2H), 3.24 (t, J = 7.1 Hz, 2H), 4.06 (q, J = 7.1 Hz, 2H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.8, 21.0, 21.4, 21.6, 32.7, 45.0, 52.9, 58.4, 87.45, 159.2, 168.8 ppm.

*Ethyl 2,3,5,6,7,8-Hexahydro-1H-pyrrolo[1,2-a]azepine-9-carboxylate (**9b**).* Yield: 96% (402 mg). Eluents: n-hexane/EtOAc = 3/1 to 2/1. Viscous colorless liquid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.25 (t, J = 7.1 Hz, 3H), 1.62−1.75 (m, 4H), 1.89 (tt, J = 7.7, 7.7 Hz, 2H), 2.04−2.15 (m, 2H), 2.17−2.27 (m, 2H), 2.46−2.53 (m, 2H), 3.81−3.86 (m, 2H), 4.17 (q, J = 7.1 Hz, 2H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ 14.1, 23.1, 24.9, 34.4, 34.8, 58.5, 60.5, 60.9, 174.7, 177.6 ppm. HRMS Calcd m/z for $C_{12}H_{20}NO_2$[M + H]$^+$: 210.1494. Found: 210.1493.

*Ethyl 2-tert-Butyl-dimethyl-silanyloxy-1,2,3,5,6,7-hexahydroindolizine-8-carboxylate (**9c**).* Yield: 67% (436 mg). Eluents: n-hexane/

dx.doi.org/10.1021/jo201964a | J. Org. Chem. 2012, 77, 1560−1565

EtOAc = 10/1 to 5/1. Viscous colorless liquid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.07 (d, J = 1.5 Hz, 6H), 0.88 (s, 6H), 1.25 (t, J = 7.1 Hz, 3H), 1.77−1.89 (m, 2H), 2.34 (t, J = 6.1 Hz, 2H), 2.98−3.18 (m, 4H), 3.27 (dd, J = 18.1, 6.9 Hz, 1H), 3.45 (dd, J = 10.0, 6.0 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 4.42−4.47 (m, 1H) ppm; ^{13}C NMR (63 MHz, $CDCl_3$) δ −4.7, −4.6, 14.9, 18.2, 21.3, 21.5, 25.9, 42.9, 44.9, 58.6, 61.3, 68.3, 88.1, 157.3, 168.8 ppm. HRMS Calcd m/z for $C_{17}H_{32}NO_3Si$ $[M + H]^+$: 326.2151. Found: 326.2153.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for **4**, **5**, **6**, **7**, **8**, and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: sanggi@ewha.ac.kr; hisin@lgls.com.

■ ACKNOWLEDGMENTS

This research was supported by the National Research Foundation of Korea, funded by the Ministry of Education, Science and Technology (NRF-20110002962 and NRF-20110016344)

■ REFERENCES

(1) For useful reviews, see: (a) Lue, P.; Greenhill, J. V. *Adv. Heterocycl. Chem.* **1997**, *67*, 207. (b) Granik, V. G.; Makarov, V. A.; Pärkänyi, C. *Adv. Heterocycl. Chem.* **1999**, *72*, 283. (c) Elliott, M. C.; Wood, J. L.; Wordingham, S. V. *Trends Heterocycl. Chem.* **2005**, *10*, 73.

(2) (a) Roth, M.; Dubs, P.; Götschi, E.; Eschenmoser, A. *Helv. Chim. Acta* **1971**, *54*, 710. (b) Michael, J. P.; Gravestock, D. *J. Chem. Soc., Perkin Trans.1* **2000**, 1919 andreferences therein.

(3) (a) Yamaguchi, M.; Hirao, I. *J. Org. Chem.* **1985**, *50*, 1975. (b) Lee, H. K.; Kim, J.; Park, C. S. *Tetrahedron Lett.* **1999**, *40*, 2173. (c) Matsumura, Y.; Fujiwara, J.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1983**, *105*, 6312. (d) Jain, S.; Jain, R.; Singh, J.; Anand, N. *Tetrahedron Lett.* **1994**, *35*, 2951.

(4) (a) Celerier, J.-P.; Deloisy, E.; Lhommet, G.; Maitte, P. *J. Org. Chem.* **1979**, *44*, 3089. (b) Gugelchuk, M. M.; Hart, D. J.; Tsai, Y.-M. *J. Org. Chem.* **1981**, *46*, 3671. (c) Celerier, J. P.; Richaud, M. G.; Lhommet, G. *Synthesis* **1983**, 195.

(5) (a) Lambert, P. H.; Vaultier, M.; Carrie, R. *J. Org. Chem.* **1985**, *50*, 5352. (b) Bellur, E.; Görls, H.; Langer, P. *J. Org. Chem.* **2005**, *70*, 4751.

(6) (a) Lygo, B. *Synlett* **1993**, 764. (b) Elliot, M. C.; Wordingham, S. V. *Synthesis* **2006**, 1162. (c) Wang, M.-X.; Liu, Y.; Gao, H.-Y.; Zhang, Y.; Yu, C.-Y.; Huang, Z.-T.; Fleet, G. W. J. *J. Org. Chem.* **2003**, *68*, 3281.

(7) (a) Blaise, E. E. *C. R. Hebd. Seances Acad. Sci.* **1901**, *132*, 478. (b) Blaise, E. E. *C. R. Hebd. Seances Acad. Sci.* **1901**, *132*, 987. (c) Rathke, M. W.; Weipert, P. In *Zinc Enolates: The Reformatsky and Blaise Reaction in Comprehensive Organic Reactions*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 2, pp 277−299. (d) Rao, H. S. P.; Rafi, S.; Padmavathy, K. *Tetrahedron* **2008**, *64*, 8037.

(8) (a) Chun, Y. S.; Lee, K. K.; Ko, Y. O.; Shin, H.; Lee, S.-g. *Chem. Commun.* **2008**, 5098. (b) Ko, Y. O.; Chun, Y. S.; Park, C.-L.; Kim, Y.; Shin, H.; Ahn, S.; Hong, J.; Lee, S.-g. *Org. Biomol. Chem.* **2009**, *7*, 1132. (c) Chun, Y. S.; Ko, Y. O.; Shin, H.; Lee, S.-g. *Org. Lett.* **2009**, *11*, 3414. (d) Chun, Y. S.; Ryu, K. Y.; Ko, Y. O.; Hong, J. Y.; Hong, J.; Shin, H.; Lee, S.-g. *J. Org. Chem.* **2009**, *74*, 7556. (e) Ko, Y. O.; Chun, Y. S.; Kim, Y.; Kim, S. J.; Shin, H.; Lee, S.-g. *Tetrahedron Lett.* **2010**, *51*, 6893.

(9) Hannick, S. M.; Kishi, Y. *J. Org. Chem.* **1983**, *48*, 3833.

(10) Proton exchange between HMDS and zinc enoate of amide, see: de Filippis, A.; Pardo, D. G.; Cossy, J. *Tetrahedron* **2004**, *60*, 9757.

(11) Kim, J. H.; Lee, S.-g. *Org. Lett.* **2011**, *13*, 1350.

(12) Fraley, M. E.; Garbaccio, R. M.; Arrington, K. L.; Hoffman, W. F.; Tasber, E. S.; Coleman, P. J.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Fernandes, C.; Schaber, M. D.; Lobell, R. B.; Tao, W.; South, V. J.; Yan, Y.; Kuo, L. C.; Prueksaritanont, T.; Shu, C.; Torrent, M.; Heimbrook, D. C.; Kohl, N. E.; Huber, H. E.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 1775.

(13) Velezheva, V. S.; Kornienko, A. G; Topilin, S. V.; Turashev, A. D.; Peregudov, A. S.; Brennan, P. J. *J. Heterocycl. Chem.* **2006**, *43*, 873.

(14) Zhao, X.; Hoesl, C. E.; Hoefner, G. C.; Wanner, K. T. *Eur. J. Org. Chem.* **2005**, *40*, 231.

(15) Bellur, E.; Freifeld, I.; Böttcher, D.; Bornscheuer, U. T.; Lange, P. *Tetrahedron* **2006**, *62*, 7132.

(16) (a) Gregson, S. J.; Howard, P. W.; Corcoran, K. E.; Barcella, S.; Yasin, M. M.; Hurst, A. A.; Jenkins, T. C.; Kelland, L. R.; Thurston, D. E. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1845. (b) Kamal, A.; Reddy, G. S. K.; Reddy, K. L.; Raghavan, S. *Tetrahedron Lett.* **2002**, *43*, 2103. (c) Clerici, F.; Erba, E.; Pocar, D. *Tetrahedron* **2003**, *59*, 1667.

(17) Perron, J.; Joseph, B.; Merour, J.-Y. *Tetrahedron Lett.* **2003**, *44*, 6553.

(18) Recent papers for the synthesis of indolizidines, see: (a) Barluenga, J.; Mateos, C.; Aznar, F.; Valdés, C. *Org. Lett.* **2002**, *4*, 1971. (b) Reddy, P. G.; Varghese, B.; Baskaran, S. *Org. Lett.* **2003**, *5*, 583. (c) Molander, G. A.; Pack, S. K. *J. Org. Chem.* **2003**, *68*, 9214. (d) Lindsay, K. B.; Pyne, S. G. *J. Org. Chem.* **2002**, *67*, 7774. (e) Randl, S.; Blechert, S. *J. Org. Chem.* **2003**, *68*, 8879. (f) Smith, A. B. III *J. Org. Chem.* **2006**, *71*, 2547. (g) Back, T. G.; Parvez, M.; Zhai, H. *J. Org. Chem.* **2003**, *68*, 9389. (h) Alcaide, B.; Almendros, P.; Alonso, J. M.; Aly, M. F. *Chem.—Eur. J.* **2003**, *9*, 3415. (i) Davis, F. A.; Yang, B. *Org. Lett.* **2003**, *5*, 5011. (j) Zhu, W.; Dong, D.; Pu, X.; Ma, D. *Org. Lett.* **2005**, *7*, 705. (k) Cai, G.; Zhu, W.; Ma, D. *Tetrahedron* **2006**, *62*, 5697.