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NHC-catalyzed efficient synthesis of β′-amino enones via carbonyl umpolung reaction of enals with aziridines

Lal Dhar S. Yadav [a,*], Vijai K. Rai [a,b], Santosh Singh [a], Pankaj Singh [a]

[a] Green Synthesis Lab, Department of Chemistry, University of Allahabad, Allahabad 211 002, India
[b] College of Science, Shri Mata Vaishno Devi University, Katra, Jammu & Kashmir 182 320, India

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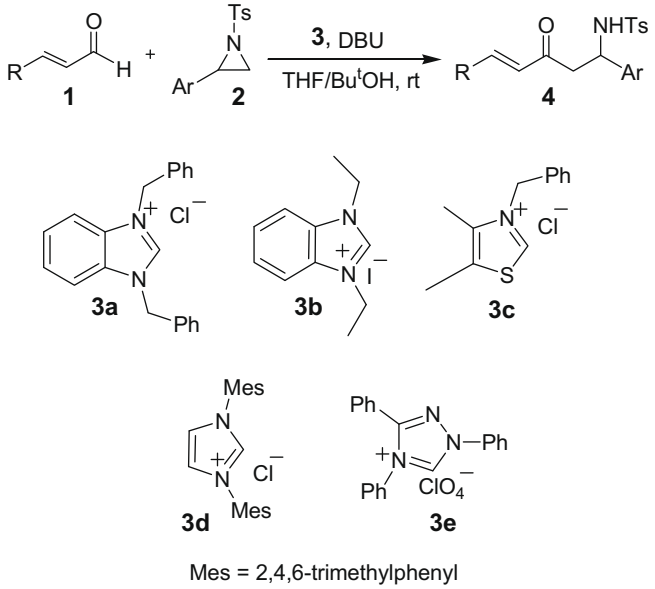
ABSTRACT

The first example of *N*-heterocyclic carbene-catalyzed synthesis of β′-amino-α,β-unsaturated ketones via regioselective ring-opening of terminal aziridines with enals is reported. The protocol involves carbonyl umpolung reactivity of enals in which the carbonyl carbon attacks nucleophilically on electrophilic terminal aziridines. No by-product formation, operational simplicity, ambient temperature, good to excellent yields (76–94%), and regioselectivity are the salient features of the present procedure.

Reversing the reactivity of aldehydes also known as umpolung[1] by nucleophilic *N*-heterocyclic carbene (NHC) has become an area of intense interest recently, providing unconventional access to some important target molecules.[2] NHC-catalyzed umpolung reactivity of α,β-unsaturated aldehydes (enals) via Breslow or homoenolate intermediate has been well documented,[3–5] where addition of an appropriate NHC to an enal renders it a d^3 nucleophile. Stetter et al. published as early as 1979 a few examples of the Michael addition of enals as acyl anions.[6] Since then, there has been no report on NHC-catalyzed umpolung reactivity of enals rendering them acyl anion equivalents (d^1 nucleophiles) although it would be of considerable synthetic utility. In an attempt to fill this remarkable gap in the literature, we report herein an NHC-catalyzed efficient synthesis of hitherto unknown β′-amino ketones **4** via carbonyl umpolung reaction of enals **1** with terminal aziridines **2** (Scheme 1). Moreover, the present reaction is a novel addition to the nucleophilic ring-opening reactions already reported in the literature.[7]

β-Amino carbonyl compounds are ubiquitous in the natural product arena and have been used as building blocks for many N-containing biologically important compounds[8] such as 1,2-diamines and β-lactams.[9,10] They are also useful precursors for the generation of β-amino alcohols, which are common intermediates in the preparation of fine chemicals and pharmaceuticals.[9] In corollary of the interesting synthetic and pharmaceutical utility, substantial interest has been demonstrated toward the synthesis of β-amino ketones including Mannich reaction[11] and aza-Michael addition of an N-centered nucleophile to an α,β-unsaturated ketones.[12]



Scheme 1. NHC-catalyzed synthesis of β′-amino ketones **4**.

* Corresponding author. Tel.: +91 5322500652; fax: +91 5322460533.
E-mail address: ldsyadav@hotmail.com (L.D.S. Yadav).

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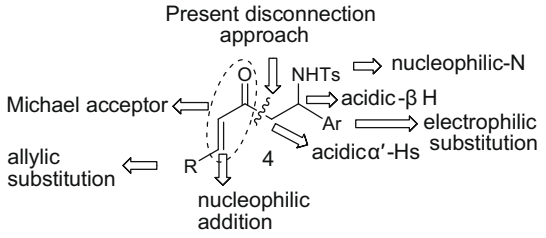
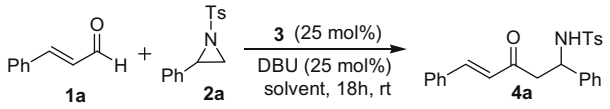


Figure 1. Diversely functionalized products **4**.

Table 1
Optimization of reaction conditions for the formation of representative compound **4a**[a]



Entry	Precatalyst	mol %	Solvent	Yield[b] (%)
1	**3a**	25	THF	45
2	**3a**	25	CH_2Cl_2	26
3	**3a**	25	THF/H_2O[c]	57
4	**3a**	25	THF/Bu^{t}OH[c]	91
5	**3b**	25	THF/Bu^{t}OH	62
6	**3c**	25	THF/Bu^{t}OH	40
7	**3d**	25	THF/Bu^{t}OH	0
8	**3e**	25	THF/Bu^{t}OH	12
9	**3a**	30	THF/Bu^{t}OH	91
10	**3a**	20	THF/Bu^{t}OH	84
11	—	—	THF/Bu^{t}OH	0

[a] For the experimental procedure, see Ref. [15].
[b] Yield of isolated and purified product.
[c] THF/H_2O; 10:01 and THF/Bu^{t}OH; 10:01 were used.

The present reaction products β′-amino ketones **4** incorporate densely populated chemo-specific functional groups including amino, α,β-unsaturated carbonyl (Michael acceptor) and active methylene groups, thereby provide handles for further manipulation in a multitude of synthetic organic transformations (Fig. 1). Interestingly, the unprecedented synthesis of target β′-amino-α,β-unsaturated ketones **4** involves carbonyl umpolung reactivity of enals **1** in which the carbonyl carbon attacks nucleophilically on electrophilic terminal aziridines **2** regioselectively, which is our new finding and is an outcome of our quest for developing convenient synthetic routes.[13]

For a model experiment, we investigated the optimization of reaction conditions with regard to both NHC-catalyst and solvent. Here, cinnamaldehyde **1a** and aziridine **2a** were chosen as substrates for the synthesis of representative β-amino ketone **4a** and the reaction was performed at room temperature under positive pressure of nitrogen (Table 1). Different types of *N*-heterocyclic carbene precursors **3a–e** were tested and **3a** was found to be the most effective precatalyst for the preparation of **4a** under the present reaction conditions (Table 1, entries 4–8).

The optimum loading for the precatalyst **3a** was found to be 25 mol % along with 25 mol % of DBU. When the amount of the precatalyst was decreased from 25 mol % to 20 mol % relative to substrate **1a**, the yield of the ketone **4a** reduced (Table 1, entry 10), but the use of 30 mol % of **3a** did not affect the yield (Table 1, entries 4 and 9). The reaction did not occur without using the precatalyst **3** (Table 1, entry 11). It was also noted that a higher reaction temperature, for example, in a refluxing solvent instead of room temperature did not increase the yield. Optimization of solvents for the synthesis of **4a** employing the precatalyst **3a** was also undertaken and it was found that amongst THF, CH_2Cl_2, THF/H_2O, and THF/Bu^{t}OH (Table 1, entries 1–4), the best solvent-system in terms of yield was THF/Bu^{t}OH (Table 1, entry 4) and we used this solvent-system (THF/Bu^{t}OH) throughout the present study. Next, in order to investigate the substrate scope and general validity of the reaction, a variety of α,β-unsaturated aldehydes **1** and aziridines **2** were used employing the present optimized reaction conditions and the yields were found to be good to excellent (Table 2), the highest yield of **4** being 94% (Table 2, **4o**).

Table 2
Reaction of *E*-enals **1** with aziridines **2** yielding β′-amino ketones **4**

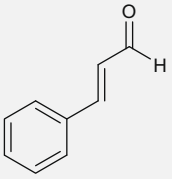
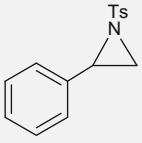
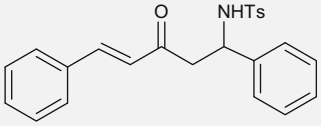
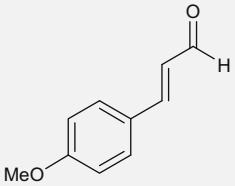
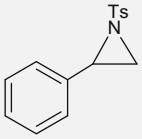
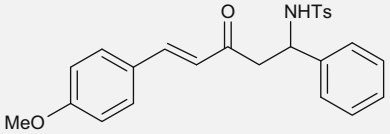
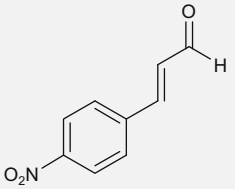
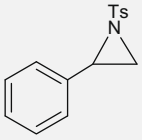
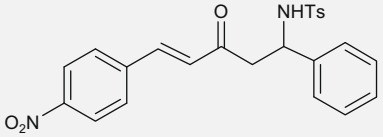
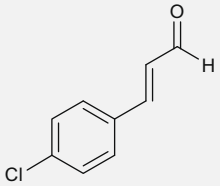
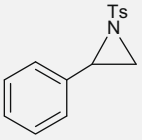
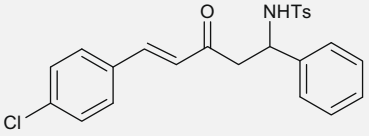
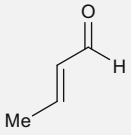
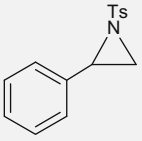
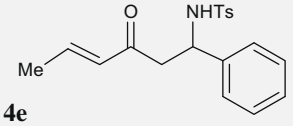
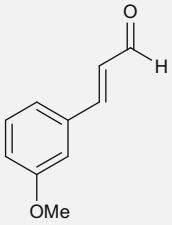
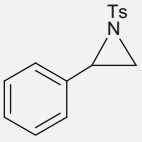
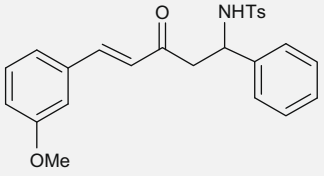
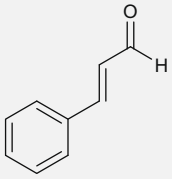
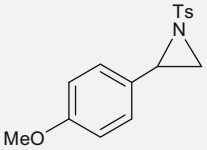
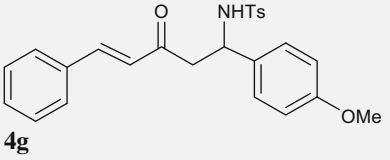
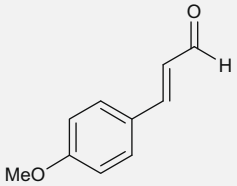
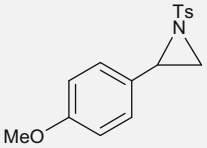
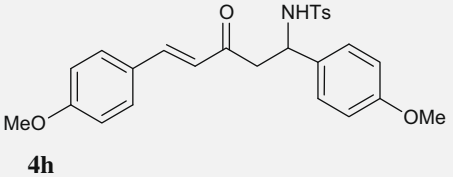
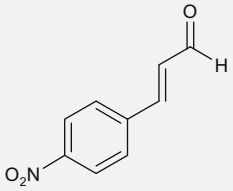
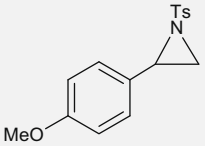
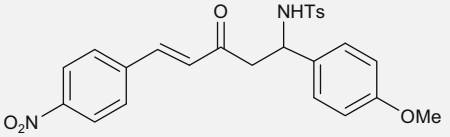
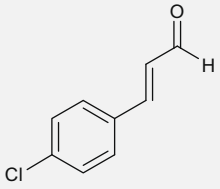
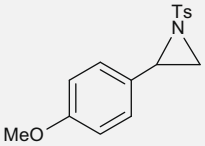
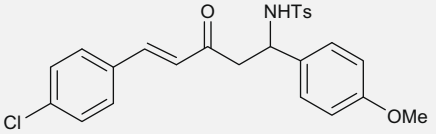
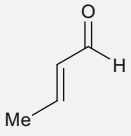
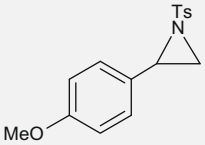
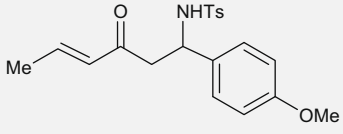
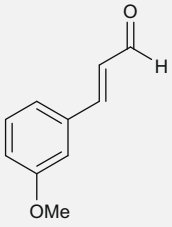
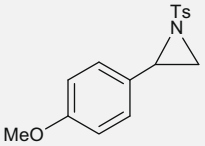
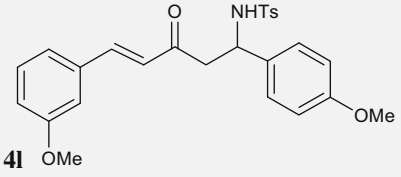
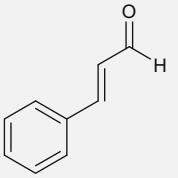
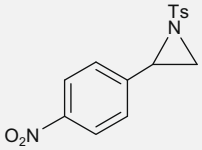
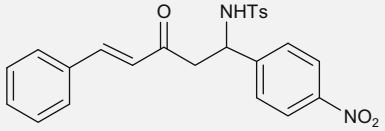
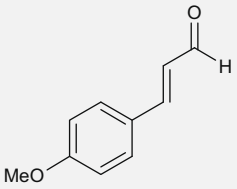
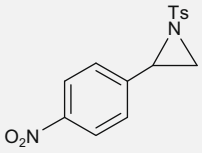
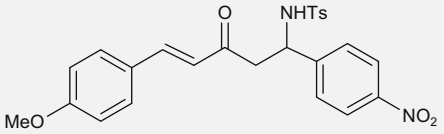
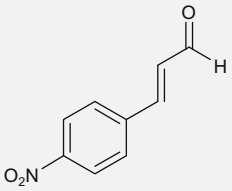
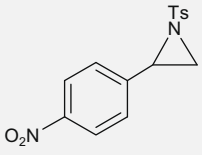
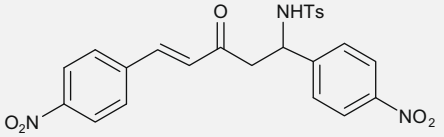
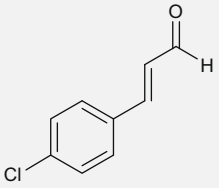
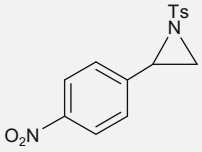
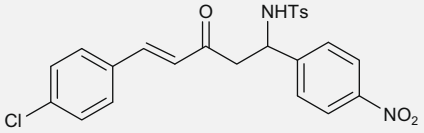
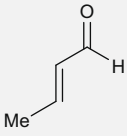
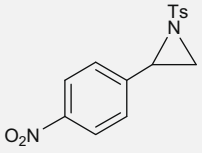
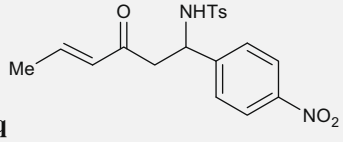
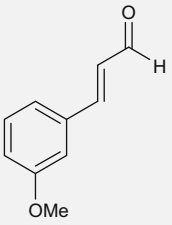
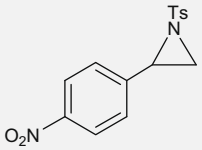
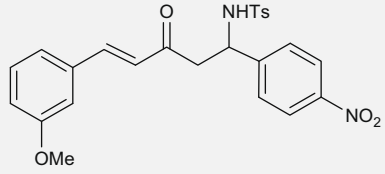
Entry	Enal **1**	Aziridine **2**	Time[a] (h)	Product **4**	Yield[b,c] (%)
1			18	 **4a**	91
2			16	 **4b**	86
3			16	 **4c**	90

Table 2 (*continued*)

Entry	Enal **1**	Aziridine **2**	Time[a] (h)	Product **4**	Yield[b,c] (%)
4			18	 **4d**	87
5			16	 **4e**	78
6			16	 **4f**	91
7			17	 **4g**	81
8			16	 **4h**	80
9			16	 **4i**	85
10			17	 **4j**	82
11			18	 **4k**	76
12			17	 **4l**	83

(*continued on next page*)

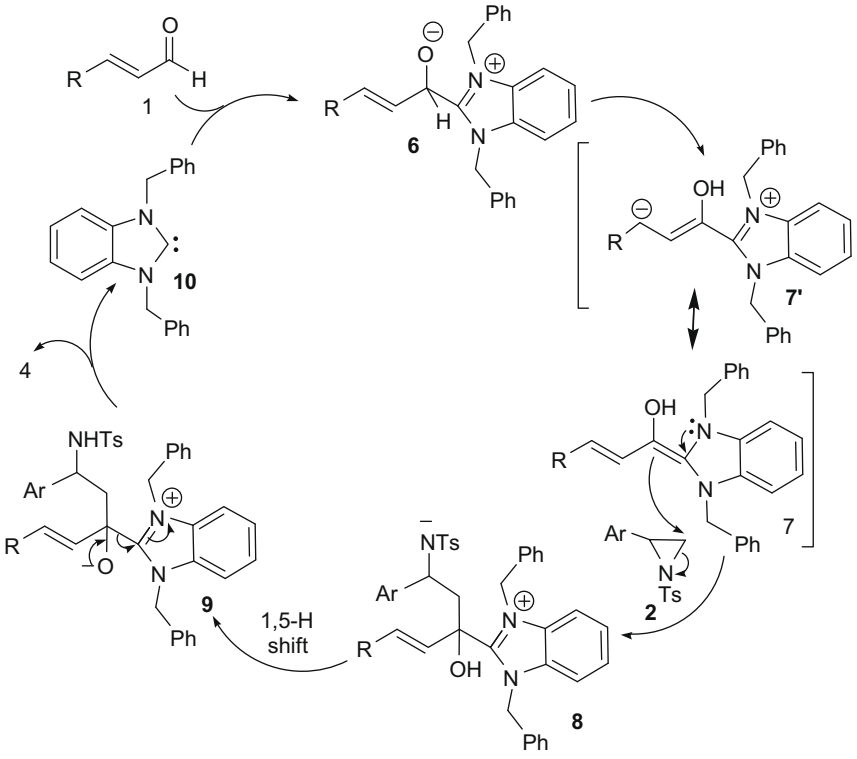
Table 2 (*continued*)

Entry	Enal **1**	Aziridine **2**	Time[a] (h)	Product **4**	Yield[b,c] (%)
13			16	 **4m**	92
14			17	 **4n**	90
15			18	 **4o**	94
16			18	 **4p**	89
17			16	 **4q**	79
18			16	 **4r**	92

[a] Stirring time at room temperature.
[b] Yield of isolated and purified product.
[c] All compounds gave C, H, and N analyses ±0.37% and satisfactory spectral (IR, ^{1}H NMR, ^{13}C NMR, and EIMS) data.

The formation of ketones **4** may be tentatively rationalized by initial addition of NHC **10** to α,β-unsaturated aldehyde **1** followed by proton shift in **6** to generate conjugated acyl anion equivalent **7** (Scheme 2). In previous similar reports, the equilibrium was shifted mostly toward homoenolate **7′** employing an appropriate, highly hindered catalyst.[9,10,14] On the basis of the literature reports[9,10,14] and the work of Stetter and co-workers[6] on enals, we reasoned that an appropriately substituted NHC could shepherd the umpolung reactivity of enals to the carbonyl group presumably by sterically blocking the β-position without posing any significant steric hindrance at the acyl carbon. To our delight, the NHC **3a** mediated reaction of enals **1** with aziridines **2** proceeded well via acyl anion to afford β′-amino ketones **4** in excellent yields (Table 2).[15] Formation of any product via homoenolate ion **7′** was not observed. However, only trace amounts of undesired benzoin product were observed in the case of crotonaldehyde.

In summary, our work fills a remarkable gap in the literature on the NHC-catalyzed carbonyl umpolung reactivity of enals. It offers a general and elegant method for the preparation of synthetically and pharmaceutically important functionally rich β′-amino enones via regioselective ring-opening of aziridines with enals. The present atom-economic reaction would be a practical procedure for the synthesis of such kinds of fine chemicals.



Scheme 2. Tentative mechanism for the formation of β′-amino ketones **4**.

Acknowledgments

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References and notes

1. (a) Seebach, D. *Angew. Chem., Int. Ed.* **1979**, *18*, 239; (b) Enders, D.; Balensiefer, T. *Acc. Chem. Res.* **2004**, *37*, 534.
2. (a) Maki, B. E.; Chan, A.; Scheidt, K. A. *Synthesis* **2008**, 1306; (b) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606; (c) Marion, N.; Díez-González, S.; Nolan, I. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2988; (d) Zeitler, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 7506; (e) Johnson, J. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 1326.
3. Sohn, S. S.; Rosen, E. L.; Bode, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 14370.
4. Burstein, C.; Glorius, F. *Angew. Chem., Int. Ed.* **2004**, *43*, 6205.
5. (a) Chan, A.; Scheidt, K. A. *Org. Lett.* **2005**, *7*, 905; (b) He, M.; Bode, J. W. *Org. Lett.* **2005**, *7*, 3131; (c) He, M.; Struble, J. R.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 8418; (d) Nair, V.; Vellalath, S.; Poonoth, M.; Suresh, E. *J. Am. Chem. Soc.* **2006**, *128*, 8736; (e) Burstein, C.; Tschan, S.; Xie, X.; Glorius, F. *Synthesis* **2006**, 2418; (f) Chiang, P.-C.; Kaeobamrung, J.; Bode, J. W. *J. Am. Chem. Soc.* **2007**, *129*, 3520; (g) Chan, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 2740.
6. Stetter, H.; Hilboll, G.; Kuhlmann, H. *Chem. Ber.* **1979**, *112*, 84.
7. For reactions of aziridines, see: (a) McCoull, W.; Davis, F. A. *Synthesis* **2000**, 1347; (b) Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247; (c) Yadav, J. S.; Reddy, B. V. S.; Abraham, S.; Sabitha, G. *Tetrahedron Lett.* **2002**, *43*, 1565; (d) Hu, X. E. *Tetrahedron* **2004**, *60*, 2701; (e) Ma, L. G.; Xu, J. X. *Prog. Chem.* **2004**, *16*, 220; (f) Yadav, V. K.; Sriramurthy, V. *J. Am. Chem. Soc.* **2005**, *127*, 16366; (g) Sureshkumar, D.; Koutha, S. M.; Chandrasekaran, S. *J. Am. Chem. Soc.* **2005**, *127*, 12760; (h) Liu, Y.-K.; Li, R.; Yue, L.; Li, B.-J.; Chen, Y.-C.; Wu, Y.; Ding, L.-S. *Org. Lett.* **2006**, *8*, 1521; (i) Sun, X.; Ye, S.; Wu, J. *Eur. J. Org. Chem.* **2006**, 4787; (j) Wang, Z.; Cui, Z.-T.; Xu, Z.-B.; Qu, J. *J. Org. Chem.* **2008**, *73*, 2270; (k) Wang, L.; Liu, Q.-B.; Wang, D.-S.; Han, X.-W.; Xiao, W.-J.; Zhou, Y.-G. *Org. Lett.* **2009**, *11*, 1119.
8. (a) Misra, M.; Luthra, R.; Singh, K. L.; Sushil, K. In *Comprehensive Natural Products Chemistry*; Barton, D. H. R., Nakanishi, K., Meth-Cohn, O., Eds.; Pergamon: Oxford, 1999; Vol. 4, p 25; (b) *Enantioselective Synthesis of β-Amino Acids*; Juaristi, E., Ed.; Wiley-VCH: New York, NY, 1997; (c) Liu, M.; Sibi, M. P. *Tetrahedron* **2002**, *58*, 7991; (d) Cardillo, G.; Tomasini, C. *Chem. Soc. Rev.* **1996**, *25*, 117.
9. (a) Kleinmann, E. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: New York, NY, 1991; Vol. 2, p 893; (b) *The Organic Chemistry of β-Lactams*; Georg, G. I., Ed.; VCH: New York, NY, 1993; (c) Devine, P. N.; Heid, R. M.; Tschaen, D. M. *Tetrahedron* **1997**, *53*, 6739.
10. (a) Abele, S.; Seebach, D. *Eur. J. Org. Chem.* **2000**, 1; (b) Sewald, N. *Amino Acids* **1996**, *11*, 397.
11. (a) Jung, M. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 4, p 30; (b) Kobayashi, S.; Ishitani, H. *Chem. Rev.* **1999**, *99*, 1069; (c) Manabe, K.; Kobayashi, S. *Org. Lett.* **1999**, *1*, 1965; (d) Okitsu, O.; Oyamada, H.; Furuta, T.; Kobayashi, S. *Heterocycles* **2000**, *52*, 1143; (e) Ishitani, H.; Ueno, M.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 8180.
12. (a) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon: New York, 1992; (b) Gomtsyan, A. *Org. Lett.* **2000**, *2*, 11; (c) Gomtsyan, A.; Koenig, R. J.; Lee, C.-H. *J. Org. Chem.* **2001**, *66*, 3613; (d) Wang, B. M.; Song, Z. L.; Fan, C. A.; Tu, Y. Q.; Shi, Y. *Org. Lett.* **2002**, *4*, 363; (e) Bartoli, G.; Bosco, M.; Marcantoni, E.; Petrini, M.; Sambri, L.; Torregiani, E. *J. Org. Chem.* **2001**, *66*, 9052; (f) Xu, L.-W.; Xia, C.-G. *Eur. J. Org. Chem.* **2005**, 633; (g) Hultzsch, K. C. *Adv. Synth. Catal.* **2005**, *347*, 367.
13. (a) Yadav, L. D. S.; Kapoor, R. *J. Org. Chem.* **2004**, *69*, 8118; (b) Yadav, L. D. S.; Yadav, S.; Rai, V. K. *Tetrahedron* **2005**, *61*, 10013; (c) Yadav, L. D. S.; Rai, V. K. *Tetrahedron Lett.* **2006**, *47*, 395; (d) Yadav, L. D. S.; Rai, V. K. *Synlett* **2007**, 1227; (e) Yadav, L. D. S.; Rai, V. K. *Tetrahedron Lett.* **2008**, *49*, 5553; (f) Yadav, L. D. S.; Yadav, S.; Rai, A.; Rai, V. K.; Awasthi, C. *Tetrahedron* **2008**, *64*, 1420; (g) Yadav, L. D. S.; Singh, S.; Rai, V. K. *Green Chem.* **2009**, *11*, 878; (h) Yadav, L. D. S.; Rai, V. K.; Singh, S. *Synlett* **2009**, 1423.
14. (a) Nair, V.; Vellalath, S.; Babu, B. P. *Chem. Soc. Rev.* **2008**, *37*, 2691; (b) Sohn, S. S.; Bode, J. W. *Org. Lett.* **2005**, *7*, 3873.
15. *General procedure for the synthesis of β′-amino ketones* **4a**–**r**: A flame-dried round bottom flask was charged with benzimidazolium salt **3a** (0.25 mmol). α,βÙunsaturated aldehyde **1** (1.0 mmol), aziridine **2** (1.5 mmol), and 5 mL of THF/Bu^{t}OH; 10:1 under positive pressure of nitrogen followed by addition of DBU (0.25 mmol) with a syringe. The resulting yellow–orange solution was stirred for 16–18 h at room temperature (Table 2). After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel using hexane/EtOAc (10:1) as eluent to afford analytically pure **4**. Physical data of representative compounds. *Compound* **4a**: Colorless solid, yield 91%, mp 125–126 °C. IR (KBr) ν_{max} 3273, 3024, 2928, 1671, 1621, 1605, 1583, 1458 cm^{-1}. ^{1}H NMR (400 MHz; $CDCl_3$/TMS) δ: 2.62 (s, 3H, Me), 4.28 (dd, 1H, J = 11.9, 8.6 Hz, α′-H_a), 4.36 (dd, 1H, J = 11.9, 3.2 Hz, α′-H_b), 4.62 (dd, 1H, J = 8.6, 3.2 Hz, β′-H), 5.39 (br s, 1H, NH), 6.25 (d, 1H, J = 16.3 Hz, α-H), 7.11–7.26 (m, 10H_{arom}), 7.36 (d, 2H, J = 8.5 Hz, H_{arom}), 7.61 (d, 1H, J = 16.3 Hz, β-H), 7.81 (d, 2H, J = 8.5 Hz, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ: = 26.1, 45.6, 52.2, 125.6, 126.8, 127.5, 128.2, 128.9, 129.6, 130.3, 130.9, 131.8, 134.8, 136.3, 140.1, 141.9, 144.2, 199.7. EIMS (m/z): 405 (M$^+$). Anal. Calcd for $C_{24}H_{23}NO_3S$: C, 71.09; H, 5.72; N, 3.45. Found: C, 71.39; H, 5.41; N, 3.27. *Compound* **4d**: Colorless solid,

yield 87%, mp 141–143 °C. IR (KBr) ν_{max} 3281, 3019, 2921, 1675, 1619, 1603, 1588, 1449 cm^{-1}. ^1H NMR (400 MHz; $CDCl_3$/TMS) δ: 2.59 (s, 3H, Me), 4.30 (dd, 1H, J = 12.2, 8.5 Hz, α′-H_a), 4.37 (dd, 1H, J = 12.2, 3.4 Hz, α′-H_b), 4.65 (dd, 1H, J = 8.5, 3.4 Hz β′-H), 5.43 (br s, 1H, NH), 6.31 (d, 1H, J = 16.4 Hz, α-H), 7.09–7.28 (m, 7H_{arom}), 7.38 (d, 2H, J = 8.7 Hz, H_{arom}), 7.67 (d, 2H, J = 8.5 Hz, H_{arom}), 7.59 (d, 1H, J = 16.4 Hz, β-H), 7.85 (d, 2H, J = 8.7 Hz, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ: = 25.8, 47.3, 52.7, 125.9, 126.7, 127.5, 128.2, 128.9, 129.6, 130.2, 131.3, 132.4, 134.5, 136.7, 141.3, 142.6, 145.1, 200.1. EIMS (m/z): 439, 441 (M^+, M^+ + 2). Anal. Calcd for $C_{24}H_{22}ClNO_3S$: C, 65.52; H, 5.04; N, 3.18. Found: C, 65.15; H, 5.31; N, 2.90. *Compound* **4g***:* Colorless solid, yield 81%, mp 134–136 °C. IR (KBr) ν_{max} 3281, 3019, 2933, 1680, 1617, 1603, 1587, 1459 cm^{-1}. ^1H NMR (400 MHz; $CDCl_3$/TMS) δ: 2.59 (s, 3H, Me), 3.73 (s, 3H, OMe), 4.28 (dd, 1H, J = 12.0, 8.6 Hz, α′-H_a), 4.31 (dd, 1H, J = 12.0, 3.2 Hz, α′-H_b), 4.60 (dd, 1H, J = 8.6, 3.2 Hz, β′-H), 5.39 (br s, 1H, NH), 6.33 (d, 1H, J = 16.5 Hz, α-H), 6.93 (d, 2H, J = 8.7 Hz, H_{arom}), 7.12–7.31 (m, 5H_{arom}), 7.21 (d, 2H, J = 8.7 Hz, H_{arom}), 7.36 (d, 2H, J = 8.4 Hz, H_{arom}), 7.54 (d, 1H, J = 16.5 Hz, β-H), 7.83 (d, 2H, J = 8.4 Hz, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ: = 25.4, 46.8, 53.4, 56.7, 115.3, 125.7, 126.6, 127.4, 128.4, 129.1, 129.8, 130.7, 134.7, 135.8, 136.4, 142.4, 143.1, 159.2, 200.1. EIMS (m/z): 435 (M^+). Anal. Calcd for $C_{25}H_{25}NO_4S$: C, 68.94; H, 5.79; N, 3.22. Found: C, 68.66; H, 6.09; N, 3.41.

Compound **4m***:* Colorless solid, yield 92%, mp 153–155 °C. IR (KBr) ν_{max} 3286, 3021, 2931, 1681, 1621, 1607, 1581, 1456 cm^{-1}. ^1H NMR (400 MHz; $CDCl_3$/TMS) δ: 2.61 (s, 3H, Me), 4.33 (dd, 1H, J = 12.3, 8.8 Hz, α′-H_a), 4.39 (dd, 1H, J = 12.3, 3.3 Hz, α′-H_b), 4.67 (dd, 1H, J = 8.8, 3.3 Hz, β′-H), 5.39 (br s, 1H, NH), 6.35 (d, 1H, J = 16.3 Hz, α-H), 7.11–7.33 (m, 7H_{arom}), 7.56 (d, 1H, J = 16.3 Hz, β-H), 7.69 (d, 2H, J = 8.8 Hz, H_{arom}), 7.88 (d, 2H, J = 8.5 Hz, H_{arom}), 8.31 (d, 2H, J = 8.8 Hz, H_{arom}). ^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ: = 26.1, 46.8, 52.4, 121.6, 126.3, 126.9, 127.7, 128.4, 129.3, 130.5, 134.3, 135.6, 136.7, 139.8, 141.7, 145.3, 148.5, 199.7. EIMS (m/z): 450 (M^+). Anal. Calcd for $C_{24}H_{22}N_2O_5S$: C, 63.98; H, 4.92; N, 6.22. Found: C, 64.26; H, 5.26; N, 6.01.