CHEMISTRY
A EUROPEAN JOURNAL

COMMUNICATION

DOI: 10.1002/chem.201203756

Baylis–Hillman Bromides as a Source of 1,3-Dipoles: Sterically Directed Synthesis of Oxindole-Fused Spirooxirane and Spirodihydrofuran Frameworks

Deevi Basavaiah,* Satpal Singh Badsara, and Bharat Chandra Sahu[a]

The spirooxindole moiety is one of the most important structural frameworks and is frequently found in many natural products[1a–i] and clinical pharmaceuticals.[1d,j–l] Therefore, the development of simple synthetic strategies for obtaining spirooxindole derivatives has been and continues to be an attractive area in synthetic and medicinal chemistry.[1f–i,2a–f] As part of our ongoing research into the Baylis–Hillman (BH) reaction, herein, we report the interesting sterically directed cycloaddition reactions of the dipoles that are generated from Baylis–Hillman bromides with isatins as dipolarophiles, thus providing a facile strategy for the synthesis of spiroepoxy oxindoles and spirodihydrofuran oxindoles in a one-pot operation.

The Baylis–Hillman reaction provides diverse classes of densely functionalized molecules, typically known as Baylis–Hillman adducts, through the coupling of activated alkenes with electrophiles under the influence of a catalyst in an operationally simple atom-economical process.[3] The Baylis–Hillman adducts and their derivatives (in particular, their bromides and acetates) have become useful as synthons for the development of a number of organic-transformation methodologies that lead to the synthesis of various building blocks and bioactive compounds.[3,4] These Baylis–Hillman adducts and their derivatives have also been successfully employed as dipolarophiles[3c,h] (with benzonitrile oxide,[5a] azomethine ylides,[5b,c] etc. as dipoles) in [3+2] cycloaddition reactions and also as a source for generating dipoles (with methyleneindolinones,[4c] isatylidene malononitriles,[4d] *N*-phenylmaleimide,[4a,6a] enones,[4g] diethyl azodicarboxylate (DEAD)/diisopropyl azodicarboxylate (DIAD),[6b] propargyl sulfones,[4e] etc. as dipolarophiles), thereby producing a variety of heterocyclic and carbocylic compounds of medicinal importance.[3c,d]

It has been well documented in the literature that Baylis–Hillman adducts (or their derivatives) that contain ester (prepared from alkyl acrylates) and nitrile groups (prepared from acrylonitrile) show remarkable opposite stereochemical directions in various chemical transformations.[7] This reversal has been mostly been attributed to the steric difference between the (smaller) nitrile and (larger) ester functionalities. To the best of our knowledge, there has been no systematic study in understanding the stereochemical directions in the cycloaddition reactions of Baylis–Hillman adducts (or their derivatives) that contain ester and nitrile groups. It occurred to us that the dipoles that are generated from Baylis–Hillman bromides that contain ester and nitrile groups should, in principle, show different reactivities in their cycloaddition reactions with isatin derivatives. Thus, we selected three types of the Baylis–Hillman bromides (**1**–**3**) and various isatin derivatives (**4**) as reaction partners for our study (Figure 1).

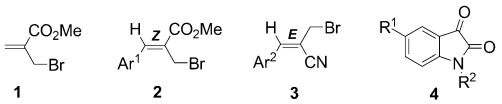


Figure 1. Reaction partners Baylis–Hillman bromides and isatin derivatives.

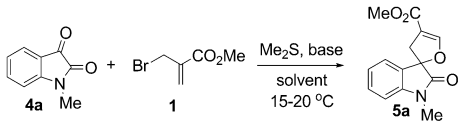
First, we investigated the cycloaddition reaction between Baylis–Hillman bromide methyl-2-(bromomethyl)prop-2-enoate (**1**) and 1-methylisatin (**4a**). In our initial studies, the reaction between compounds **1** and **4a** in the presence of Me_2S and K_2CO_3 in DMF gave spirodihydrofuran oxindole **5a** in 74% yield (Table 1, entry 1). To optimize this reaction, we tested various conditions (Table 1) and the best results were obtained when the allyl bromide **1** (3 mmol) was treated with compound **4a** (2 mmol) in DMF (5 mL) at 15–20 °C in the presence of Me_2S (4 mmol) and Cs_2CO_3 (4 mmol) for 8 h, thus providing the desired spirodihydrofuran oxindole **5a** in 83% yield (Table 1, entry 5). To understand the scope of this method, we used several N-substituted isatins (**4a**–**g**) in the cycloaddition reaction with compound **1**; the resulting spirodihydrofuran oxindoles **5a**–**g**[8a] were obtained in 78–86% yield (Table 2).

Next, we directed our attention to examining the potential of Baylis–Hillman bromide[9] methyl-(2*Z*)-2-bromomethyl-3-phenyl-prop-2-enoate (**2a**) in the cycloaddition reaction with 1-methylisatin (**4a**) under similar conditions.[10]

[a] Prof. D. Basavaiah, S. S. Badsara, B. C. Sahu
School of Chemistry, University of Hyderabad
Hyderabad-500 046 (India)
Fax: (+91) 40-23012460
E-mail: dbsc@uohyd.ernet.in

Supporting information for this article, including experimental details, spectroscopic data, ^1H and ^{13}C NMR spectra for compounds **5**, **6**, **7**, and **8**, and X-ray crystallographic data for compounds **5a**, **6a**, **7a**, **6h**, **7h**, **8d**, and **8e**, is available on the WWW under http://dx.doi.org/10.1002/chem.201203756.

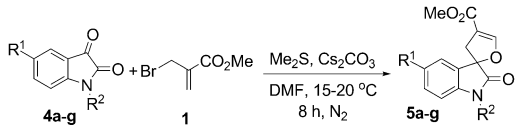
Table 1. Optimization: treatment of methyl-2-(bromomethyl)prop-2-enoate (**1**, 3 mmol) with 1-methylisatin (**4a**, 2 mmol) in the presence of Me_2S (4 mmol) and base (4 mmol) to provide the spirodihydrofuran oxindole **5a**.



Entry	Base	Solvent (5 mL)	*t* [h]	Yield [%]
1	K_2CO_3	DMF	48	74
2	K_2CO_3	$CHCl_3$	72	38
3	K_2CO_3	CH_3CN	36	43
4	K_2CO_3	THF	60	38
5	Cs_2CO_3	DMF	8	83
6	Cs_2CO_3	THF	24	65
7	Cs_2CO_3	DMF	12	78[a]
8	Cs_2CO_3	CH_3CN	24	71
9	NaOH	DMF	14	76

[a] 1 equiv of base was used.

Table 2. Synthesis of spirodihydrofuran oxindoles **5a–g**.[a]



Entry	R^1	R^2	Isatin	Product[b]	Yield [%][c]
1	H	Me	**4a**	**5a**[d]	83
2	H	Et	**4b**	**5b**	78
3	Cl	Me	**4c**	**5c**	78
4	Cl	Et	**4d**	**5d**	82
5	Br	Me	**4e**	**5e**	86
6	Br	Et	**4f**	**5f**	81
7	Me	Bn	**4g**	**5g**	80

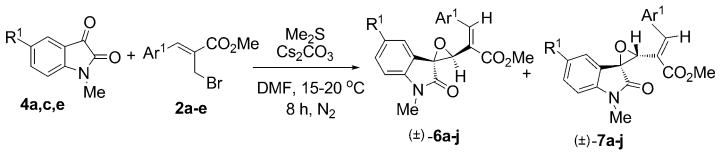
[a] All reactions were performed on a 3 mmol scale with respect to Baylis–Hillman bromide **1** with isatins **4a–g** (2 mmol) in the presence of Me_2S (4 mmol) and Cs_2CO_3 (4 mmol) in DMF (5 mL) at 15–20 °C. [b] All of these compounds were obtained as solids and were fully characterized (see the Supporting Information). [c] Yield of isolated product, based on the isatin. [d] The structure of this compound was further confirmed by single-crystal X-ray analysis (see the Supporting Information).[8b] Bn = benzyl.

However, we did not obtain the expected spirodihydrofuran oxindole; instead, spiroepoxy oxindoles **6a** and **7a**[8a] were obtained in a 27:46 ratio (separated by column chromatography) and an overall 73% yield (Table 3, entry 1). Interestingly, allyl bromide **1** provided spirodihydrofuran oxindoles **5**, whereas sterically more demanding allyl bromide **2a** gave spiroepoxy oxindoles **6a** and **7a**.[11] These reactions clearly indicated the influence of steric factors in directing the reaction pathway, thus leading to the formation of different products. Then, we extended this strategy to the use of Baylis–Hillman bromides **2a–e** in cycloaddition reactions with representative isatin derivatives **4a**, **c**, and **e**; the resulting spiroepoxy oxindoles **6a–j** and **7a–j**[8a,11] were obtained as separable mixtures of diastereomers in 65–75% yield (Table 3).

The significant differences in reactivity between allyl bromides **1** and **2** in these reactions led us to investigate the reaction of (2*E*)-2-bromomethyl-3-(4-methylphenyl)prop-2-enenitrile (**3a**)[9] with 5-chloro-1-methylisatin (**4c**) under similar conditions. In this case, the spiroepoxy oxindole was not obtained; instead spirodihydrofuran oxindole **8a** [3*R*-(2′*R*),5′*R*]/[3*S*(2′*S*),5′*S*]-(1-methyl-5-chloroindolin-2-one)-3-spiro-2′-[4′-cyano-5′-(4-methylphenyl)-2′,5′-dihydrofuran] was isolated as a single diastereomer (Table 4, entry 1).[12] We were pleased to observe high stereoselectivity in this reaction. To understand the applicability of this strategy, we subjected allyl bromide **3a** to the reaction with isatin derivatives **4d** and **e**, which gave spirodihydrofuran oxindoles **8b** and **c** in 73% and 67% yield, respectively.[8a,12] Similarly, the reactions of allyl bromide **3b** with **4a**, **c**, and **e** provided the desired spirodihydrofuran oxindoles **8d–f** in 65–71% yield.[8a,12]

The different reactivities of allyl bromides **1–3** might be attributed to steric factors, as shown in the mechanistic pathway (Schemes 1–3). Thus, in the case of allyl bromides **2a–e**, spirodihydrofuran oxindoles were not formed. This result is probably due to the *Z* stereochemistry of the bromide, which might prevent the attack of the oxygen anion on the olefinic carbon atom α to the aryl group (owing to steric hindrance), thus leading to the formation of an oxirane ring. In the case of allyl bromides **3a** and **b**, *E* stereochemistry might facilitate the formation of the spirodihydrofuran oxindole framework, (±)-**8**, with high diastereoselectivity (see transition states **T-1** and **T-2**, Scheme 3). Path A3, which leads to the formation of com-

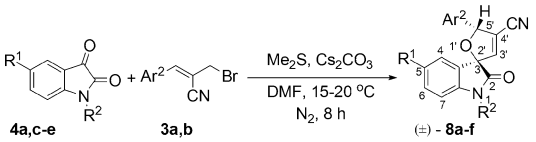
Table 3. Synthesis of spiroepoxy oxindoles **6a–j** and **7a–j**.[a,b,c]



Entry	Isatin	R^1	BH bromide	Ar^1	Product **6**	Yield [%]	Product **7**	Yield [%]
1	**4a**	H	**2a**	C_6H_5	**6a**[d]	27	**7a**[d]	46
2	**4e**	Br	**2a**	C_6H_5	**6b**	30	**7b**	43
3	**4a**	H	**2b**	4-ClC_6H_4	**6c**	19	**7c**	52
4	**4a**	H	**2c**	4-MeC_6H_4	**6d**	30	**7d**	43
5	**4c**	Cl	**2c**	4-MeC_6H_4	**6e**	25	**7e**	42
6	**4a**	H	**2d**	2-ClC_6H_4	**6f**	25	**7f**	50
7	**4e**	Br	**2d**	2-ClC_6H_4	**6g**	26	**7g**	42
8	**4a**	H	**2e**	4-$MeOC_6H_4$	**6h**[d]	41	**7h**[d]	29
9	**4c**	Cl	**2e**	4-$MeOC_6H_4$	**6i**	36	**7i**	31
10	**4e**	Br	**2e**	4-$MeOC_6H_4$	**6j**[e]	41	**7j**	24

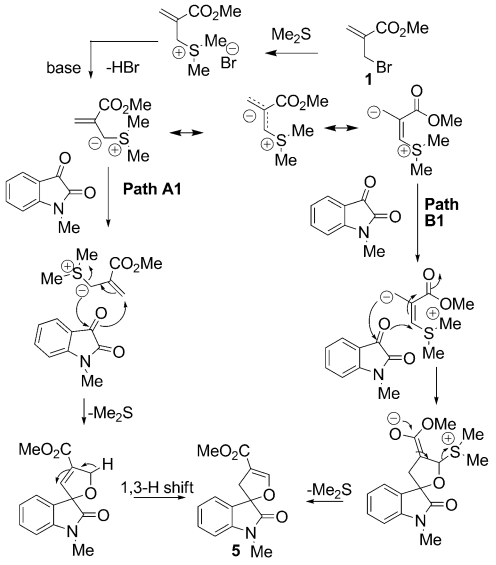
[a] All reactions were performed on a 3 mmol scale with respect to Baylis–Hillman bromides **2a–e** with isatins **4a**, **c** and **e** (2 mmol) in the presence of Me_2S (4 mmol) and Cs_2CO_3 (4 mmol) in DMF (5 mL) at 15–20 °C. [b] Pure diastereomers **6** and **7** were separated and obtained as solids and were fully characterized (see the Supporting Information). [c] Yield of isolated product, based on the isatin. [d] The structure of this compound was further confirmed by single-crystal X-ray analysis (see the Supporting Information).[8b] [e] This compound was obtained as a viscous liquid.

Table 4. Synthesis of spirodihydrofuran oxindoles **8a–f**.[a]



Entry	Isatin	R^1	R^2	BH bromide	Ar^2	Product[b]	Yield[c] [%]
1	**4c**	Cl	Me	**3a**	4-MeC_6H_4	**8a**	66
2	**4d**	Cl	Et	**3a**	4-MeC_6H_4	**8b**	73
3	**4e**	Br	Me	**3a**	4-MeC_6H_4	**8c**	67
4	**4a**	H	Me	**3b**	2-ClC_6H_4	**8d**[d]	69
5	**4c**	Cl	Me	**3b**	2-ClC_6H_4	**8e**[d]	65
6	**4e**	Br	Me	**3b**	2-ClC_6H_4	**8f**	71

[a] All reactions were performed on a 3 mmol scale with respect to Baylis–Hillman bromides **3a** and **b** with isatins **4a** and **c**–**e** (2 mmol) in the presence of Me_2S (4 mmol) and Cs_2CO_3 (4 mmol) in DMF (5 mL) at 15–20 °C. [b] All of these compounds were obtained as solids and were fully characterized (see the Supporting Information). [c] Yield of isolated product, based on the isatin. [d] The structure of this compound was further confirmed by single-crystal X-ray analysis (see the Supporting Information).[8b]



Scheme 1. Plausible mechanism for the formation of spirodihydrofuran oxindole **5**.

pound (±)-**8**, is probably favored, owing to the possible steric repulsions in path B3.

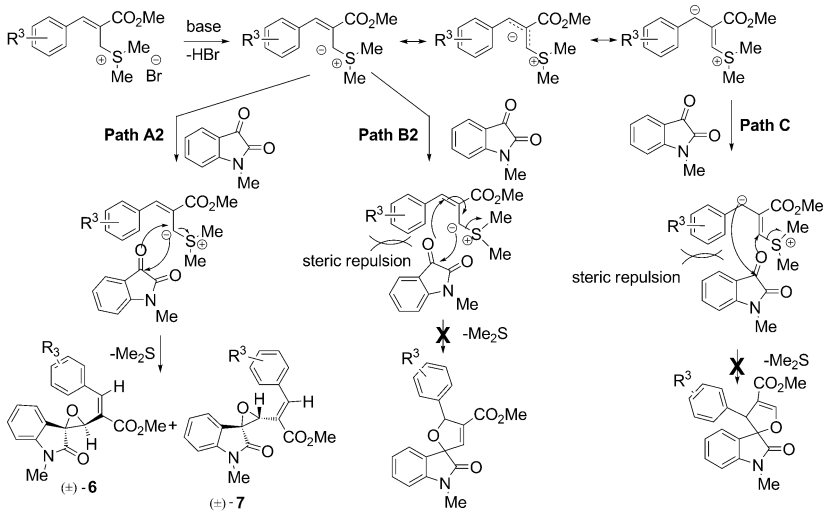
In conclusion, we have demonstrated that steric factors direct the cycloaddition reactions between dipoles that are generated from Baylis–Hillman bromides **1**–**3** and isatins **4** as dipolarophiles, thus providing an interesting method for the synthesis of spiroepoxy oxindoles and spirodihydrofuran oxindoles.

Experimental Section

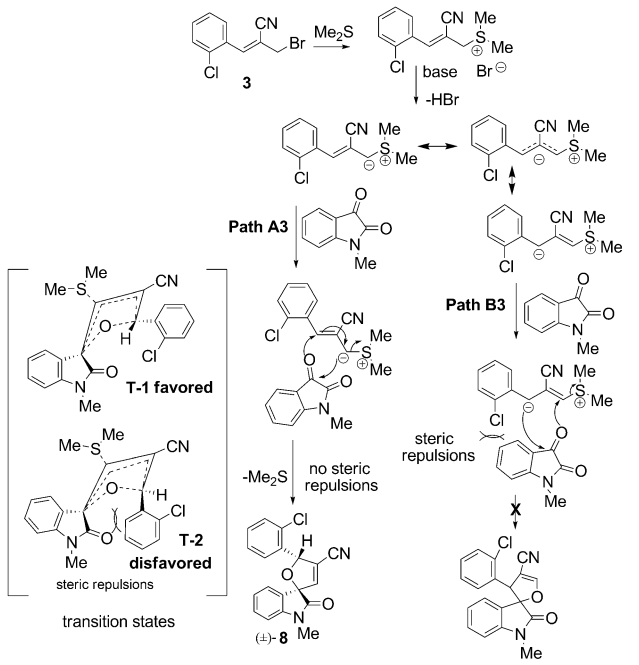
To a stirring solution of methyl-2-(bromomethyl)prop-2-enoate (**1**, 3 mmol, 0.537 g) in DMF (5 mL) were added Me_2S (4.0 mmol, 0.248 g, 0.3 mL), Cs_2CO_3 (4.0 mmol, 1.303 g), and 1-methylisatin (**4a**, 2.0 mmol, 0.322 g) at 15–20 °C. After stirring for 8 h, the reaction mixture was diluted with water (3 mL) and extracted with EtOAc (3×10 mL). The combined organic layer was washed with water (2×5 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated and the crude product was purified by column chromatography on silica gel (EtOAc/hexanes, 20%) to provide compound **5a** as a white solid (0.431 g, 83% yield).

Acknowledgements

We thank the DST (New Delhi) for funding this project. S.S.B. thanks the CSIR (New Delhi) for a fellowship and B.C.S. thanks the UGC (New Delhi) for a Kothari fellowship. We thank the UGC for providing some instrumental facilities. We thank the National Single-Crystal X-ray and HRMS Facility funded by the DST. We also thank Professors T. P. Radhakrishnan and S. Pal at the School of Chemistry, the University of Hyderabad, for their helpful discussions regarding analysis of the X-ray data.



Scheme 2. Plausible mechanism for the formation of spiroepoxy oxindoles **6** and **7**.



Scheme 3. Plausible mechanism for the formation of spirodihydrofuran oxindoles **8**.

Keywords: cycloaddition · dipoles · fused-ring systems · heterocycles · spiro compounds

[1] a) M. N. G. James, G. J. B. Williams, *Can. J. Chem.* **1972**, *50*, 2407–2412; b) R. C. Elderfield, R. E. Gilman, *Phytochemistry* **1972**, *11*, 339–343; c) C.-B. Cui, H. Kakeya, H. Osada, *Tetrahedron* **1996**, *52*, 12651–12666; d) C. V. Galliford, K. A. Scheidt, *Angew. Chem.* **2007**, *119*, 8902–8912; *Angew. Chem. Int. Ed.* **2007**, *46*, 8748–8758; e) J. M. Finefield, J. C. Frisvad, D. H. Sherman, R. M. Williams, *J. Nat. Prod.* **2012**, *75*, 812–833; f) C. Marti, E. M. Carreira, *Eur. J. Org. Chem.* **2003**, 2209–2219; g) N. R. Ball-Jones, J. J. Badillo, A. K. Franz, *Org. Biomol. Chem.* **2012**, *10*, 5165–5181; h) L. E. Overman, M. D. Rosen, *Angew. Chem.* **2000**, *112*, 4768–4771; *Angew. Chem. Int. Ed.* **2000**, *39*, 4596–4599; i) P. S. Baran, J. M. Richter, *J. Am. Chem. Soc.* **2005**, *127*, 15394–15396; j) V. V. Vintonyak, K. Warburg, H. Kruse, S. Grimme, K. Hubel, D. Rauh, H. Waldmann, *Angew. Chem.* **2010**, *122*, 6038–6041; *Angew. Chem. Int. Ed.* **2010**, *49*, 5902–5905; k) K. Ding, Y. Lu, Z. Nikolovska-Coleska, G. Wang, S. Qiu, S. Shangary, W. Gao, D. Qin, J. Stuckey, K. Krajewski, P. P. Roller, S. Wang, *J. Med. Chem.* **2006**, *49*, 3432–3435; l) S. M. Rajesh, S. Perumal, J. C. Menéndez, P. Yogeeswari, D. Sriram, *Med. Chem. Commun.* **2011**, *2*, 626–630.

[2] a) J. Li, Y. Liu, C. Li, X. Jia, *Chem. Eur. J.* **2011**, *17*, 7409–7413; b) A. P. Antonchick, C. Gerding-Reimers, M. Catarinella, M. Schurmann, H. Preut, S. Ziegler, D. Rauh, H. Waldmann, *Nat. Chem.* **2010**, *2*, 735–740; c) V. Schulz, M. Davoust, M. Lemarié, J.-F. Lohier, J. S. O. Santos, P. Metzner, J.-F. Brière, *Org. Lett.* **2007**, *9*, 1745–1748; d) D. Basavaiah, K. R. Reddy, *Org. Lett.* **2007**, *9*, 57–60; e) Z. Lian, M. Shi, *Org. Biomol. Chem.* **2012**, *10*, 8048–8050; f) X.-C. Zhang, S.-H. Cao, Y. Wei, M. Shi, *Chem. Commun.* **2011**, *47*, 1548–1550.

[3] a) T. Y. Liu, M. Xie, Y.-C. Chen, *Chem. Soc. Rev.* **2012**, *41*, 4101–4112; b) D. Basavaiah, G. Veeraraghavaiah, *Chem. Soc. Rev.* **2012**, *41*, 68–78; c) D. Basavaiah, B. S. Reddy, S. S. Badsara, *Chem. Rev.* **2010**, *110*, 5447–5674; d) V. Declerck, J. Martinez, F. Lamaty, *Chem. Rev.* **2009**, *109*, 1–48; e) C. E. Aroyan, A. Dermenci, S. J. Miller, *Tetrahedron* **2009**, *65*, 4069–4084; f) V. Singh, S. Batra, *Tetrahedron* **2008**, *64*, 4511–4574; g) D. Basavaiah, K. V. Rao, R. J. Reddy, *Chem. Soc. Rev.* **2007**, *36*, 1581–1588; h) D. Basavaiah, A. J. Rao, T. Satyanarayana, *Chem. Rev.* **2003**, *103*, 811–891.

[4] a) Y. Wang, L. Liu, N.-J. Zhong, D. Wang, Y.-J. Chen, *J. Org. Chem.* **2012**, *77*, 4143–4147; b) M. S. Santos, F. Coelho, *RSC Adv.* **2012**, *2*, 3237–3241; c) B. Tan, N. R. Candeias, C. F. Barbas III, *J. Am. Chem. Soc.* **2011**, *133*, 4672–4675; d) F. Zhong, X. Han, Y. Wang, Y. Lu, *Angew. Chem.* **2011**, *123*, 7983–7987; *Angew. Chem. Int. Ed.* **2011**, *50*, 7837–7841; e) J. Peng, X. Huang, L. Jiang, H.-L. Cui, Y.-C. Chen, *Org. Lett.* **2011**, *13*, 4584–4587; f) H.-P. Deng, Y. Wei, M. Shi, *Org. Lett.* **2011**, *13*, 3348–3351; g) R. Zhou, J. Wang, H. Song, Z. He, *Org. Lett.* **2011**, *13*, 580–583; h) K. R. L. Freire, C. F. Tormena, F. Coelho, *Synlett* **2011**, 2059–2063; i) P. Shanbhag, P. R. Nareddy, M. Dadwal, S. M. Mobin, I. N. N. Namboothiri, *Org. Biomol. Chem.* **2010**, *8*, 4867–4873; j) D. Basavaiah, B. Devendar, K. Aravindu, A. Veerendhar, *Chem. Eur. J.* **2010**, *16*, 2031–2035; k) M. Bakthadoss, G. Sivakumar, D. Kannan, *Org. Lett.* **2009**, *11*, 4466–4469; l) Y. Q. Jiang, Y. L. Shi, M. Shi, *J. Am. Chem. Soc.* **2008**, *130*, 7202–7203; m) M. E. Krafft, T. F. N. Haxell, K. A. Seibert, K. A. Abboud, *J. Am. Chem. Soc.* **2006**, *128*, 4174–4175; n) V. K. Aggarwal, A. Patin, S. Tisserand, *Org. Lett.* **2005**, *7*, 2555–2557; o) S. R. S. S. Kotti, X. Xu, G. Li, A. D. Headley, *Tetrahedron Lett.* **2004**, *45*, 1427–1431; p) L. Navarre, S. Darses, J.-P. Genet, *Chem. Commun.* **2004**, 1108–1109; q) D. Basavaiah, T. Satyanarayana, *Org. Lett.* **2001**, *3*, 3619–3622; r) D. Basavaiah, M. Bakthadoss, S. Pandiaraju, *Chem. Commun.* **1998**, 1639–1640; s) A. Chamakh, H. Amri, *Tetrahedron Lett.* **1998**, *39*, 375–378.

[5] a) S. Kanemasa, S. Kobayashi, *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2685–2693; b) P. Shanmugam, B. Viswambharan, S. Madhavan, *Org. Lett.* **2007**, *9*, 4095–4098; c) M. Bakthadoss, N. Sivakumar, A. Devaraj, D. S. Sharada, *Synthesis* **2011**, 2136–2146.

[6] a) Y. Du, X. Lu, C. Zhang, *Angew. Chem.* **2003**, *115*, 1065–1067; *Angew. Chem. Int. Ed.* **2003**, *42*, 1035–1037; b) D. Basavaiah, S. Roy, *Org. Lett.* **2008**, *10*, 1819–1822.

[7] a) A. Gruiec, A. Foucaud, *New J. Chem.* **1991**, *15*, 943–947; b) D. Basavaiah, P. K. S. Sarma, *J. Chem. Soc. Chem. Commun.* **1992**, 955–957; c) D. Basavaiah, P. K. S. Sarma, A. K. D. Bhavani, *J. Chem. Soc. Chem. Commun.* **1994**, 1091–1092; d) D. Basavaiah, A. K. D. Bhavani, S. Pandiaraju, P. K. S. Sarma, *Synlett* **1995**, 243–244; e) D. Basavaiah, S. Pandiaraju, *Tetrahedron* **1996**, *52*, 2261–2268; f) D. Basavaiah, M. Krishnamacharyulu, R. S. Hyma, S. Pandiaraju, *Tetrahedron Lett.* **1997**, *38*, 2141–2144; g) H. J. Lee, M. R. Seong, J. N. Kim, *Tetrahedron Lett.* **1998**, *39*, 6223–6226; h) G. W. Kabalka, B. Venkataiah, G. Dong, *Org. Lett.* **2003**, *5*, 3803–3805; i) G. W. Kabalka, G. Dong, B. Venkataiah, C. Chen, *J. Org. Chem.* **2005**, *70*, 9207–9210; j) B. C. Ranu, K. Chattopadhyay, R. Jana, *Tetrahedron Lett.* **2007**, *48*, 3847–3850; k) M. L. Kantam, K. B. S. Kumar, B. Sreedhar, *J. Org. Chem.* **2008**, *73*, 320–322.

[8] a) For the names of the compounds, see the Supporting Information; b) CCDC-898730 (**5a**), CCDC-898579 (**6a**), CCDC-898580 (**7a**), CCDC-898731 (**6h**), CCDC-898732 (**7h**), CCDC-898386 (**8d**), and CCDC-898387 (**8e**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[9] a) S. E. Drewes, N. D. Emslie, *J. Chem. Soc. Perkin Trans. 1* **1982**, 2079–2083; b) R. Buchholz, H. M. R. Hoffmann, *Helv. Chim. Acta* **1991**, *74*, 1213–1220; c) D. Basavaiah, K. R. Reddy, N. Kumaragurubaran, *Nat. Prot.* **2007**, *2*, 2665–2676.

[10] The reactions of BH-bromides with methyl vinyl ketone in the presence of Me_2S and a base provided cyclopropanes; see: K. Y. Lee, S. C. Kim, J. N. Kim, *Bull. Korean Chem. Soc.* **2006**, *27*, 319–321; similar reactions of BH-bromides with *N*-tosyl amines provided aziridines; see: K. Y. Lee, S. C. Kim, J. N. Kim, *Tetrahedron Lett.* **2006**, *47*, 977–980.

[11] Interestingly, in the ^{1}H NMR spectra of compounds **6a–j**, the *N*-methyl protons appeared in the range of $\delta = 3.13$–3.24 ppm, whereas in the case of compounds **7a–j**, they appeared in the range of $\delta = 2.87$–2.99 ppm. Similarly, the aromatic proton (probably the C-4

proton) for compounds **6a–j** appeared in the range of $\delta = 6.74$–6.97 ppm, whereas in the case of compounds **7a–j**, it was deshielded and appeared at $\delta > 7.00$ ppm. Although this observation is not significant, it is worth noting that in the ^{13}C NMR spectra of compounds **6a–j** the ester cabonyl carbon atom appeared in the range of $\delta = 170.56$–171.44 ppm, whereas in the case of compounds **7a–j**, the same atom appeared in the range of $\delta = 169.09$–169.74 ppm.

[12] a) The stereochemistry was assigned on the basis of the single-crystal X-ray structures of compounds **8d** and **e**.[8] b) We have retained "[3*R*(2′*R*),5′*R*]/[3*S*(2′*S*),5′*S*]" before the names of compounds **8a–c** and "[3*R*(2′*R*),5′*S*]/[3*S*(2′*S*),5′*R*]" before the names of compounds **8d–f** to indicate their racemic nature and also their stereochemistry. The difference in configuration (*R* versus *S*) at the 5′ position was due to a change in priority groups.

Received: October 20, 2012
Published online: February 1, 2013

