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Ionic liquid [Hmim]HSO_4-promoted one-pot oxidative conjugate addition of sulfur-centred nucleophiles to Baylis–Hillman adducts

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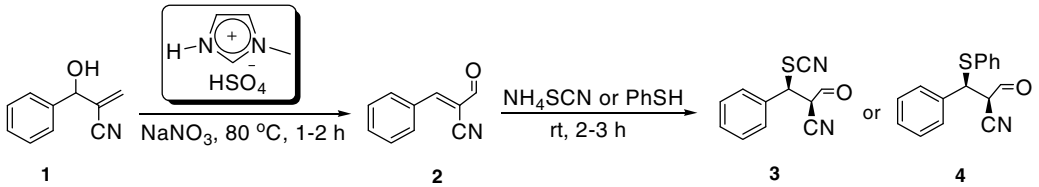
Abstract

The first example of the one-pot oxidative conjugate addition of sulfur-centred nucleophiles to Baylis–Hillman adducts is reported. The reaction involves oxidation of Baylis–Hillman adducts with $NaNO_3$ in the Brønsted acidic ionic liquid [Hmim]HSO_4 to give [*E*]-α-cyanocinnamaldehydes followed by conjugate hydrothiocyanation/hydrosulfenylation with NH_4SCN/PhSH to afford the corresponding β-thiocyanato (or β-phenylsulfenyl)-α-cyanohydrocinnamaldehydes diastereoselectively in 76–89% yields in a one-pot procedure. After isolation of the product, the ionic liquid [Hmim]HSO_4 could be easily recycled for further use.

Keywords: Baylis–Hillman adducts; Conjugate addition; Oxidation; Ionic liquids; Cinnamaldehydes; Stereoselective synthesis

The formation of carbon–sulfur bond constitutes a key reaction in biosynthetic processes as well as in organic synthesis.[1] The conjugate addition of sulfur-centred nucleophiles to α,β-unsaturated carbonyl compounds is one of the most important methods for the synthesis of β-sulfur functionalized carbonyl compounds. Sulfur functionalities, viz. thiocyanate and thioether, are well known in various areas of organo-sulfur chemistry and are of considerable importance from both chemical and biological viewpoints.

The thioether structural fragment is an important molecular tool as bioisosteric replacements in rational drug design.[2] Organic thiocyanates, representing a masked mercapto group, are useful scaffolds for various organic transformations especially in the synthesis of heterocycles such as thiazoles, thiazines and as biocides.[3] The thiocyanato group is a prominent functional motif found in certain anticancer natural products formed by the deglycosylation of glucosinolates derived from cruciferous vegetables.[4]



1 2 3 4

Scheme 1. Ionic liquid-promoted oxidative conjugate addition to BH adducts.

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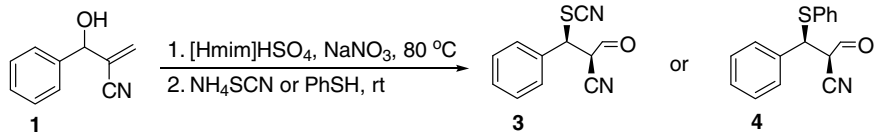
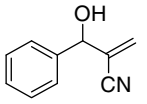
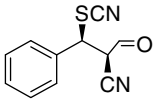
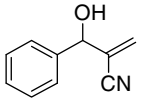
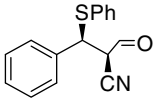
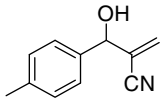
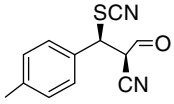
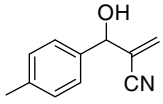
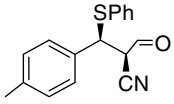
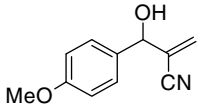
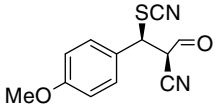
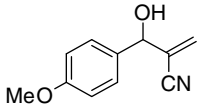
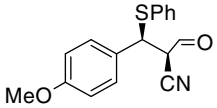
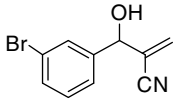
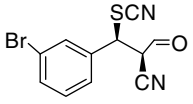
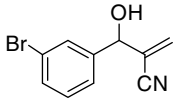
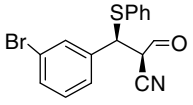
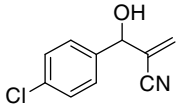
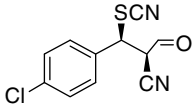
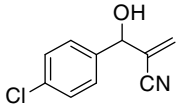
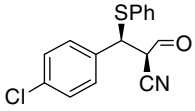
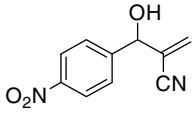
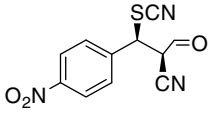
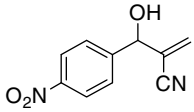
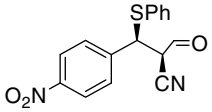
Table 1
One-pot oxidative conjugate addition of sulfur-centred nucleophiles to BH adducts



1 3 4

Entry	BH adduct	Nucleophile	Product	Reaction time (h)	Yield[a,b] (%)
3a		NH_4SCN		4	80
4a		PhSH		3.5	81
3b		NH_4SCN		3	84
4b		PhSH		3.5	85
3c		NH_4SCN		3	87
4c		PhSH		3	89
3d		NH_4SCN		5	84
4d		PhSH		4	86
3e		NH_4SCN		4	86
4e		PhSH		3.5	88
3f		NH_4SCN		5	76
4f		PhSH		4.5	79

[a] Yield refers to pure products after column chromatography.
[b] All compounds gave C, H and N analyses within ±0.35% and satisfactory spectral (IR, ^1H NMR, ^{13}C NMR and EIMS) data.

Furthermore, β-thiocyanated and β-sulfenylated carbonyl compounds are an important class of synthons for a wide variety of compounds and thus, enhance the versatility of molecules containing sulfur functionalities.[5] Hence, the development of a simple, convenient and efficient methodology for their synthesis is highly desirable. Herein, Baylis–Hillman chemistry has been applied for this purpose.

The Baylis–Hillman reaction is an efficient carbon–carbon bond forming reaction yielding densely functionalized molecules,[6] thereby providing handles for further manipulation in a multitude of synthetic organic transformations.[7] The utility of Baylis–Hillman (BH) adducts, particularly in the form of their modified version (e.g., acetyl derivatives) as carbon electrophiles, and their derivatization with various nucleophilic reagents including thiocyanates, alkyl or aryl thiolates providing a wide range of potential synthetic intermediates and precursors for the synthesis of a variety of biologically active natural and unnatural products has been well documented in the literature.[8–10]

Unmodified BH adducts have been employed as Michael acceptors to produce functionalized aldol products with oxygen, sulfur, nitrogen and carbon-centred nucleophiles.[11] Recently, oxidative conjugate addition of carbon-centred nucleophiles to BH adducts has been reported.[12] However, there has been no report on oxidative conjugate addition of sulfur-centred nucleophiles to BH adducts.

Ionic liquids (ILs) have gained considerable interest as environmentally benign reaction media, catalysts and reagents, and are easy to recycle.[13] Recently, Brønsted acidic ionic liquids have been deemed as promising alternatives for acid catalyzed reactions and play a dual solvent–catalyst role in a variety of reactions including esterification of carboxylic acids, protection of alcohols and carbonyl groups, oxidation of alcohols, alcohol dehydrodimerization, pinocol/benzopinocol rearrangement, in Mannich reactions and cleavage of ethers.[14]

One-pot sequential multi-step reactions are of increasing academic, economical and ecological interest because they address fundamental principles of synthetic efficiency and reaction design. The continued interest of synthetic chemists in the BH reaction and our ongoing efforts to devise one-pot protocols involving conjugate addition[15] have encouraged us to develop the present Brønsted acidic ionic liquid-promoted oxidative sulfur functionalization of BH adducts (Scheme 1), opens a new aspect of their synthetic utility.

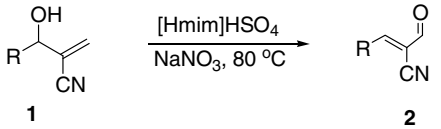
The present one-pot procedure for oxidative hydrothiocyanation/hydrosulfenylation involves stirring an equimolar mixture of $NaNO_3$ and BH adduct **1** in 1-methylimidazolinium hydrogen sulfate [Hmim]HSO_4 at 80 °C for 1–2 h followed by the addition of 1.1 equiv of NH_4 SCN or PhSH and stirring at rt for a further 2–3 h to afford the corresponding hitherto unknown β-thiocyanated product **3** in 76–87% yields or β-sulfenylated compounds **4** in 79–89% yields (Table 1).[16] The process proceeds through the formation of isolable [*E*]-α-cyanocinnamaldehydes **2**. The formation of **3** and **4** was highly diastereoselective in favour of the *syn* isomers. The diastereomeric ratios in the crude isolates were determined by ^{1}H NMR spectroscopy to note any inadvertent alteration of these ratios during subsequent purification. As determined by ^{1}H NMR spectroscopy, the crude isolates of **3** and **4** were found to be diastereomeric mixtures containing 91–95% and 93–96% of the *syn* isomer, respectively.

It is worth mentioning here that the synthesis of [*E*]-α-cyanocinnamaldehydes, representing an important class of synthons for the synthesis of various biologically active and heterocyclic molecules,[17] has been achieved previously from BH adducts in two steps, that is, an aqueous sulfuric acid mediated isomerization of the BH adducts to [*E*]-α-cyanocinnamyl alcohols and subsequent oxidation with PCC to afford **2**.[18] The present method advantageously provides an easy access to [*E*]-α-cyanocinnamaldehydes **2** from BH adducts with sole *E*-stereoselectivity in a one-pot reaction using the $NaNO_3$-[Hmim]HSO_4 reagent–solvent system (Table 2).[19] The *E*-stereoselectivity of molecules **2** was assigned on the basis of ^{1}H NMR spectra and literature precedent.[18]

We also attempted the oxidative conjugate hydrothiocyanation/hydrosulfenylation using $NaNO_3$–[Hmim]NO_3 as well as $NaNO_3$–[Hmim]H_2PO_4 separately under the same reaction conditions (Table 1). The reaction was unsuccessful in the former case indicating the need for an acidic hydrogen which is absent in [Hmim]NO_3 to catalyze the oxidation of the BH adducts into [*E*]-α-cyanocinnamaldehydes **2** (Scheme 2). However, the reaction proceeded with the $NaNO_3$–[Hmim]H_2PO_4 system but relatively low yields of **3** and **4** (28–39%) were obtained. This is probably due to the lower Brønsted acidity associated with [H_2PO_4]. Thus [Hmim]HSO_4 plays a dual role, that is, as an acid catalyst and solvent for both oxidation and hydrothiocyanation/hydrosulfenylation.

After isolation of products **2**–**4**, the ionic liquid [Hmim]HSO_4 could be recycled for four times up to 71% recovery and reused without any loss of efficiency.[16,19]

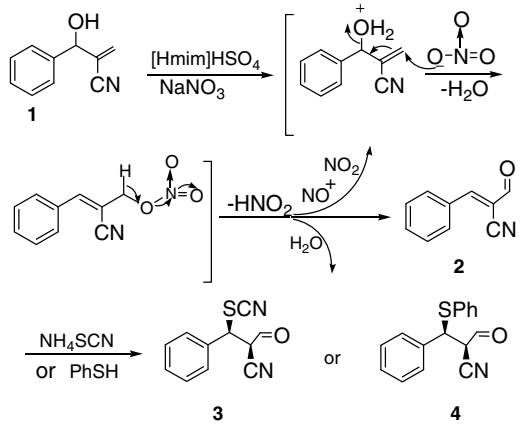
Table 2
Synthesis of [*E*]-α-cyanocinnamaldehydes **2** from BH adducts **1**



1 **2**

Product[a]	R	Time (h)	Yield[b] (%)
2a	Ph	1.5	82
2b	4-$CH_3C_6H_4$	1.3	80
2c	4-$CH_3OC_6H_4$	1	84
2d	3-BrC_6H_4	1.7	77
2e	4-ClC_6H_4	1.2	79
2f	4-$NO_2C_6H_4$	2	75

[a] **2a**, **2b** and **2e** are known compounds.[18]
[b] Yields of isolated and purified products.



Scheme 2. A plausible mechanism for the formation of **3** and **4**.

The requisite BH adducts and Brønsted acidic ionic liquids were prepared employing the known methods.[20,21]

In summary, we have reported the first example of the one-pot oxidative conjugate addition of sulfur-centred nucleophiles to BH adducts using the $NaNO_3$–[Hmim]-HSO_4 system to afford β-thiocyanato (or β-phenylsulfenyl)-α-cyanohydrocinnamaldehydes, diastereoselectively. Furthermore, application of the same reagent–solvent system for the one-pot isomerization–oxidation of BH adducts to afford [*E*]-α-cyanocinnamaldehydes has also been demonstrated, which is advantageous over the existing two-step method.[18]

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References and notes

1. (a) Fluharty, A. L. In *The Chemistry of the Thiol Group*; Patai, S., Ed.; Wiley: New York, 1974; Part 2; p 589; (b) Clark, J. H. *Chem. Rev.* **1980**, *80*, 429–452; (c) Fujita, E.; Nagao, Y. J. *Bioorg. Chem.* **1977**, *6*, 287–309; (d) Trost, B. M.; Keeley, D. E. *J. Org. Chem.* **1975**, *40*, 2013; (e) Shono, T.; Matsumura, Y.; Kashimura, S.; Hatanaka, K. *J. Am. Chem. Soc.* **1979**, *101*, 4752–4753; (f) Nishimura, K.; Ono, M.; Nagaoka, Y.; Tomioka, K. *J. Am. Chem. Soc.* **1997**, *119*, 12974–12975.
2. Patani, G. A. *Chem. Rev.* **1996**, *96*, 3147–3176.
3. (a) Kelly, T. R.; Kim, M. H.; Curtis, A. D. M. *J. Org. Chem.* **1993**, *58*, 5855–5857; (b) Leblanc, B. L.; Jursic, B. C. *Synth. Commun.* **1998**, *28*, 3591–3599; (c) Toste, F. D.; Laronde, F.; Still, W. J. *Tetrahedron Lett.* **1995**, *36*, 2949–2952; (d) Metzer, J. B. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A., Ed.; Pergamon: Oxford, 1984; Vol. 6, p 235; (e) Newman, A. A. In *Chemistry and Biochemistry of Thiocyanic Acid and its Derivatives*; Academic Press, 1975.
4. Mehta, R. G.; Liu, J.; Constantinou, A.; Thomas, C. F.; Hawthorne, M.; You, M.; Gerhaeusers, C.; Pezzuto, J. M.; Moon, R. C.; Moriarty, R. M. *Carcinogenesis* **1995**, *16*, 399–404.
5. Bakuzis, P.; Bakuzis, M. L. F. *J. Org. Chem.* **1981**, *46*, 235–239.
6. (a) Baylis, A. B.; Hillaman, M. E. D. *Offenlegungsschrift* **1972**, 2155113; Baylis, A. B.; Hillaman, M. E. D., **1973**, U.S. Patent 3,743,669; *Chem. Abstr.* **1972**, *77*, 34174; (b) Ciganek, E. In *Organic Reactions*; Wiley: New York, NY, 1997; Vol. 51. pp 201–305; (c) Ghosh, A. K.; Bilcer, G.; Schiltz, G. *Synthesis* **2001**, 2203–2229.
7. (a) Basavaiah, D.; Rao, K. V.; Reddy, R. J. *Chem. Soc. Rev.* **2007**, *36*, 1581–1588; (b) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811–891; (c) Langer, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 3049–3052; (d) Basavaiah, D.; Rao, P. D. *Tetrahedron* **1996**, *52*, 8001–8062; (e) Drewes, S. E.; Roos, G. H. P. *Tetrahedron* **1988**, *44*, 4653–4670.
8. (a) Yadav, J. S.; Gupta, M. K.; Pandey, S. K.; Reddy, B. V. S.; Sarma, A. V. S. *Tetrahedron Lett.* **2005**, *46*, 2761–2763; (b) Basavaiah, D.; Hyma, R. S.; Muthukumaran, K.; Kumaragurubaran, N. *Synthesis* **2000**, 217–219; (c) Roy, O.; Riahi, A.; Hénin, F.; Muzart, J. *Tetrahedron* **2000**, *56*, 8133–8140; (d) Basavaiah, D.; Satyanarayana, T. *Tetrahedron Lett.* **2002**, *43*, 4301–4303; (e) Kundu, M. K.; Bhat, S. V. *Synth. Commun.* **1999**, *29*, 93–101; (f) Basavaiah, D.; Bhavani, A. K. D.; Pandiaraju, S.; Sarma, P. K. S. *Synlett* **1995**, 243–244.
9. (a) Basavaiah, D.; Krishnamacharyulu, M.; Hyma, R. S.; Sarma, P. K. S.; Kumaragurabaran, N. *J. Org. Chem.* **1999**, *64*, 1197–1200; (b) Park, D. Y.; Gowarisankar, S.; Kim, J. N. *Tetrahedron Lett.* **2006**, *47*, 6641–6645; (c) Das, B.; Banerjee, J.; Chowdhury, N.; Majhi, A.; Mahender, G. *Helv. Chim. Acta* **2006**, *89*, 876–883; (d) Kim, J. N.; Chung, Y. M.; Im, Y. J. *Tetrahedron Lett.* **2002**, *43*, 6209–6211; (e) Hbaïeb, S.; Latiri, Z.; Amri, H. *Synth. Commun.* **1999**, *29*, 981–988.
10. (a) Liu, Y.; Xu, X.; Zheng, H.; Xu, D.; Xu, Z.; Zhang, Y. *Synlett* **2006**, 571–574; (b) Srihari, P.; Singh, A. P.; Jain, R.; Yadav, J. S. *Synthesis* **2006**, 2772–2776; (c) Das, B.; Chowdhury, N.; Damodar, K.; Banerjee, J. *Chem. Pharm. Bull.* **2007**, *55*, 1274–1276; (d) Kim, J. N.; Kim, J. M.; Lee, K. Y. *Synlett* **2003**, 821–824; (e) Kim, J. N.; Kim, H. S.; Gong, J. H.; Chung, Y. M. *Tetrahedron Lett.* **2001**, *42*, 8341–8344.
11. (a) Bhuniya, D.; Gujjary, S.; Sengupta, S. *Synth. Commun.* **2006**, *36*, 151–164; (b) Wang, W.; Yu, M. *Tetrahedron Lett.* **2004**, *45*, 7141–7143; (c) Azizi, N.; Saidi, M. R. *Tetrahedron Lett.* **2002**, *43*, 4305–4308; (d) Kamimura, A.; Morita, R.; Matsuura, K.; Omata, Y.; Shirai, M. *Tetrahedron Lett.* **2002**, *43*, 6189–6191.
12. (a) Yadav, J. S.; Reddy, B. V. S.; Singh, A. P.; Basak, A. K. *Synthesis* **2008**, 469–473; (b) Yadav, J. S.; Reddy, B. V. S.; Singh, A. P.; Basak, A. K. *Tetrahedron Lett.* **2007**, *48*, 4169–4172. and 7546–7548.
13. (a) Chowdhury, S.; Mohan, R. S.; Scott, J. L. *Tetrahedron* **2007**, *63*, 2363–2389; (b) Bao, W.; Wang, Z. *Green Chem.* **2006**, *8*, 1028–1033; (c) Zhao, D.; Wu, M.; Kou, Y.; Min, E. *Catal. Today* **2002**, *74*, 157–189; (d) Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667–3692; (e) Qiao, K.; Yakoyama, C. *Chem. Lett.* **2004**, *33*, 472–473; (f) Sun, W.; Xia, C.-G.; Wang, H.-W. *Tetrahedron Lett.* **2003**, *44*, 2409–2411; (d) Kamal, A.; Chouhan, G. *Tetrahedron Lett.* **2005**, *46*, 1489–1491; (e) Earle, M. J.; Katdare, S. P.; Seddon, K. R. *Org. Lett.* **2004**, *6*, 707–710.
14. (a) Cole, A. C.; Jensen, J. L.; Ntai, I.; Tran, K. L. T.; Weaver, K. J.; Forbes, D. C.; Davis, J. H., Jr. *J. Am. Chem. Soc.* **2002**, *124*, 5962–5963; (b) Welton, T. *Chem. Rev.* **1999**, *99*, 2071–2084; Sheldon, R. *Chem. Commun.* **2001**, *23*, 2399–2407; (c) Zhu, H. P.; Yang, F.; Tang, J.; He, M. Y. *Green Chem.* **2003**, *5*, 38–39; Hajipour, A. R.; Rafiee, F.; Ruoho, A. E. *Synlett* **2007**, 1118–1120; (d) Zhao, G.; Jiang, T.; Gao, H.; Han, B.; Huang, J.; Sun, D. *Green Chem.* **2004**, *6*, 75–77.
15. (a) Yadav, L. D. S.; Awasthi, C.; Rai, V. K.; Rai, A. *Tetrahedron Lett.* **2007**, *48*, 4899–4902 and 8037–8039; (b) Yadav, L. D. S.; Patel, R.; Rai, V. K.; Srivasatava, V. P. *Tetrahedron Lett.* **2007**, *48*, 7793–7795; (c) Yadav, L. D. S.; Rai, A.; Rai, V. K.; Awasthi, C. *Synlett* **2007**, 1905–1908; (d) Yadav, L. D. S.; Yadav, S.; Rai, V. K. *Green Chem.* **2006**, *8*, 455–458; (e) Yadav, L. D. S.; Rai, V. K.; Yadav, S. *Tetrahedron* **2006**, *62*, 5464–5468.
16. General procedure for the synthesis of β-thiocyanato-α-cyanohydrocinnamaldehydes (**3**) and β-phenylsulfenyl-α-cyanohydrocinnamaldehydes (**4**): A mixture of BH adduct **1** (1 mmol) and $NaNO_3$ (1 mmol) was stirred in 1 mL of [Hmim]HSO_4 at 80 °C for 1–2 h (Table 2). The reaction mixture was cooled to rt, and NH_4SCN or

PhSH (1.1 mmol) was added. The mixture was further stirred at rt for 2–3 h. After completion of the reaction (monitored by TLC), the product was extracted with ether/ethyl acetate (3 × 10 mL). The combined extract was dried over $MgSO_4$, filtered, concentrated under reduced pressure and purified by silica gel column chromatography (hexane/ethyl acetate 9.5:0.5) to afford the desired product (**3**) or (**4**). After isolation of the product, the remaining ionic liquid was washed with diethyl ether (2 × 10 mL) to remove any organic impurity, then H_2SO_4 (2.1 mmol in the case of compound **3** and 1 mmol in the case of **4**) was added, the mixture was stirred at 80 °C for 1 h, cooled to about −5 °C in an ice-salt bath. The precipitated solid was filtered out and the filtrate was dried under vacuum to afford the IL [Hmim]HSO_4 which was used in subsequent runs. Physical data of representative compounds. Compound **3a**: Yellowish solid, yield 80%, mp 102–103 °C. IR (KBr) ν_{max} 3022, 2241, 2116, 1731, 1603, 1579, 1456, 764, 710 cm^{-1}. ^1H NMR (400 MHz; $CDCl_3$/TMS) δ: 3.66 (dd, 1H, $J = 3.9$ Hz, $J = 2.1$ Hz, 2-H), 4.82 (d, 1H, $J = 3.9$ Hz, 3-H), 7.11–7.33 (m, $5H_{arom}$), 9.54 (d, 1H, $J = 2.1$ Hz, CHO). ^{13}C NMR (100 MHz; $CDCl_3$/TMS): δ 36.6, 50.9, 112.3, 116.1, 126.9, 128.6, 129.2, 140.9, 197.8. EIMS (*m*/*z*): 216 (M^+). Anal. Calcd for $C_{11}H_8N_2OS$: C, 61.09; H, 3.73; N, 12.95. Found: C, 60.82; H, 4.08; N, 12.83.

Compound **4f**: Yellowish solid, yield 79%, mp 122–123 °C. IR (KBr) ν_{max} 3055, 2932, 2245, 1728, 1586, 1520, 1345, 760, 714. ^1H NMR (400 MHz; $CDCl_3$/TMS): δ 3.71 (dd, 1H, $J = 3.9$ Hz, $J = 2.1$ Hz, 2-H), 4.69 (d, 1H, $J = 3.9$ Hz, 3-H), 7.24–8.27 (m, $9H_{arom}$), 9.56 (d, 1H, $J = 2.1$ Hz, CHO). ^{13}C NMR (100 MHz; $CDCl_3$/TMS): δ 30.7, 51.3, 117.2, 121.6, 124.9, 127.4, 129.2, 129.8, 135.8, 148.2, 149.4, 198.2. EIMS (*m*/*z*): 312 (M^+). Anal. Calcd for $C_{16}H_{12}N_2O_3S$: C, 61.53; H, 3.87; N, 8.97. Found: C, 61.69; H, 3.98; N, 8.62.

17. (a) Montgomery, J. A.; Niwas, S.; Rose, J. D.; Secrist, J. A., III; Babu, Y. S.; Bugg, C. E.; Erion, M. D.; Guida, W. C.; Ealick, S. E. *J. Med. Chem.* **1993**, *36*, 55–69; (b) Elliott, A. J.; Morris, P. E.; Petty, S. L.; Williams, C. H. *J. Org. Chem.* **1997**, *62*, 8071–8075.
18. Basavaiah, D.; Kumaragurubaran, N.; Padmaja, K. *Synlett* **1999**, 1630–1632.
19. *General procedure for the synthesis of* [*E*]-α-*cyanocinnamaldehydes* (**2**): A stirred solution of BH adduct **1** (1 mmol) and $NaNO_3$ (1 mmol) in 1 mL of [Hmim]HSO_4 was heated at 80 °C for 1–2 h (Table 2). The reaction progress was monitored by TLC. Upon completion, the reaction mixture was cooled to rt and extracted with ether/ethyl acetate (3 × 10 mL). The combined organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting crude product was purified by silica gel column chromatography using a gradient mixture of hexane/ethyl acetate (9:1) as eluent to give the pure aldehydes **2**. The remaining ionic liquid was recycled for subsequent runs as described above using H_2SO_4 (1 mmol).[16] Physical data of a representative compound. Compound **2c**: White solid, yield 84%, mp 112–113 °C. IR (KBr) ν_{max} 3078, 2221, 2740, 2809, 1686, 1602, 1576, 1508, 1464, 833 cm^{-1}. ^1H NMR (400 MHz; $CDCl_3$/TMS): δ 3.87 (s, 3H, OMe), 6.88 (d, $2H_{arom}$, $J = 8.6$ Hz), 7.36 (d, $2H_{arom}$, $J = 8.6$ Hz), 7.96 (s, 1H, CHPh), 9.63 (s, 1H, CHO). ^{13}C NMR (100 MHz; $CDCl_3$/TMS): δ 55.4, 112.2, 113.6, 114.8, 126.9, 128.1, 158.5, 160.1, 187.1. EIMS (*m*/*z*): 187 (M^+). Anal. Calcd for $C_{11}H_9NO_2$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.79; H, 4.56; N, 7.26.
20. Mehdi, H.; Bodor, A.; Lantos, D.; Horváth, I. T.; de Vas, D. E.; Binnemans, K. *J. Org. Chem.* **2007**, *72*, 1517–1524.
21. Cai, J.; Zhou, Z.; Zhao, G.; Tang, C. *Org. Lett.* **2002**, *4*, 4723–4725.