Tetrahedron Letters 53 (2012) 5136–5140

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

The direct thioesterification of aldehydes with disulfides via NHC-catalyzed carbonyl umpolung strategy

Santosh Singh, Lal Dhar S. Yadav *

Green Synthesis Lab, Department of Chemistry, University of Allahabad, Allahabad 211 002, India

ARTICLE INFO

Article history:
Received 17 May 2012
Revised 9 July 2012
Accepted 11 July 2012
Available online 15 July 2012

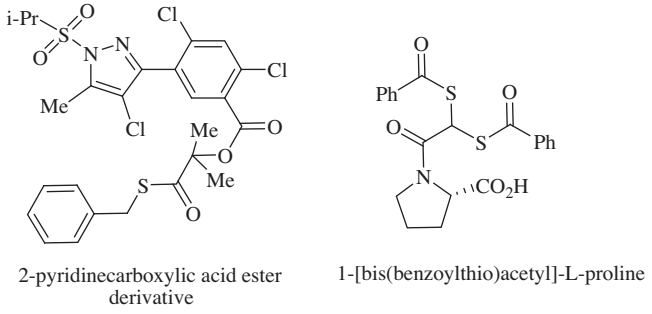
Keywords:
N-heterocyclic carbenes
Acylation
Umpolung
Disulfides
Thioesters
Aldehydes

ABSTRACT

An efficient N-heterocyclic carbene (NHC)-catalyzed direct thioesterification of aldehydes and α,β-unsaturated aldehydes (enals) with diaryl disulfides is reported. The protocol involves carbonyl umpolung reactivity of aldehydes and enals in which the carbonyl carbon attacks nucleophilically on diaryl disulfides to afford thioesters and α,β-unsaturated thioesters, respectively. However, aliphatic aldehydes are not suitable substrates for this reaction. No by-product formation, complete atom-economy, shorter reaction time, ambient temperature, operational simplicity, and high yields are the salient features of the present procedure.

The development of mild and efficient new catalytic methods for carbon–sulfur (C–S) bond formation without transition-metal catalyst remains a formidable challenge. Thioesters are important synthetic intermediates in organic synthesis[1] and used as mild acyl transfer reagents,[2] building blocks of heterocyclic compounds,[3] for aldol reactions,[4] protecting groups for thiols,[5] for peptide coupling,[6] for the synthesis of ketones,[7] amides,[8] and also as coupling partners in organometallic reactions.[9] They are also key intermediates in various biological processes[10] and find broad application in medicinal chemistry[11] (Fig. 1). The biologically active thioesters play central roles in living cells serving as essential metabolic intermediates due to their ability to act as excellent acyl group transfer agents. In addition, biosynthesis of polyketides and non-ribosomal polypeptides is achieved via thioester intermediates of fatty acids and amino acids.[12]

Due to the chemical and biological importance of thioesters, a number of methods for their synthesis have been described in the past few years. The most common method involves the acylation reaction of thiols with acids, anhydrides, aldehydes, acyl chlorides, *N*-acylphthalimides, and *N*-acylbenzotriazoles.[13] Recently, Alper and co-workers introduced a new procedure for the preparation of thioesters utilizing palladium-catalyzed thiocarbonylation of iodoarenes with thiols in ionic liquid.[14] However, the use of highly volatile and unpleasant smelling free thiols leads to serious environmental safety problems and also limits the use of these methods



2-pyridinecarboxylic acid ester derivative

1-[bis(benzoylthio)acetyl]-L-proline

Figure 1. Examples of medicinally important thioesters.

for large-scale operations. Furthermore, these methodologies are associated with undesirable side reactions owing to the oxidation of thiols. In order to minimize or eliminate the encountered problems, the acylation of disulfides with anhydrides or acyl halides in the presence of various promoting agents, such as In or InI,[15a,15b] Sm/$CoCl_2$,[15c,15d] SmI_2,[15e–g] Sm/Cp_2TiCl_2,[15h] Sm/$NiCl_2$,[15i] Zn/$AlCl_3$,[15j,15k] Zn/$ZrCl_4$,[15l] V(O)$(OTf)_2$,[15m] and $RhCl(PPh_3)_3/H_2$ (1 atm)[15n] has been developed as an alternative method for the synthesis of thioesters. Recently, Yamaguchi and co-workers have reported a rhodium-catalyzed alkylthio exchange reaction of thioester with disulfide.[16]

In view of the above points, the direct synthesis of thioesters from aldehydes appears to be an interesting target of investigation.

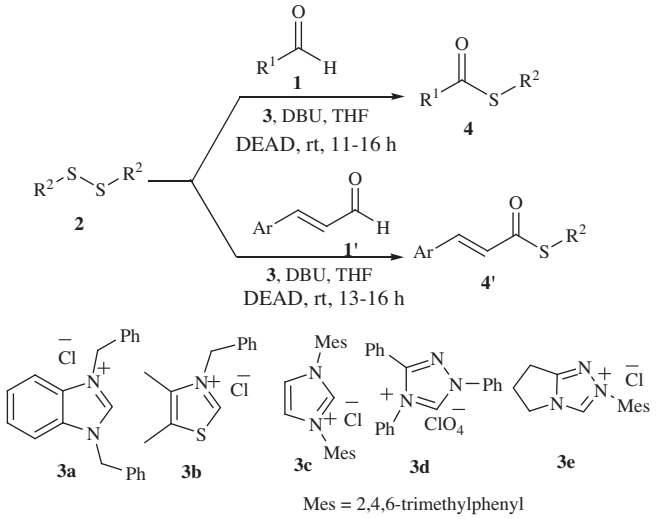
* Corresponding author. Tel.: +91 532 2500652; fax: +91 532 2460533.
E-mail address: ldsyadav@hotmail.com (L.D.S. Yadav).

0040-4039/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2012.07.042

Although, a few such synthetic methods are available in the literature,[17] they usually suffer from one or more limitations, such as the use of unpleasant odorous substrates,[14,17b,13a,13d,13e,13h,13k] toxic, or metallic catalysts,[15] poor atom-economy,[15m] low reagent efficiency,[17a] use of additives,[17a,17b] as well as elevated temperature.[16] Sometimes, a large amount of the aldehyde is required, since the aldehyde must be used not only as the reagent but also as the solvent.[17a]

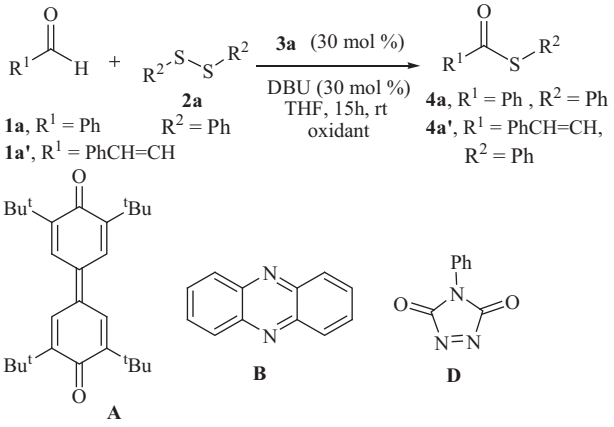
Over the past two decades, NHCs have aroused considerable interest[18] not only because of their extensive use in organocatalytic transformations, but also due to their characteristic inversion of the classical carbonyl reactivity, that is, umpolung.[19–22] Although the development of carbonyl anion addition reactions has received significant attention,[19–22] the nucleophilic substitution reactions catalyzed by NHC have received far less attention.[23–26] However, there has been no report on NHC-catalyzed acylation of disulfides via acyl anion equivalent of aldehydes and enals. Prompted by this novel C–S bond formation strategy without transition-metal catalyst and our efforts to develop synthetically useful processes,[27] we report herein a novel methodology developed for an efficient construction of both thioesters **4** and α,β-unsaturated thioesters **4′**. The protocol involves the first example of the NHC-catalyzed intermolecular acylation of disulfides **2** with aromatic aldehydes **1** and enals **1′** (Scheme 1), and it is the best example in which thioesters and α,β-unsaturated thioesters can be synthesized by the same method.

Firstly, we investigated the reaction of benzaldehyde **1a** or cinnamaldehyde **1′a** (1 equiv) with diphenyl disulfide **2a** (1 equiv) as a representative case for the synthesis of thioesters **4a** and **4a′**. The reaction underwent satisfactorily at room temperature (Table 1). However, the atom-economy of the reaction was considerably low because only half part (R^2S) of the disulfide (R^2SSR^2) was incorporated in the product and the other half (thiolate anion R^2S^-) remained as the by-product. In order to increase the atom-economy of the reaction, we searched for a selective oxidant which would oxidize the thiolate anion into the corresponding disulfide without any interference with Breslow intermediate. For this purpose, we used different oxidants, viz. azobenzene, PhTAD, DEAD, $PhI(OAc)_2$, MnO_2, IBX, **A**, and **B** (Table 1). Out of these, DEAD was the best for the synthesis of **4a** and **4′a** in terms of yield (Table 1, entry 3), whereas oxidants PhTAD **(D)** and MnO_2 gave thioesters **4a** and **4′a** in low to moderate yields (Table 1, entries 2 and 7) because they were also involved in the oxidation of the Breslow intermediate



Scheme 1. Synthesis of thioesters **4** and α,β-unsaturated thioesters **4′**.

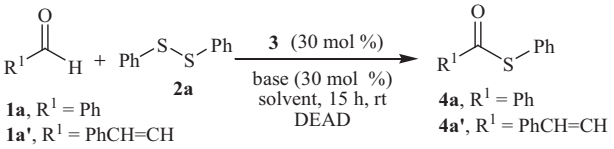
Table 1
Screening of oxidants for the formation of **4a** and **4a′**[a]



Entry	Oxidant	Yield[b] (%)	
		4a	**4a′**
1	Azobenzene	Trace	Trace
2	PhTAD **(D)**	61	56
3	DEAD	82	81
4[c]	$PhI(OAc)_2$[c]	71	67
5	**A**	18	13
6	**B**	Trace	Trace
7	MnO_2	52	33
8	IBX[c]	76	58

[a] Reaction conditions: **1a** (1 mmol), **2a** (0.5 mmol), **3a** (0.3 mmol), DBU (0.3 mmol), oxidant (1.2 equiv) in 5 mL of THF at rt.
[b] Yield of isolated and purified product.
[c] 2.2 equiv of oxidant was used.

Table 2
Optimization of reaction conditions for the formation of representative compounds **4a** and **4′a**[a]



Entry	Precatalyst (mol %)	Base	Solvent	Yield[b] (%)	
				4a	**4′a**
1	**3a** (30)	TEA	THF	52	42
2	**3a** (30)	K_2CO_3	THF	58	53
3	**3a** (30)	$CsCO_3$	THF	52	48
4	**3a** (30)	DBU	THF/Bu^tOH[c]	68	62
5	**3a** (30)	DBU	CH_2Cl_2	61	57
6	**3a** (30)	DBU	CH_3CN	51	41
7	**3a** (30)	DBU	DMF	48	39
8	**3a** (30)	DBU	THF	82	81
9	**3b** (30)	DBU	THF	29	22
10	**3c** (30)	DBU	THF	28	ND[d]
11	**3d** (30)	DBU	THF	35	31
12	**3e** (30)	DBU	THF	31	ND[d]
13	**3a** (25)	DBU	THF	74	71
14	**3a** (35)	DBU	THF	82	81
15	—	DBU	THF	—	—

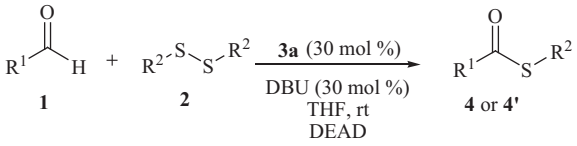
[a] For the experimental procedure, see Ref. [28].
[b] Yield of isolated and purified product.
[c] THF/Bu^tOH; 10:01 were used.
[d] Instead of α,β-unsaturated thioester, β-aryl/alkylsulfanyl thioesters was obtained in low yield.

to some extent. Although $PhI(OAc)_2$ and IBX also give good yield (Table 1, entries 4 and 8), their 2.2 equiv was required compared to 1.2 equiv in the case of DEAD. Furthermore, in case of oxidants

azobenzene and **B**, only trace amount of thioesters **4a** and **4′a** were obtained (Table 1, 1 and 6) because they oxidized the Breslow intermediate selectively instead of the thiolate ion.

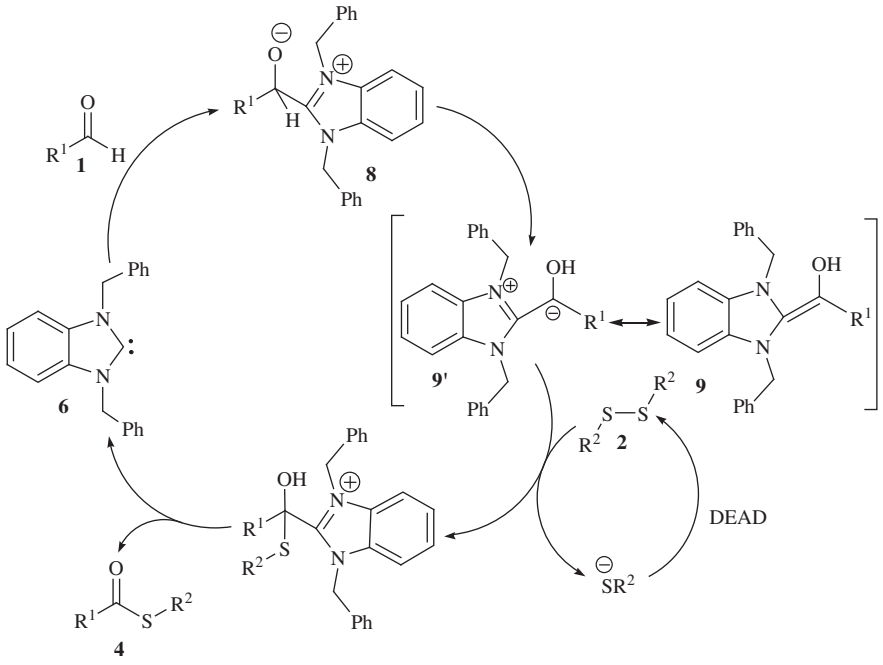
Next, we optimized the reaction conditions with regard to NHC-catalyst base, solvent, and temperature. Thus, different types of N-heterocyclic carbene precursors **3a–e** were tested and **3a** was found to be the most effective pre-catalyst for the preparation of **4a** and **4′a** under the present reaction conditions (Table 2, entry 8). The optimum loading for the pre-catalyst **3a** was found to be 30 mol % along with 30 mol % of DBU. When the amount of the pre-catalyst was decreased from 30 mol % to 25 mol % relative to substrates **1a** and **1′a**, the yield of the thioesters **4a** and **4′a** reduced (Table 2, entry 13), but the use of 35 mol % of **3a** did not affect the yield (Table 2, entries 8 and 14). The reaction did not occur without using the pre-catalyst **3** (Table 2, entry 15). Then, we optimized the base and found that DBU was the best among TEA, K_2CO_3, $CsCO_3$, and DBU (Table 2, entries 1–3 and 8). Optimization of solvents for the synthesis of **4a** and **4′a** employing the precatalyst **3a** was also undertaken and it was found that among THF, THF/Bu^{t}OH, CH_2Cl_2, CH_3CN, and DMF (Table 2, entries 3–7), the best solvent

Table 3
Reaction of aldehydes **1** with phenacyl halide **2** yielding thioesters **4** and **4′**[a]



Entry	R^1	R^2	Product **4** or **4′**	Time[b] (h)	Yield[c] (%)
1	Ph	Ph	**4a**	15	82
2	4-$NO_2C_6H_4$	Ph	**4b**	12	87
3	4-ClC_6H_4	Ph	**4c**	14	85
4	4-$MeOC_6H_4$	Ph	**4d**	16	77
5	Ph	4-ClC_6H_4	**4e**	15	83
6	4-$NO_2C_6H_4$	4-ClC_6H_4	**4f**	11	91
7	4-$MeOC_6H_4$	4-ClC_6H_4	**4g**	16	80
8	4-ClC_6H_4,	4-ClC_6H_4	**4h**	15	86
9	Ph	4-MeC_6H_4	**4i**	16	78
10	4-$NO_2C_6H_4$	4-MeC_6H_4	**4j**	13	82
11	4-$MeOC_6H_4$	4-MeC_6H_4	**4k**	16	71
12	4-ClC_6H_4	4-MeC_6H_4	**4l**	15	79
13	PhCH=CH	Ph	**4′a**	15	81
14	4-$NO_2C_6H_4$CH=CH	Ph	**4′b**	13	86
15	4-$MeOC_6H_4$CH=CH	Ph	**4′c**	16	82
16	CH_3CH=CH	Ph	**4′d**	16	66
17	CH_3CH=CH	4-ClC_6H_4	**4′e**	16	69

[a] For the experimental procedure, see Ref. [28]
[b] Stirring time at room temperature.
[c] Yield of isolated and purified product **4** or **4′**.



Scheme 2. A plausible mechanism for the formation of thioesters **4** and α,β-unsaturated thioesters **4′**.

in terms of yield was THF (Table 2, entry 8) and we used it throughout the present study. It was also noted that a higher reaction temperature, for example, in a refluxing solvent instead of room temperature did not increase the yield.

We applied the optimized conditions to the reaction of different substituted aldehydes and enals with a wide range of disulfides to produce the desired thioesters in good to excellent yields (Table 3). The presence of an electron-withdrawing substituent on the aryl moiety of aldehydes, enals, or disulfides appears to enhance the yield (Table 3, entries 3, 5, 6, 8, and 14), whereas an electron-donating group seems to reduce the yield (Table 3, entries 4, 9, 11, and 15). Besides the aromatic enals, we also attempted the reaction using aliphatic enals such as crotonaldehyde, but yields were low (66–69%) in these cases. Furthermore, we also attempted the reaction using aliphatic aldehydes such as, acetaldehyde, and propionaldehyde, but the yields were poor (10–20%) in these cases. This might be due to the side reaction like aldol reaction under the present basic conditions.

A possible catalytic cycle of the NHC-catalyzed reaction is depicted in Scheme 2. The addition of the NHC to aldehyde **1** gives intermediate **8** followed by H-migration to produce an acyl anion equivalent (Breslow intermediate) **9** which reacts with disulfide **2** to form the desired product thioester **4** and thiophenoxide ion which further oxidize into disulfide **2** by DEAD (Scheme 2). Similarly, enals **1′** also react with disulfide **2** through the Breslow intermediate **7′** (d^1 nucleophile) to afford α,β-unsaturated thioester **4′**. To our delight, the NHC **3a** mediated reaction of enals **1′** with disulfide **2** proceeded well via acyl anion to afford α,β-unsaturated thioester **4′** in good to excellent yields (Table 3) without the formation of any appreciable amount of the product through the homoenolate (d^3 nucleophile) of **1′**.

In conclusion, we have developed a convenient, efficient, and one-pot route for the synthesis of thioesters and α,β-unsaturated thioesters via direct NHC-catalyzed nucleophilic acylation of disulfides with aromatic aldehydes and enals in good to excellent yields. The method benefits from the use of cheap and safe starting materials and avoids the use of very unpleasant and noxious thiols as well as corrosive acid chlorides in the course of reaction. This is the first NHC-catalyzed intermolecular acylation reaction of disulfides. This protocol allows the transformation of aldedydes and enals to a range of thioesters and α,β-unsaturated thioesters by the same procedure.

Acknowledgments

We sincerely thank SAIF, Punjab University, Chandigarh, for providing microanalyses and spectra. S.S. is grateful to the CSIR, New Delhi, for the award of a Research Associateship (CSIR File No. 09/001/(0358)/2012/EMR-I).

References and notes

1. Field, L. *Synthesis* **1972**, *101*, 6321.
2. Mukaiyama, T.; Araki, M.; Takei, H. *J. Am. Chem. Soc.* **1973**, *95*, 4763.
3. (a) Alvarez-Ibarra, C.; Mendoza, M.; Orellana, G.; Quiroga, M. L. *Synthesis* **1989**, 560; (b) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F. *Tetrahedron Lett.* **1995**, *36*, 613.
4. (a) Mukaiyama, T.; Uchiro, H.; Shiina, I.; Kobayashi, S. *Chem. Lett.* **1990**, 1019; (b) Kobayashi, S.; Uchiro, H.; Fujishita, Y.; Shiina, I.; Mukaiyama, T. *J. Am. Chem. Soc.* **1991**, *113*, 4247.
5. Christian, F.; Bjorn, S.; Andreas, T. *Eur. J. Org. Chem.* **2007**, *6*, 1013.
6. (a) Ficht, S.; Payne, R. J.; Guy, R. T.; Wong, C. H. *Eur. J. Org. Chem.* **2008**, *14*, 3620; (b) Hojo, H.; Aimoto, S. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 111; (c) Ozawa, C.; Katayama, H.; Hojo, H.; Yuko, N.; Yoshiaki, N. *Org. Lett.* **2008**, *10*, 3531; (d) Dawson, P. E.; Muir, T. W.; Lewis, C. I.; Kent, S. B. H. *Science* **1994**, *266*, 776; (e) Dawson, P. E.; Kent, S. B. H. *Annu. Rev. Biochem.* **2000**, *69*, 923.
7. (a) McGarvey, G. J.; Williams, J. M.; Hiner, R. N.; Matsubara, Y.; Oh, T. *J. Am. Chem Soc.* **1986**, *108*, 4943; (b) Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc.* **2000**, *122*, 11260.
8. (a) Davis, A. P.; Walsh, J. *J. Tetrahedron Lett.* **1994**, *35*, 4865; (b) Davis, A. P.; Menzer, S.; Walsh, J. J.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1996**, 453.
9. (a) Villalobos, J. M.; Srogl, J.; Liebeskind, L. S. *J. Am. Chem. Soc.* **2007**, *129*, 15734; (b) Prokopcova, H.; Pisani, L.; Kappe, C. O. *Synlett* **2007**, 43; (c) Morita, A.; Kuwahara, S. *Org. Lett.* **2004**, *8*, 1613; (d) Lengar, A.; Kappe, C. O. *Org. Lett.* **2004**, *6*, 771; (e) Alphonse, F. A.; Suzenet, F.; Keromnes, A.; Lebert, B.; Guillaumet, G. *Synlett* **2002**, *3*, 447.
10. Bjorn, H. T.; Ben, F. L.; Adriaan, M. J. *Chem. Commun.* **2007**, *5*, 489.
11. (a) Metzner, P.; Thuillier, A. *Sulfur Reagents in Organic Synthesis*; Academic Press: New York, 1994; (b) Nudelman, A. *The Chemistry of Optically Active Sulfur Compoundsm*; Gordon and Breach: New York, 1984; (c) Chatgilialoglu, C.; Asmus, K. D. *Sulfur-Centered Reactive Intermediates in Chemistry and Biology*; Springer: New York, 1991.
12. (a) Stindl, A.; Keller, U. *J. Biol. Chem.* **1993**, *268*, 10612; (b) Dittmann, J.; Wenger, R. M.; Kleinkauf, H.; Lawen, A. *J. Biol. Chem.* **1994**, *269*, 2841; (c) Stachelhaus, T.; Huser, A.; Marahiel, M. A. *Chem. Biol.* **1996**, *3*, 913.
13. (a) Bandgar, B. P.; More, P. E.; Kamble, V. T.; Sawant, S. S. *Aust. J. Chem.* **2008**, *61*, 1006; (b) Iranpoor, N.; Firouzabadi, H.; Khalili, D.; Motevalli, S. *J. Org. Chem.* **2008**, *73*, 4882; (c) Katritzky, A. R.; Shestopalov, A. A.; Suzuki, K. *Synthesis* **2004**, 1806; (d) Yamada, S. I.; Yokoyama, Y.; Shioiri, T. *J. Org. Chem.* **1974**, *39*, 3302; (e) Kadam, S. T.; Kim, S. S. *Synthesis* **2008**, 3307; (g) Jeyakumar, K.; Chand, D. K. *J. Mol. Catal. A: Chem.* **2006**, *255*, 275; (h) Chakraborti, A.; Shivani, K. *J. Org. Chem.* **2006**, *71*, 5785; (i) Firouzabadi, H.; Iranpoor, N.; Farahi, S. *J. Mol. Catal. A: Chem.* **2008**, *289*, 61; (j) Ranu, B. C.; Jana, R. *Adv. Synth. Catal.* **2005**, *347*, 1811; (k) Uno, T.; Inokuma, T.; Takemoto, Y. *Chem. Commun.* **2012**, *48*, 1901.
14. Cao, H.; McNamee, L.; Alper, H. *J. Org. Chem.* **2008**, *73*, 3530.
15. (a) Peppe, C.; Castro, L. B. D. *Can. J. Chem.* **2009**, *87*, 678; (b) Ranu, B. C.; Mandal, T. *J. Org. Chem.* **2004**, *69*, 5793; (c) Chen, R. E.; Zhang, Y. M. *Synth. Commun.* **1999**, *29*, 3699; (d) Chowdhury, S.; Roy, S. *Tetrahedron Lett.* **1997**, *38*, 2149; (e) Wang, X. X.; Zou, X. F.; Du, J. X. *J. Chem. Res. Synop.* **2006**, 64; (f) Patra, P. K.; Shanmugasundaram, K.; Matoba, M.; Nishide, K.; Kajimoto, T.; Node, M. *Synthesis* **2005**, 447; (g) Bao, W. L.; Zhang, Y. M. *Synth. Commun.* **1995**, *25*, 143; (h) Jia, X. S.; Zhang, Y. M. *J. Chem. Res. Synop.* **2003**, *9*, 540; (i) Wu, H. Y.; Chen, R. E.; Zhang, Y. M. *Chin. Chem. Lett.* **1999**, *10*, 899; (j) Lakouraj, M. M.; Movassagh, B.; Fadaei, Z. *Monatsh. Chem.* **2002**, *133*, 1085; (k) Movassagh, B.; Lakouraj, M. M.; Fadaei, Z. *J. Chem. Res., Synop.* **2001**, 22; (l) Tian, F. S.; Zhu, Y. M.; Zhang, S. L.; Wang, Y. L. *J. Chem. Res., Synop.* **2002**, *11*, 582; (m) Chen, C. T.; Kuo, J. H.; Li, C. H.; Barhate, N. B.; Hon, S. W.; Li, T. W.; Chao, S. D.; Liu, C. C.; Li, Y. C.; Chang, I. H.; Lin, J. S.; Liu, C. J.; Chou, Y. C. *Org. Lett.* **2001**, *3*, 3729; (n) Ajiki, K.; Hirano, M.; Tanaka, K. *Org. Lett.* **2005**, *7*, 4193.
16. Arisawa, M.; Kubota, T.; Yamaguchi, M. *Tetrahedron Lett.* **1975**, *2008*, 49.
17. (a) Nambu, H.; Hata, K.; Matsugi, M.; Kita, Y. *Chem. Commun.* **2002**, 1082; (b) Bandgar, S. B.; Bandgar, B. P.; Korbad, B. L.; Sawant, S. S. *Tetrahedron Lett.* **2007**, *48*, 1287; (c) Sohn, S. S.; Bode, J. W. *Angew. Chem., Int. Ed.* **2006**, *45*, 6021.
18. Reviews of NHC-catalyzed reactions: (a) Mahatthananchai, J.; Bode, J. W. *Chem. Sci.* **2012**, *3*, 192; (b) Vora, H. U.; Rovis, T. *Aldrichimica Acta* **2011**, *44*, 3; (c) Biju, A.; Kuhl, N.; Glorius, F. *Acc. Chem. Res.* **2011**, *44*, 1182; (d) Zeitler, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 7506; (e) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606.
19. (a) Enders, D.; Kallfass, U. *Angew. Chem., Int. Ed.* **2002**, *41*, 1743; (b) Kerr, M. S.; de Alaniz, J. R.; Rovis, T. *J. Am. Chem. Soc.* **2002**, *124*, 10298; (c) Chow, K. Y. K.; Bode, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 8216; (d) Reynold, N. T.; de Alaniz, J. R.; Rovis, T. *J. Am. Chem. Soc.* **2004**, *126*, 9518; (e) Myers, M. C.; Bharadwaj, A. R.; Milgram, B. C.; Scheidt, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 14675.
20. (a) Burstein, C.; Glorius, F. *Angew. Chem. Int. Ed.* **2004**, *43*, 6205; (b) Sohn, S. S.; Rosen, E. L.; Bode, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 14370; (c) Chan, A.; Scheidt, K. A. *Org. Lett.* **2005**, *7*, 905; (d) Nair, V.; Vellalath, S.; Poonoth, M.; Suresh, E. *J. Am. Chem. Soc.* **2006**, *128*, 8736; (e) Chiang, P. C.; Kaeobamrung, J.; Bode, J. W. *J. Am. Chem. Soc.* **2007**, *129*, 3520; (f) Chan, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 2740.
21. (a) Grasa, G. A.; Kissling, R. M.; Nolan, S. P. *Org. Lett.* **2002**, *4*, 3583; (b) Nyce, G. W.; Lamboy, J. A.; Connor, E. F.; Waymouth, R. M.; Hedrick, J. L. *Org. Lett.* **2002**, *4*, 3587.
22. (a) He, J.; Zheng, J.; Liu, J.; She, X.; Pan, X. *Org. Lett.* **2006**, *8*, 463; (b) Suzuki, Y.; Ota, S.; Fukuta, Y.; Ueda, Y.; Sato, M. *J. Org. Chem.* **2008**, *73*, 2420.
23. (a) Suzuki, Y.; Toyota, T.; Miyashita, A.; Sato, M. *Chem. Pharm. Bull.* **2006**, *54*, 1653; (b) Miyashita, A.; Matsuda, H.; Iijima, C.; Higashino, T. *Chem. Pharm. Bull.* **1990**, *38*, 1147.
24. He, J.; Zheng, J.; Liu, J.; She, X.; Pan, X. *Org. Lett.* **2006**, *8*, 4637.
25. Lin, L.; Li, Y.; Du, W.; Deng, W. P. *Tetrahedron Lett.* **2010**, *51*, 3571.
26. Singh, S.; Singh, P.; Rai, V. K.; Yadav, L. D. S. *Tetrahedron Lett.* **2011**, *52*, 125.
27. (a) Singh, S.; Yadav, L. D. S. *Org. Biomol. Chem.* **2012**, *10*, 3932; (b) Yadav, L. D. S.; Singh, S.; Rai, V. K. *Synlett* **2010**, 240; (c) Yadav, L. D. S.; Rai, V. K.; Singh, S.; Singh, P. *Tetrahedron Lett.* **2010**, *51*, 1657; (d) Patel, R.; Srivastava, V. P.; Yadav, L. D. S. *Adv. Synth. Catal.* **2010**, *352*, 1610; (e) Yadav, L. D. S.; Singh, S.; Rai, V. K. *Green Chem.* **2009**, *11*, 878.
28. *General procedure for the synthesis of thioesters **4** and **4′***: A flame-dried round bottomed flask was charged with benzimidazolium salt **3a** (0.3 mmol), aldehyde **1** or **1′** (1.0 mmol), disulfide **2** (0.5 mmol), oxidant DEAD (1.2 mmol) and 5 mL of THF under positive pressure of nitrogen followed by addition of DBU (0.3 mmol) with a syringe. The resulting solution was stirred for 11–16 h at room temperature (Table 3). After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using hexane/EtOAc; (20:1) as eluent to afford analytically pure **4** and **4′**. Characterization data of representative compounds. Compound **4a**: The ^{1}H

NMR spectroscopic data are in agreement with those reported in the literature.[13k] IR (KBr): ν_{max} = 3058, 2931, 1666 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, J = 7.5 Hz, 2H, Ar), 7.67 (t, J = 7.5 Hz, 1H, Ar) 7.50–7.42 (m, 7H, Ar). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 126.5, 127.2, 128.4, 129.3, 130.1, 134.2, 135.8, 136.7, 189.7. MS (EI): m/z = 214 (M^+). Anal. Calcd for $C_{13}H_{10}OS$: C, 72.87; H, 4.70%. Found: 73.14; H, 4.54%. Compound **4g**: IR (KBr): ν_{max} = 3062, 2925, 1670 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, J = 8.4 Hz, 2H, Ar), 7.21 (d, J = 8.3 Hz, 2H Ar), 7.15 (d, J = 8.3 Hz, 2H, Ar), 7.02 (d, J = 8.4 Hz, 2H, Ar), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.4, 114.8, 127.3, 129.6, 130.4, 131.1, 131.8, 133.8, 168.2, 188.7. MS (EI): m/z = 278, 280 (M^+, M+2). Anal. Calcd for $C_{14}H_{11}ClO_2S$: C, 60.32; H, 3.98%. Found: 59.94; H, 4.22%. Compound **4j**: IR (KBr): ν_{max} = 3062, 2927, 1676 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.28 (d, J = 7.5 Hz, 2H, Ar), 8.16 (d, J = 7.5 Hz, 2H, Ar), 7.09 (d, J = 7.3 Hz, 2H, Ar), 6.88 (d, J = 7.3 Hz, 2H, Ar), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.1, 122.8, 129.4, 130.2, 131.4, 132.9, 136.5, 139.7, 154.2, 190.1. MS (EI): m/z = 273 (M^+). Anal. Calcd for $C_{14}H_{11}NO_3S$: C, 61.52; H, 4.06; N, 5.12%. Found: 61.81; H, 4.27; N, 4.88%. Compound **4′a**: IR (KBr): ν_{max} = 3052, 2965, 2927, 1645 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, J = 16.0 Hz, 1H), 7.60–7.49 (m, 3H, Ar), 7.31–7.22 (m, 5H, Ar), 6.88 (d, J = 7.3 Hz, 2H, Ar), 6.61 (d, J = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 124.1, 125.9, 126.8, 128.5, 129.2, 130.4, 131.2, 135.8, 136.2, 153.4, 189.6. MS (EI): m/z = 240 (M^+). Anal. Calcd for $C_{15}H_{12}OS$: C, 74.97; H, 5.03%. Found: C, 74.73; H, 4.88%.