Tetrahedron Letters 52 (2011) 6859–6864

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

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

Condensation of propargylic alcohols with 1,3-dicarbonyl compounds and 4-hydroxycoumarins in ionic liquids (ILs)

Gopalakrishnan Aridoss, Kenneth K. Laali *

Department of Chemistry, University of North Florida, 1 UNF Drive, Jacksonville, FL 32224, USA

ARTICLE INFO

Article history:
Received 13 September 2011
Revised 4 October 2011
Accepted 6 October 2011
Available online 12 October 2011

Keywords:
Propargylation
1,3-Dicarbonyl compounds
Ionic liquids
Metallic triflates
Bismuth nitrate
Tetrasubstitued furans
4-Hydroxycoumarins

ABSTRACT

Propargylic alcohols are activated toward 1,3-diketones by Lewis or Brønsted acidic ionic liquids (ILs) without an added catalyst, but significantly better conversions are achieved with metallic triflates [in particular $Sc(OTf)_3$ and $Ln(OTf)_3$] and bismuth nitrate in imidazolium ILs. The scope of this condensation reaction was investigated with a variety of propargylic alcohols and a host of acyclic and cyclic dicarbonyl compounds. Concomitant cycloisomerization leading to tetrasubstituted furans was observed with the propargylic alcohols **1b** and **1c** in reaction with 1,3-diketone **2b** and the β-ketoester **2c**. With propargylic alcohol **1c**, propargylation, cycloisomerization, or dienone formation were observed, depending on the structure of the 1,3-dicarbonyl compound. The $[BMIM][PF_6]/Bi(NO_3)_3{\cdot}5H_2O$ system proved efficient for propargylation, vinylation, and alkylation of 4-hydroxycoumarins. The recycling and reuse of the IL are added advantages of this method.

Condensation of 1,3-dicarbonyl compounds with benzylic, allylic, and propargylic moieties is an important C–C bond forming method capable of generating a wide range of valuable synthetic intermediates that are utilized in the synthesis of functional materials, natural products, and pharmaceuticals. There has been a flurry of research activity in this area in the past few years and a number of methods employing various catalysts have been reported. Thus tris(pentafluorophenyl)borane,[1] bismuth nitrate pentahydrate,[2] and phosphomolybdic acid supported on silica gel (PMA/SiO_2)[3] were employed for alkylation of 1,3-dicarbonyl compounds with benzylic alcohols, and PMA/SiO_2,[3] $FeCl_3$,[4] and $MoO_2(acac)_2/NH_4PF_6$[5] were used as catalysts in propargylation. Other workers employed an Ir-Sn bimetallic complex in DCE solvent to achieve propargylation or allenylation, depending on the structure of the propargylic alcohol.[6] The rhenium-catalyzed coupling of 2-propynyl alcohols with 1,3-diketones via dehydration was also studied.[7] Indium tribromide was employed in annulation of cyclic 1,3-diketones with aryl propargyl alcohols to synthesize 2,4-diaryldihydropyrans.[8] Cycloaddition between propargylic alcohols and cyclic 1,3-dicarbonyl compounds was effected by using thiolate-bridged diruthenium complexes via allenylidene intermediates.[9] Depending on the structure of alkynol, propargylation or allenylation products were obtained with PTS/MeCN[10] and with $Yb(OTf)_3$/MeCN.[11] Propargylation and cycloisomerization leading to furans were observed in variable amounts in the reaction of 1-phenylprop-2-yn-1-ol with 1,3-dicarbonyl compound by using Au(III) catalysis in organic solvents.[12] Tandem propargylation/cycloisomerization leading to substituted furans was observed with $FeCl_3$ in refluxing toluene.[13] A two-step process using TFA to effect propargylation followed by an allyl-ruthenium complex to effect cycloisomerization has also been reported.[14]

Propargylation of coumarins represents a related useful transformation. Alkylation of 4-hydroxycoumarin with benzylic, allylic, and propargylic alcohols was reported by using amberlite IR-120 (H^+)[15] and with $Yb(OTf)_3$.[11]

To our knowledge one study on propargylation of 1,3-dicarbonyl compounds in ILs has so far appeared,[16] in which a Brønsted acidic IL was used as catalyst with an imidazolium IL acting as solvent to effect benzylation, allylation, and propargylation of 1,3-dicarbonyl compounds at 100 °C.

In continuation of our work on electrophilic chemistry in room temperature ionic liquids (RT-IL),[17] and in relation to a recent study from this laboratory focusing on propargyl group introduction into aromatics and heteroaromatics and cross coupling of propargylic alcohols,[18] we report here on propargylation of acyclic and cyclic 1,3-dicarbonyl compounds and 4-hydroxycoumarins in ILs.[19]

With propargylation of 1,3-diphenylpropan-1,3-dione as a benchmark (Fig. 1) a survey study was performed using various ILs, with and without an added catalyst (Table 1). With

* Corresponding author. Tel.: +1 904 620 1503; fax: +1 904 620 3535.
E-mail address: kenneth.laali@UNF.edu (K.K. Laali).

0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.10.021

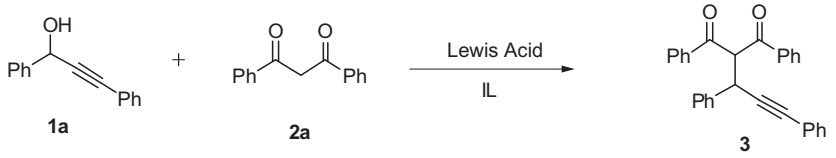
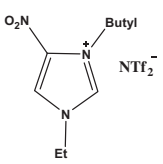
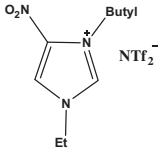


Figure 1. Screening of IL/Lewis acid systems as catalysts in condensation of **1a** with **2a** as model reaction.

Table 1
Screening of IL/Lewis acid systems as catalysts in condensation of **1a** with **2a** as model reaction

S. No.	Lewis acid	IL	Temp (°C)	Isolated yield (%)
1	$[C_2H_5NH_3][NO_3]$	$[C_2H_5NH_3][NO_3]$	50	21
2	$Bi(NO_3)_3{\cdot}5H_2O$	$[C_2H_5NH_3][NO_3]$	50	48
3	$Bi(NO_3)_3{\cdot}5H_2O$	$[BMIM][PF_6]$	30	91 (90[a], 85[a])
4	$Bi(OTf)_3$	$[BMIM][PF_6]$	50	10
5	$Al(OTf)_3$	$[BMIM][PF_6]$	60	Trace
6	$Ln(OTf)_3$	$[BMIM][PF_6]$	50	81
7	$Sc(OTf)_3$	$[BMIM][BF_4]$	40	88 (86[a], 80[a])
8	$Sc(OTf)_3$	$[BMIM][PF_6]$	40	85
9			50	52

[a] Yield corresponds to second and third runs respectively without re-loading catalyst.

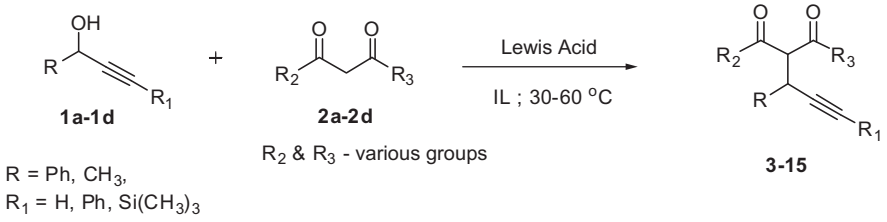


Figure 2. Condensation of propargylic alcohols with 1,3-dicarbonyl compounds with IL/Lewis acid systems.

ethylammonium nitrate (EAN) the yield was modest, but conversion was improved with EAN/$Bi(NO_3)_3$. Under comparable conditions, the Lewis acidic IL nitro-substituted butyl-ethyl-limidazolium-NTf_2 gave 52% isolated yield without an added catalyst. Among the IL/Lewis acid systems studied $[BMIM][PF_6]$/$Bi(NO_3)_3{\cdot}5H_2O$ and $[BMIM][PF_6]$/$Sc(OTf)_3$ proved most effective and were therefore selected to examine the scope of this transformation (Fig. 2 and Table 2).

In selected cases (Table 1 runs 3 and 7) the reactions were repeated in used $[BMIM][PF_6]$ IL without addition of fresh Lewis acid. A slight decrease in the isolated yields was observed for these cases.

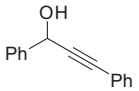
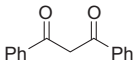
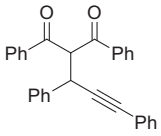
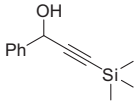
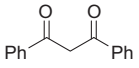
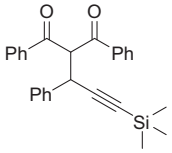
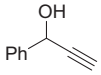
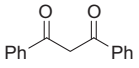
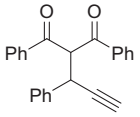
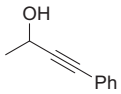
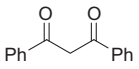
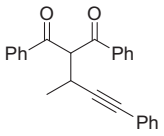
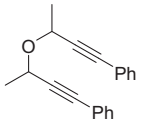
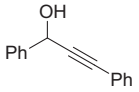
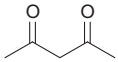
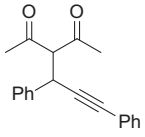
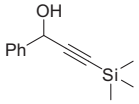
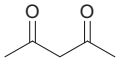
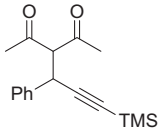
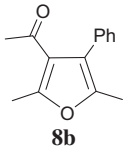
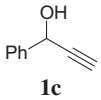
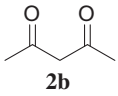
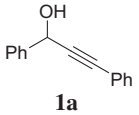
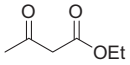
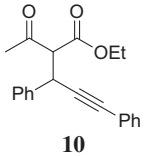
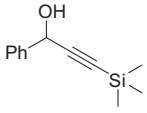
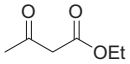
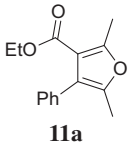
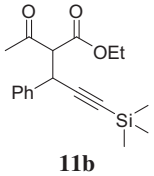
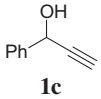
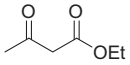
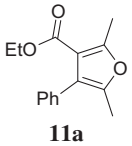
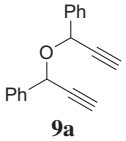
Propargylic alcohols **1a**–**1d** reacted with acyclic 1,3-diketones **2a** and **2b**, the ketoester **2c**, and the cyclic **2d**. In many cases, the direct propargylation products were obtained in respectable isolated yields under very mild conditions. The dipropargylic ethers **6b**[18] and **9a**[20] were obtained as minor byproducts (see runs 4, 7 and 10—Table 2).

Competing cycloisomerization to form tetrasubstituted furans were observed with **1b** and **1c**, depending on the structure of the 1,3-dicarbonyl compound. Furan formation became predominant in reaction with the ketoester **2c**. Condensation of **1c** with the cyclic **2d** resulted in isolation of the corresponding allene **14**. For comparison, allyl alcohol **1e** reacted with **2b** to give the condensation product **15** in 86% isolated yield. Figure 3 gives a summary of the reactions of **2b** and **2c** with **1b** and **1c** leading to the observed products.

The next phase of this study focused on propargylation of 4-hydroxycoumarins (Fig. 4). Thus 4-hydroxycoumarin **16a** and 6-chloro-4-hydroxycoumarin **16b** reacted with the propargylic alcohols **1a**–**1c**, as well as allyl alcohol **1e**, and diphenylmethanol **1f** to give the corresponding 3-substituted coumarins in isolated yields ranging from 96% to 81% except for reaction of **1a** with **16b** where the formation of byproducts **22b** and **22c** lowered the isolated yield of the desired product.

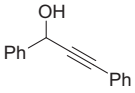
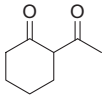
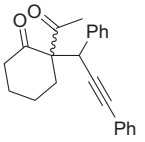
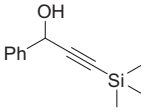
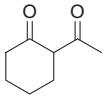
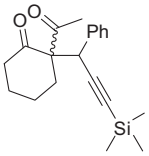
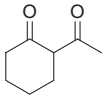
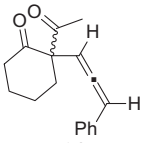
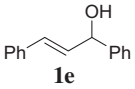
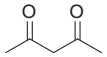
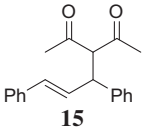
The present method offers a number of advantages over the earlier reported procedures as it avoids the use of volatile solvents and gives respectable isolated yields under very mild conditions. The recycling/reuse of the IL is an added advantage.

Table 2
Condensation of propargylic alcohols with 1,3-dicarbonyl compounds in IL/ $Bi(NO_3)_3{\cdot}5H_2O$ or IL/$Sc(OTf)_3$ systems

S. No.	Alcohol	Diketone	Products		Time (h)	Temp (°C)	Isolated yield (%)
1	 **1a**	 **2a**	 **3**	–	2.0	30	91
2	 **1b**	 **2a**	 **4**	–	1.5	30	92
3	 **1c**	 **2a**	 **5**	–	3.0	50	83
4	 **1d**	 **2a**	 **6a**	 **6b**	16	60	47 (**6a**)/36 (**6b**)[a]
5	 **1a**	 **2b**	 **7**	–	2	40	92[b]
6	 **1b**	 **2b**	 **8a**	 **8b**	4	45	79 (**8a** & **8b**)[c]
7	 **1c**	 **2b**	Mixture of products **8b**, **9a**–**9c**		9	60	Refer to Figure 3
8	 **1a**	 **2c**	 **10**	–	6	45	81[d]
9	 **1b**	 **2c**	 **11a**	 **11b**	5	45	68 (**11a** & **11b**[d])[e]
10	 **1c**	 **2c**	 **11a**	 **9a**	10	60	51 (**11a** & **9a**)[f]

(*continued on next page*)

Table 2 (*continued*)

S. No.	Alcohol	Diketone	Products	Time (h)	Temp (°C)	Isolated yield (%)
11	 **1a**	 **2d**	 **12**	–	3	40	88[d]
12	 **1b**	 **2d**	 **13**	–	3.5	40	82[d]
13	 **1c**	 **2d**	 **14**	–	6	40	67[d]
14	 **1e**	 **2b**	 **15**	–	1.5	35	86[g]

[a] Dipropargylic ether (**6b**) exists in two geometrical isomers (in 1:0.74 ratio by NMR) and the unreacted alcohol (**1d**) was recovered.
[b] 90% yield was achieved with [BMIM][BF_4]/$Sc(OTf)_3$.
[c] GC yield (**8a**:**8b** = 60.7:39.3).
[d] Exists as two diastereomers.
[e] GC–MS yield (**11a**:**11b** = 92.2:7.8).
[f] GC–MS yield (**11a**:**9a** = 73.5:26.5).
[g] 82% yield was achieved with [BMIM][BF_4]/$Sc(OTf)_3$.

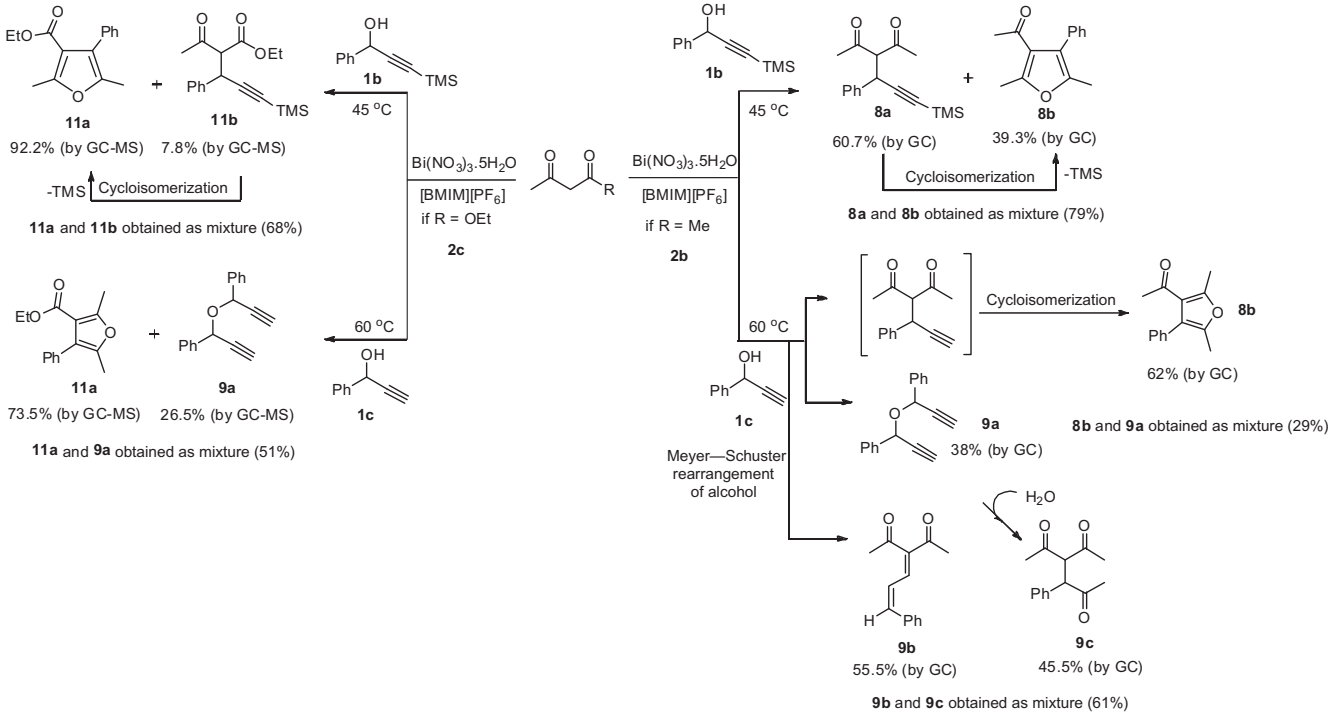


Figure 3. Product distribution as a function of propargylic alcohol.

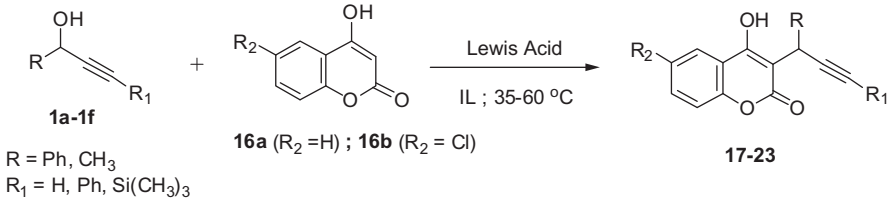
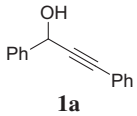
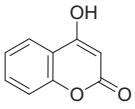
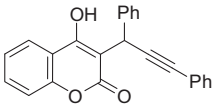
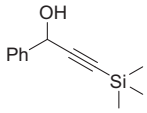
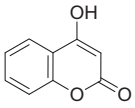
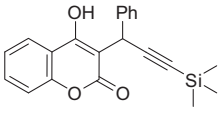
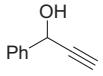
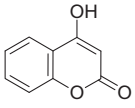
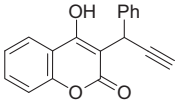
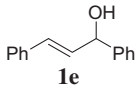
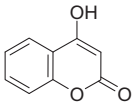
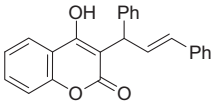
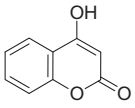
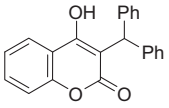
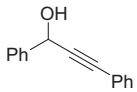
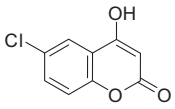
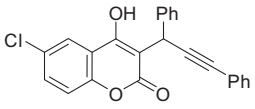
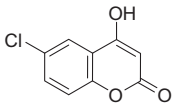
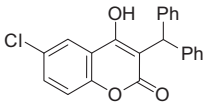
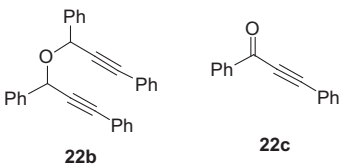


Figure 4. Propargylation of 4-hydroxycoumarins in IL/Lewis acid systems.

Table 3
C-3 alkylation of 4-hydroxycoumarins in IL/$Bi(NO_3)_3{\cdot}5H_2O$ system

Entry	Alcohol	Coumarin	Product	Temp (°C)	Time (h)	Isolated yield (%)
15	 **1a**	 **16a**	 **17**	35	1	90
16	 **1b**	 **16a**	 **18**	35	1.5	92
17	 **1c**	 **16a**	 **19**	40	4	87
18	 **1e**	 **16a**	 **20**	35	1.5	81
19	 **1f**	 **16a**	 **21**	35	1	93
20	 **1a**	 **16b**	 **22a**	60	10	43[a]
21	 **1f**	 **16b**	 **23**	40	5	96

[a] Dipropargylic ether **22b** [present as a mixture of two geometrical isomers (1:0.74)] and ketone **22c** were also formed (in 1:1 ratio; 48%), unreacted alcohol (**1a**) was also recovered.



Acknowledgment

We thank University of North Florida for support and Dr. Nelson Zhao of this department for NMR assistance.

Supplementary data

Supplementary data (NMR analysis of the products and other characterization data for the new compounds are furnished) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.10.021.

References and notes

1. Reddy, C. R.; Vijaykumar, J.; Grée, R. *Synthesis* **2010**, *21*, 3715–3723.
2. J. Escano, D. Bandyopadhyay, B.K. Banik, *Abstracts of Papers*, 238th, National Meeting of the American Chemical Society, Washington, DC, Aug 16–20, 2009; American Chemical Society: Washington, DC, 2009; ORGN-107.
3. Yadav, J. S.; Subba Reddy, B. V.; Pandurangam, T.; Raghavendra Rao, K. V.; Praneeth, K.; Narayana Kumar, G. G. K. S.; Madavi, C.; Kunwar, A. C. *Tetrahedron Lett.* **2008**, *49*, 4296–4301.
4. Maiti, S.; Biswas, S.; Jana, U. *Synth. Commun.* **2011**, *41*, 243–254.
5. Zhang, M.; Yang, H.; Cheng, Y.; Zhu, Y.; Zhu, C. *Tetrahedron Lett.* **2010**, *51*, 1176–1179.
6. Chatterjee, P. N.; Roy, S. *Tetrahedron* **2011**, *67*, 4569–4577.
7. Kuninobu, Y.; Ueda, H.; Takai, K. *Chem. Lett.* **2008**, *37*(8), 878–879.
8. Yadav, J. S.; Subba Reddy, B. V.; Raghavendra Rao, K. V.; Narender, R. *Tetrahedron Lett.* **2009**, *50*, 3963–3965.
9. Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Hidai, M.; Uemura, S. *J. Org. Chem.* **2004**, *69*, 3408–3412.
10. Sanz, R.; Miguel, D.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríuez, F. *Org. Lett.* **2007**, *9*(4), 727–730.
11. Huang, W.; Wang, J.; Shen, Q.; Zhou, X. *Tetrahedron* **2007**, *63*, 11636–11643.
12. Arcadi, A.; Alfonsi, M.; Chiarini, M.; Marinelli, F. *J. Organomet. Chem.* **2009**, *694*, 576–582.
13. Ji, W.-h.; Pan, Y.-m.; Zhao, S.-y.; Zhan, Z.-p. *Synlett* **2008**, 3046–3052.
14. Cadierno, V.; Gimeno, J.; Nebra, N. *Adv. Synth. Catal.* **2007**, *349*, 382–394.
15. Reddy, C. R.; Srikanth, B.; Narsimha Rao, N.; Shin, D.-S. *Tetrahedron* **2008**, *64*, 11666–11672.
16. Funabiki, K.; Komeda, T.; Kubota, K.; Matsui, M. *Tetrahedron* **2009**, *65*, 7457–7463.
17. (a) Laali, K. K.; Gettwert, V. J. *J. Org. Chem.* **2001**, *66*, 35–40; (b) Laali, K. K.; Gettwert, V. J. *J. Fluorine. Chem.* **2001**, *107*, 31–34; (c) Laali, K. K.; Borodkin, G. I. *J. Chem. Soc. Perkin Trans. 2* **2002**, 953–957; (d) Sarca, V. D.; Laali, K. K. *Green Chemistry* **2004**, *6*, 245–248; (e) Laali, K. K.; Sarca, V. D.; Okazaki, T.; Brock, A.; Der, P. *Org. Biomol. Chem.* **2005**, *3*, 1034–1042; (f) Sarca, V. D.; Laali, K. K. *Green Chemistry* **2006**, *8*, 615–620; (g) Laali, K. K.; Okazaki, T.; Bunge, S. *J. Org. Chem.* **2007**, *72*, 6758–6762; (h) Hubbard, A.; Okazaki, T.; Laali, K. K. *Aust. J. Chem.* **2007**, *60*, 923–927; (i) Hubbard, A.; Okazaki, T.; Laali, K. K. *J. Org. Chem.* **2008**, *73*, 316–319; (j) Pavlinac, J.; Laali, K. K.; Zupan, M.; Stavber, S. *Aust. J. Chem.* **2008**, *61*, 946–955; (k) Pavlinac, J.; Zupan, M.; Laali, K. K.; Stavber, S. *Tetrahedron* **2009**, *65*, 5625–5662; (l) Kalkhambkar, R. G.; Waters, S. N.; Laali, K. K. *Tetrahedron Lett.* **2011**, *52*, 867–871; (m) Kalkhambkar, R. G.; Laali, K. K. *Tetrahedron Lett.* **2011**, *52*, 1733–1737; (n) Aridoss, G.; Laali, K. K. *Eur. J. Org. Chem.* **2011**, 2827–2835; (o) Aridoss, G.; Laali, K. K. *Eur. J. Org. Chem.* **2011**, *2*, 6343–6355; (p) Aridoss, G.; Laali, K. K. *J. Org. Chem.* **2011**, *76*, 8088–8094.
18. Aridoss, G.; Sarca, V. D.; Ponder, J. F., Jr.; Crowe, J.; Laali, K. K. *Org. Biomol. Chem.* **2011**, *9*, 2518–2529.
19. *General procedure for propargylation of diketones and 4-hydroxycoumarins*: The desired ionic liquid (2 mL if the reactants were liquids and 3.00–3.5 mL for solids) was charged into an oven-dried Schlenk tube under a nitrogen atmosphere. The Lewis acid (10 mol %) was then introduced and was dissolved or immobilized in the IL upon sonication (for about 15 min). No catalyst was used in entries 1 and 9 in Table 1. The respective 1,3-diketone or the 4-hydroxycoumarin was then introduced into the Schlenk tube under a nitrogen atmosphere followed by the desired propargylic alcohol. The reaction mixture was magnetically stirred, initially at rt for about 10 min followed by stirring in a pre-heated oil bath at 30–60 °C (as specified; refer to Tables 1–3), until completion (monitored by TLC). Once the reaction was over, the contents were cooled to rt and extracted with dry diethyl ether or with EtOAc–Hexane (2:3)—(until the final extraction showed no spot corresponding to the starting material or to the product). The combined organic extracts were washed with DI water, dried with $MgSO_4$ and concentrated to give the crude product, which upon purification through column chromatography furnished the desired products. In some cases the crude reaction mixture obtained upon evaporation of the combined organic extracts was directly charged onto a column for purification without a water wash.
Re-use and recycling of IL: After extraction, the ionic liquid was dried under high-vacuum at 60–70 °C for about 6 h and re-used for successive runs.
20. Maraval, V.; Duhayon, C.; Coppel, Y.; Chauvin, R. *Eur. J. Org. Chem.* **2008**, 5144–5156.