Tetrahedron Letters 54 (2013) 4973–4974

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

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

A novel copper-catalyzed synthesis of functionalized alkynyl imidates and alkynyl thioimidates

Issa Yavari *, Manijeh Nematpour

Department of Chemistry, Tarbiat Modares University, PO Box 14115-175, Tehran, Iran

ARTICLE INFO

Article history:
Received 23 May 2013
Revised 25 June 2013
Accepted 5 July 2013
Available online 13 July 2013

Keywords:
Cross-coupling
Alkynyl imidates
Alkynyl thioimidates
Copper iodide
Trichloroimidates
Terminal alkynes

ABSTRACT

A copper-catalyzed one-pot synthesis of alkynyl imidates and alkynyl thioimidates via coupling reactions of terminal alkynes with trichloroimidates, generated in situ from trichloroacetonitrile and benzyl alcohols or thiols, is reported.

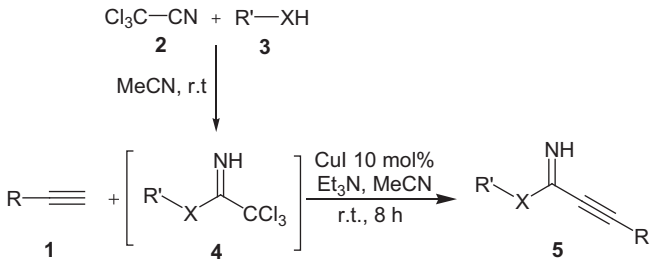
Alkynyl imines and alkynyl imidates represent an important class of functionalized alkynes because of their applications in the synthesis of a broad range of biologically important compounds. Alkynyl imidates are versatile intermediates, which are used to synthesize different types of N-heterocyclic systems.[1–8] Furthermore, they can react with conjugated dienes to give bicyclic compounds.[9,10]

Despite their synthetic importance, relatively few methods have been described for the preparation of alkynyl imidates and alkynyl thioimidates. One such important methodology involves metal-catalyzed coupling reactions of imidoyl halides,[11,12] diarylnitrones,[13] or the palladium-catalyzed reaction product of bromobenzene and *tert*-butyl isocyanide[14] with organometallic reagents derived from 1-alkynes. Alternatively, alkynyl imines have been prepared via imination of the corresponding alkynyl ketones.[2,15]

Herein, we report an efficient procedure for the synthesis of alkynyl imidates and alkynyl thioimidates via the Cu-catalyzed, three-component coupling reaction of trichloroacetonitrile, benzyl alcohol (thiol), and terminal alkynes (Scheme 1).[16]

In our initial investigations, phenylacetylene (**1a**), trichloroacetonitrile (**2**), and benzyl alcohol (**3a**) were selected as model substrates. Several catalysts including CuI, CuBr, CuCl, and copper powder were tested with CuI giving the best results. Among several solvents screened, acetonitrile proved to be the best. When this reaction was performed in MeCN in the presence of one equivalent of Et_3N at room temperature for eight hours, the desired product, benzyl 3-phenylpropiolimidate (**5a**), was obtained in 84% yield (Scheme 1). Thus, the optimized reaction conditions are as follows: 10 mol % of CuI, 1 mmol of alkyne, 1 mmol of Et_3N, 1 mmol of benzyl alcohol (thiol), and 1 mmol of trichloroacetonitrile in MeCN at room temperature.

Phenylacetylene readily participates in the coupling to furnish the corresponding 3-phenylpropiolimidates in good yields

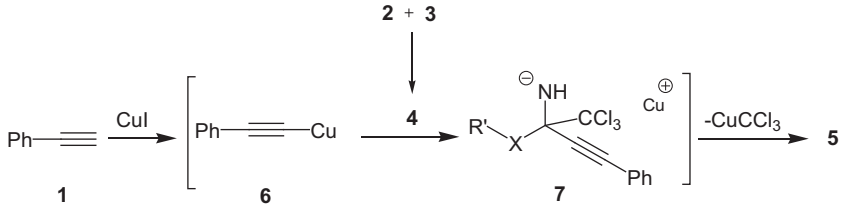


1,3,5	X	R	R'	Yield (%) of **5**
a	O	Ph	Bn	84
b	O	Ph	4-Cl-$C_6H_4CH_2$	80
c	O	Ph	4-Me-$C_6H_4CH_2$	74
d	O	*n*-Pr	4-Cl-$C_6H_4CH_2$	67
e	O	*n*-Bu	4-Cl-$C_6H_4CH_2$	63
f	O	*n*-Bu	4-Me-$C_6H_4CH_2$	62
g	S	Ph	Bn	81
h	S	*n*-Pr	Bn	68
i	S	*n*-Bu	Bn	61

Scheme 1. Synthesis of compounds **5**.

* Corresponding author. Tel.: +98 21 82883465; fax: +98 21 82883455.
E-mail address: yavarisa@modares.ac.ir (I. Yavari).

0040-4039/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2013.07.029



Scheme 2. A mechanism for the formation of products **5**.

(Scheme 1). Aliphatic acetylenes served as low yielding substrates compared to phenylacetylene.

The structures of products **5a–i** were assigned by IR, ^{1}H NMR, and ^{13}C NMR spectroscopies and by mass spectrometry data. The ^{1}H NMR spectrum of **5a** exhibited two singlets for the methylene (4.45 ppm) and NH (5.10 ppm) protons, along with characteristic multiplets for the phenyl protons. The ^{13}C NMR spectrum of **5a** exhibited 12 signals in agreement with the proposed structure. The mass spectrum of **5a** displayed a molecular ion peak at $m/z = 235$. The NMR spectra of compounds **5b–i** were similar to those of **5a**, except for the substituents, which showed characteristic signals in the appropriate regions of the spectra.

A mechanism for the formation of products **5** is given in Scheme 2. Yellow copper acetylide **6**, formed from **1** and CuI, takes part in a nucleophilic addition reaction with trichloroimidates **4**, generated in situ from trichloroacetonitrile and benzyl alcohols or thiols, to afford tetrahedral intermediate **7**. This intermediate is converted into **5** by the elimination of $CuCCl_3$.

In conclusion, we have demonstrated that under ligand-free conditions, CuI catalyzes the coupling reaction of trichloroacetonitrile and benzyl alcohols with terminal alkynes to produce alkynyl imidates. Replacement of the alcohols with benzyl thiols furnishes alkynyl thioimidates. The potential diversity of this type of reaction and readily available starting materials and catalyst are the main advantages of this methodology.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.07.029.

References and notes

1. Sromek, A. W.; Rheingold, A. L.; Wink, D. J.; Gevorgyan, V. *Synlett* **2006**, 2325.
2. Kel'in, A. V.; Sromek, A. W.; Gevorgyan, V. *J. Am. Chem. Soc.* **2001**, *123*, 2074.
3. Lihar, P. R.; Subhas, M. S.; Roy, S.; Kantam, M. L. *Org. Biomol. Chem.* **2009**, *7*, 85.
4. Sha, F.; Wu, L.; Huang, X. *Angew. Chem., Int. Ed.* **2009**, *48*, 3458.
5. Hachiya, I.; Minami, Y.; Aramaki, T.; Shimizu, M. *Eur. J. Org. Chem.* **2008**, *8*, 1411.
6. Ueda, M.; Ikeda, Y.; Sato, A.; Ito, Y.; Kakiuchi, M.; Shono, H.; Miyoshi, T.; Naito, T.; Miyata, O. *Tetrahedron* **2011**, *67*, 4612.
7. Mangelinckx, S.; Rooryck, S.; Jacobs, J.; De Kimpe, N. *Tetrahedron Lett.* **2007**, *48*, 6535.
8. Zhang, F. G.; Ma, H.; Zheng, Y.; Ma, J. A. *Tetrahedron* **2012**, *68*, 7663.
9. Rahm, R.; Espenlaub, S.; Werz, U. R.; Maas, G. *Heteroatom Chem.* **2005**, *16*, 437.
10. Feng, L.; Kerwin, S. M. *Tetrahedron Lett.* **2003**, *44*, 3463.
11. Gerster, H.; Espenlaub, S.; Maas, G. *Synthesis* **2006**, 2251.
12. Schlegel, J.; Maas, G. *Synthesis* **1999**, 100.
13. Miura, M.; Enna, M.; Okuro, K.; Nomura, M. *J. Org. Chem.* **1995**, *60*, 4999.
14. Kosugi, M.; Ogata, T.; Tamura, H.; Sano, H.; Migita, T. *Chem. Lett.* **1986**, 1197.
15. Bishop, B. C.; Brands, K. M. J.; Gibb, A. D.; Kennedy, D. J. *Synthesis* **2004**, 43.
16. *General procedure for the synthesis of compounds* ***5***: A solution of **2** (1 mmol) and **3** (1 mmol) in MeCN (2 mL) was stirred for 30 min. Next, a mixture of alkyne **1** (1 mmol), CuI (0.1 mmol) and Et_3N (1 mmol) in MeCN (3 mL) was added slowly at room temperature under an N_2 atmosphere. After completion of the reaction [about 8 h; TLC (EtOAc/hexane, 1:5) monitoring], the mixture was diluted with CH_2Cl_2 (2 mL) and aqueous NH_4Cl solution (3 mL), stirred for 30 min, and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 3 mL) and the combined organic fractions were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash column chromatography [silica gel (230–400 mesh; Merck), hexane/EtOAc, 5:1] to give the product. Benzyl 3-Phenylpropiolimidate (**5a**): Cream powder, mp: 121–124 °C; yield: 0.20 g (84%). IR (K Br) (ν_{max}, cm^{-1}): 3438, 2123, 1611, 1396, 1270, 1139, 1081. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta_H = 4.45$ (2H, s, CH_2), 5.10 (1H, s, NH), 7.25–7.34 (3H, m, Ph), 7.47–7.50 (4H, m, Ph), 7.60 (1H, t, $^3J = 7.5$ Hz, Ar), 7.97 (2H, d, $^3J = 7.9$ Hz, Ar). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta_C = 47.0$ (CH_2), 77.6 (C), 85.4 (C), 122.5 (C), 128.7 (2 CH), 129.2 (CH), 129.3 (2 CH), 129.4 (2 CH), 132.5 (2 CH), 134.4 (CH), 135.3 (C), 161.7 (C). MS: m/z (%) = 235 (M$^+$, 2), 158 (8), 144 (43), 134 (23), 101 (100), 91 (70), 77 (54). Anal. Calcd for $C_{16}H_{13}NO$ (235.10): C, 81.68; H, 5.57; N, 5.95. Found: C, 81.39; H, 5.63; N, 6.04. Benzyl 3-Phenylprop-2-ynimidothioate (**5g**): Pale yellow powder, mp: 151–153 °C; yield: 0.20 g (81%). IR (K Br) (ν_{max}, cm^{-1}): 3452, 2133, 1620, 1401, 1370, 1218. ^{1}H NMR (500 MHz, $CDCl_3$): $\delta_H = 4.39$ (2 H, s, CH_2), 5.10 (1H, s, NH), 7.25–7.33 (4H, m, Ph), 7.43 (2H, d, $^3J = 7.5$ Hz, Ar), 7.48 (2H, d, $^3J = 7.5$ Hz, Ar), 7.90 (2H, d, $^3J = 7.9$ Hz, Ar). ^{13}C NMR (125.7 MHz, $CDCl_3$): $\delta_C = 46.7$ (CH_2), 77.7 (C), 85.4 (C), 122.5 (C), 128.8 (2 CH), 129.2 (CH), 129.3 (2 CH), 130.8 (2 CH), 132.5 (2 CH), 132.7 (CH), 141.0 (C), 160.7 (C). MS: m/z (%) = 251 (M$^+$, 6), 174 (8), 160 (43), 123 (53), 101 (100), 91 (72), 77 (34). Anal. Calcd for $C_{16}H_{13}NS$ (251.35): C, 76.46; H, 5.21; N, 5.57. Found: C, 76.79; H, 5.26; N, 5.63.