Tetrahedron Letters 52 (2011) 6217–6219

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

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

Effect of halogenation reagents on halocyclization and Overman rearrangement of allylic trichloroacetimidates

Na Liu, Casi M. Schienebeck, Michelle D. Collier, Weiping Tang *

School of Pharmacy, University of Wisconsin, Madison, WI 53705, USA

ARTICLE INFO

Article history:
Received 19 August 2011
Revised 10 September 2011
Accepted 13 September 2011
Available online 19 September 2011

Keywords:
Overman rearrangement
Halocyclization
Allylic alcohols
Allylic amide
Halogen

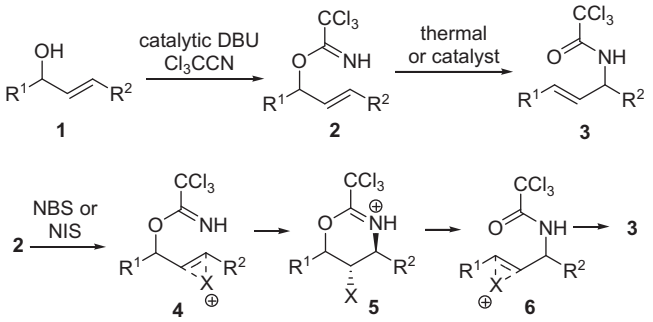
ABSTRACT

Electrophilic halogen can promote either halocyclization or Overman rearrangement of allylic trichloroacetimidates. We found that the chemoselectivity was dependent on the nature of the halogenation reagents for primary allylic trichloroacetimidates. A one-pot procedure was developed for the preparation of allylic trichloroacetamides directly from allylic alcohols at room temperature.

The [3,3]-sigmatropic rearrangement of allylic trichloroacetimidate **2** (Overman rearrangement) has been widely used for the preparation of protected allylic amine **3** from allylic alcohol **1** (Scheme 1).[1–3] The thermal and Hg(II)-catalyzed process was first reported by Overman in 1974.[4] The same group also developed the enantioselective process for the rearrangement of primary allylic trichloroacetimidate **2** employing a chiral Pd(II) catalyst.[5] Metal complexes including Hg(II), Pd(II), Pt(II), Pt(IV), Au(I), and Au(III) salts can lower the temperature required for the rearrangement of allylic trichloroacetimidates and allow the reaction to be carried out at room temperature or lower.[1,4,6]

It has been reported that N-bromosuccinimide (NBS) or N-iodosuccinimide (NIS) could promote Overman rearrangement if R^1 in trichloroacetimidate **2** is an electron withdrawing group such as phosphonate or cyano groups.[7] The proposed mechanism of this halogen-promoted Overman rearrangement is shown in Scheme 1.[7] On the other hand, numerous examples of halogen-promoted halocyclization of allylic trichloroacetimidates were also known.[8] The occurrence of the unusual halogen-promoted Overman rearrangement was attributed to the electron withdrawing R^1 substituent (phosphonate or cyano groups) in compound **2**.[7] We herein report that primary allylic trichloroacetimidates (**2**, R^1 = H) can also undergo halogen-promoted Overman rearrangement at room temperature in the presence of amine catalysts. The choice of electrophilic halogenation reagents is critical for chemoselective Overman rearrangement over halocyclization.

During our development of stereoselective halocyclization reactions,[9,10] we became interested in using trichloroacetimidates as nitrogen nucleophiles. When allylic trichloroacetimidate **2a** was treated with NCS, no reaction was observed (Table 1, entry 1). We[9,10] and others[11] have found that various catalysts can facilitate the halogen-promoted cyclization or addition reactions. We then screened different catalysts and halogenation reagents. Overman rearrangement product **3a** was isolated in 34% yield together with 50% of recovered **2a** after 10 h in the presence of quinine catalyst **10** (entry 2). The yield of product **3a** was improved to 76% using 1,3-dichloro-5,5-dimethylhydantoin (DCDMH) **9** as the halogenation reagent and quinine **10** as the catalyst (entry 4). The yield of product **3a** dropped slightly with substoichiometric amount of halogen reagents (entry 5). DBU and catalyst **11** all provided lower yields of product **3a** (entries 6 and 7), indicating that the hydroxyl

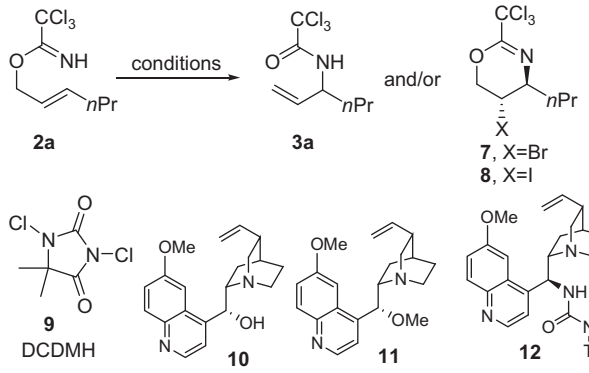


Scheme 1. Overman rearrangement.

* Corresponding author. Tel.: +1 608 890 1846; fax: +1 608 262 5345.
E-mail address: wtang@pharmacy.wisc.edu (W. Tang).

0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.09.057

Table 1
Effect of halogen on Overman rearrangement and halocyclization of allylic trichloroacetimidates



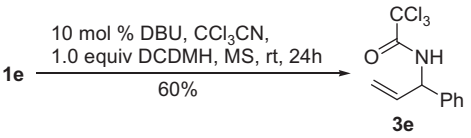
Entry	Conditions	Yield of **3a**	Yield of **7** or **8**
1	1.2 equiv NCS	No reaction	
2	1.2 equiv NCS, 10 mol % **10**	34%	—
3	1.2 equiv **9**	No reaction	
4	1.2 equiv **9**, 10 mol % **10**	76%	—
5	0.4 equiv **9**, 10 mol % **10**	67%	—
6	1.2 equiv **9**, 10 mol % DBU	50%	
7	1.2 equiv **9**, 10 mol % **11**	50%	—
8	1.2 equiv **9**, 10 mol % **12**	32%	—
9	1.2 equiv NBS	No reaction	
10	1.2 equiv NBS, 10 mol % **10**	73% yield of **3a** and **7** (**3a**:**7** = 1.4:1)	
11	1.2 equiv NIS	—	63% of **8**

group in quinine **10** is beneficial for the reaction. Much lower conversion was observed in the presence of chiral catalyst **12** (entry 8).[10] Interestingly, an inseparable mixture of Overman rearrangement product **3a** and bromocyclization product **7** was observed when NBS and quinine were used as the halogenation reagent and catalyst respectively (entry 10). Treatment of **2a** with NIS in the absence of quinine yielded 6-endo-cyclization product **8** together with small amount of 5-exo-cyclization product (entry 11).

Since DBU is also the catalyst for the preparation of allylic trichloroacetimidate **2** from the corresponding alcohol **1**, we then examined the one-pot procedure for the preparation of allylic amides from allylic alcohols (Table 2). Allylic trichloroacetamide **3a** can be directly prepared in 72% yield from allylic alcohol **1a** by sequential addition of trichloroacetonitrile and DCDMH in the presence of 4 Å molecular sieves (MS) and a catalytic amount of DBU (entry 1). We then explored the scope of this protocol for the preparation of allylic trichloroacetamides. The reaction tolerated various alkyl and aryl substituted primary allylic alcohols (entries 2–10).

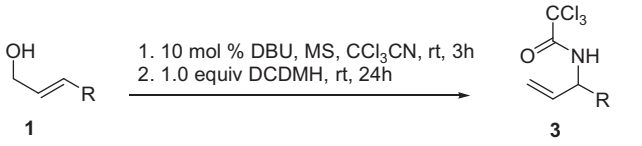
A complex mixture was obtained for substrate **1k**, which has an electron-rich aryl substituent. No rearrangement product was observed for secondary cyclic or acyclic allylic alcohols **1l** and **1m**.

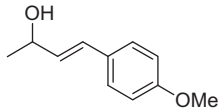
When DBU, trichloroacetonitrile, and DCDMH were added together to allylic alcohol **1e**, product **3e** could be isolated in 60% yield (Eq. 1), which was lower than that obtained from sequential additions as shown in Table 2 (entry 5). Under the identical condition shown in (Eq. 1), substrate **1a** only yielded trace amounts of rearrangement product and most of the starting material was recovered. This suggested that the introduction of halogenation reagent in the first step was detrimental for substrates with an alkyl substituent.



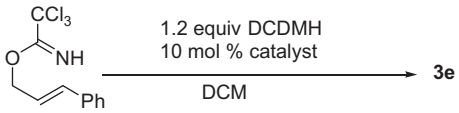
(1)

Table 2
Preparation of allylic amides from allylic alcohols via halogen-promoted Overman rearrangement in a one-pot procedure



Entry	Structure of substrates	Yields
1	**1a**, R = *n*Pr	72%
2	**1b**, R = *c*Hex	78%
3	**1c**, R = Me	64%
4	**1d**, R = $PhCH_2CH_2$	54%
5	**1e**, R = Ph	81%
6	**1f**, R = 4-ClC_6H_4	59%
7	**1g**, R = 4-$(NO_2)C_6H_4$	55%
8	**1h**, R = 3-$(NO_2)C_6H_4$	53%
9	**1i**, R = 4-BrC_6H_4	71%
10	**1j**, R = 2-BrC_6H_4	62%
11	**1k**, R = 4-$(CH_3O)C_6H_4$	See text
12	**1l**, Cyclohex-2-en-1-ol	NR
13	 **1m,**	NR

Our preliminary study showed that good yield and observable enantioselectivity could be achieved for allylic amide **3e** (Eq. 2). This halogen-promoted process has the potential to become an alternative metal-free approach for enantioselective Overman rearrangement.



chiral catalysts:	isolated yield	ee
catalyst **10**	63%	<1%
catalyst **11**	72%	10-13%
catalyst **12**	44%	<1%
$(DHQD)_2PHAL$	58%	<1%

(2)

In summary, we found that the chemoselectivity for halocyclization or Overman rearrangement of allylic trichloroacetimidates is highly dependent on the halogenation reagent. We demonstrated, for the first time, that a halogen could promote Overman rearrangement of trichloroacetimidates derived from primary allylic alcohols. A one-pot procedure was developed for the preparation of allylic trichloroacetamides from primary allylic alcohols at room temperature.

Acknowledgment

We thank University of Wisconsin-Madison for start up funding.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.09.057.

References and notes

1. Overman, L. E. *Acc. Chem. Res.* **1980**, *13*, 218.
2. (a) Overman, L. E. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 579; (b) Overman, L. E. *Tetrahedron* **2009**, *65*, 6432; (c) Majumdar, K. C.; Bhattacharyya, T.; Chattopadhyay, B.; Sinha, B. *Synthesis* **2009**, 2117.
3. Overman, L. E.; Carpenter, N. E. In *Organic Reactions*; Overman, L. E., Ed.; Wiley: New York, NY, 2005; Vol. 66, p. 1.

4. (a) Overman, L. E. *J. Am. Chem. Soc.* **1974**, *96*, 597; (b) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901.
5. (a) Anderson, C. E.; Overman, L. E. *J. Am. Chem. Soc.* **2003**, *125*, 12412; (b) Overman, L. E.; Owen, C. E.; Pavan, M. M.; Richards, C. J. *Org. Lett.* **2003**, *5*, 1809; (c) Kirsch, S. F.; Overman, L. E.; Watson, M. P. *J. Org. Chem.* **2004**, *69*, 8101; (d) Watson, M. P.; Overman, L. E.; Bergman, R. G. *J. Am. Chem. Soc.* **2007**, *129*, 5031.
6. (a) Metz, P.; Mues, C.; Schoop, A. *Tetrahedron* **1992**, *48*, 1071; (b) Mehmandoust, M.; Petit, Y.; Larcheveque, M. *Tetrahedron Lett.* **1992**, *33*, 4313; (c) Doherty, A. M.; Kornberg, B. E.; Reily, M. D. *J. Org. Chem.* **1993**, *58*, 795; (d) Jaunzeme, I.; Jirgensons, A. *Synlett* **2005**, 2984; (e) Jaunzeme, I.; Jirgensons, A. *Tetrahedron* **2008**, *64*, 5794.
7. Shabany, H.; Spilling, C. D. *Tetrahedron Lett.* **1998**, *39*, 1465.
8. (a) Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Chem. Soc., Perkin Trans. 1* **1985**, 935; (b) Pauls, H. W.; Fraserreid, B. *Carbohydr. Res.* **1986**, *150*, 111; (c) Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1339; (d) Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1345; (e) Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Org. Chem.* **1986**, *51*, 4905.
9. (a) Zhang, W.; Xu, H.-D.; Xu, H.; Tang, W. *J. Am. Chem. Soc.* **2009**, *131*, 3832; (b) Werness, J. B.; Tang, W. *Sci. Chin. Chem.* **2011**, *54*, 56; (c) Liu, N.; Werness, J. B.; Guzei, I. A.; Tang, W. *Tetrahedron* **2011**, *67*, 4385.
10. Zhang, W.; Zheng, S.; Liu, N.; Werness, J. B.; Guzei, I. A.; Tang, W. *J. Am. Chem. Soc.* **2010**, *132*, 3664.
11. (a) Braddock, D. C.; Cansell, G.; Hermitage, S. A. *Chem. Commun.* **2006**, 2483; (b) Ahmad, S. M.; Braddock, D. C.; Cansell, G.; Hermitage, S. A.; Redmond, J. M.; White, A. J. P. *Tetrahedron Lett.* **2007**, *48*, 5948; (c) Ahmad, S. M.; Braddock, D. C.; Cansell, G.; Hermitage, S. A. *Tetrahedron Lett.* **2007**, *48*, 915; (d) Sakakura, A.; Ukai, A.; Ishihara, K. *Nature* **2007**, *445*, 900; (e) Hennecke, U.; Muller, C. H.; Frohlich, R. *Org. Lett.* **2010**, *13*, 860; (f) Yousefi, R.; Whitehead, D. C.; Mueller, J. M.; Staples, R. J.; Borhan, B. *Org. Lett.* **2010**, *13*, 608; (g) Murai, K.; Matsushita, T.; Nakamura, A.; Fukushima, S.; Shimura, M.; Fujioka, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 9174; (h) Zhou, L.; Tan, C. K.; Jiang, X. J.; Chen, F.; Yeung, Y. Y. *J. Am. Chem. Soc.* **2010**, *132*, 15474; (i) Veitch, G. E.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2010**, *49*, 7332; (j) Denmark, S. E.; Kalyani, D.; Collins, W. R. *J. Am. Chem. Soc.* **2010**, *132*, 15752; (k) Denmark, S. E.; Burk, M. T. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 20655; (l) Gustafson, J. L.; Lim, D.; Miller, S. J. *Science* **2010**, *328*, 1251; (m) Jaganathan, A.; Garzan, A.; Whitehead, D. C.; Staples, R. J.; Borhan, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 2593; (n) Chen, Z.-M.; Zhang, Q.-W.; Chen, Z.-H.; Li, H.; Tu, Y.-Q.; Zhang, F.-M.; Tian, J.-M. *J. Am. Chem. Soc.* **2011**, *133*, 8818; (o) Nicolaou, K. C.; Simmons, N. L.; Ying, Y.; Heretsch, P. M.; Chen, J. S. *J. Am. Chem. Soc.* **2011**, *133*, 8134.