$GaCl_3$-Catalyzed Chloroacylation of Alkynes: A Simple, Convenient and Efficient Method to β-Chlorovinyl Ketones

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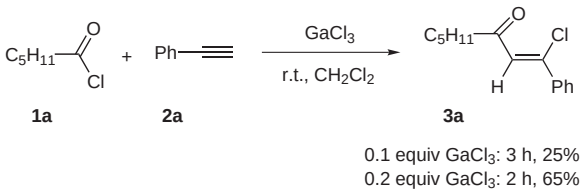
Abstract: Gallium chloride catalyzed acylation of alkynes was studied to afford one of the most atom-economic and efficient methodologies for the preparation of β-chlorovinyl ketones. In contrast to the Friedel–Crafts acylation, only a catalytic amount of $GaCl_3$ was needed to produce the target products in high stereoselectivity.

Key words: gallium trichloride, acylation, alkyne, β-chlorovinyl ketone

In the past decade, gallium chloride ($GaCl_3$), for a long time considered to be analogous to aluminum chloride ($AlCl_3$) but with a lower reactivity, has been revealed to be a reagent used for generating organogallium compounds, which can carbometalate unactivated unsaturated bonds.[1] Recently, Yamaguchi and co-workers reported many interesting $GaCl_3$-promoted reactions, such as the insertion of Ga(III) complexes into alkynes to produce vinylgalliums as important synthetic intermediates.[2]

β-Chlorovinyl ketones are very useful intermediates for the synthesis of a variety of compounds.[3] Although β-chlorovinyl ketones are a class of simple compounds, there are not many synthetic routes to these compounds.[3b–3g] In the early 1970s, the Friedel–Crafts addition of acid chloride–$AlCl_3$ complexes to acetylenes leading to β-chlorovinyl ketones had been reported.[4] The major products from the Friedel–Crafts addition, which requires equimolar amounts of acid chloride–$AlCl_3$ complex, have the chlorine and the carbonyl groups configured in a *trans* relationship.[4b] Herein we wish to report a $GaCl_3$-catalyzed acylation of alkynes for the synthesis of β-chlorovinyl ketones in which the major products contain a *cis* configuration.

As a first attempt, we examined the reaction of hexanoyl chloride (**1a**) with phenylacetylene (**2a**) using 0.1 equivalent of $GaCl_3$ as catalyst and dichloromethane as solvent at room temperature. 1-Chloro-1-phenyloct-1-en-3-one (**3a**) was isolated in 25% yield together with 42% of recovered phenylacetylene. The stereochemistry of the product **3a** was established by 2D NOE experiment which clearly showed an NOE effect between the aromatic protons and the vinyl proton. It was notable that we did not observe the *trans* isomer even in the ^1H NMR spectra of crude products, demonstrating that this reaction took a different reaction route from the $AlCl_3$-promoted Friedel–Crafts addition. Considering the moisture-sensitivity and low turnover number (TON) of the catalyst $GaCl_3$,[5] we tried the experiment under nitrogen atmosphere using 0.2 equivalent of $GaCl_3$. To our delight, the reaction was complete in two hours and compound **3a** was obtained in 65% yield (Scheme 1).



Scheme 1

Encouraged by this result, we turned our attention to other acid chlorides and alkynes (Table 1). However, we observed that the *trans* isomers could be isolated in cases when the acid chlorides used were sterically non-hindered or aromatic acid chlorides (entries 6–11, Table 1). Moreover, to our surprise, in those cases prolonging the reaction time also changed the *cis*/*trans* ratio (entries 12–16, Table 1), indicating that this type of β-chlorovinyl ketones was sensitive to *cis*/*trans* isomerization in the presence of $GaCl_3$.[4c]

Recently, Yadav et al. reported a stereoselective condensation of phenylacetylene with benzaldehyde in the presence of gallium trihalides but no mechanism was proposed.[7] Yamaguchi et al. has also developed an interesting $GaCl_3$-promoted C2-olefination of aromatic hydrocarbons with silylacetylene, in which a novel organogallium intermediate was reported.[8] Considering the absence of β-silicon-stabilization to vinyl cation, we suggested the possibility of a C1-vinyl cation intermediate mechanism for the reaction (Scheme 2).

At first a $GaCl_3$-complexed alkyne is formed, generating a vinyl cation intermediate **A**.[8] The intermediate **A** is attacked by a chloride anion to afford vinylgallium intermediate **B**. The vinylgallium intermediate **B** reacts with acid chloride to give **3**. Due to the sensitivity to *cis*/*trans* isomerization,[4c] **3** may rearrange to give a mixture.

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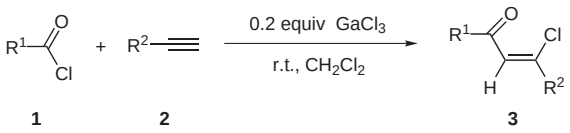
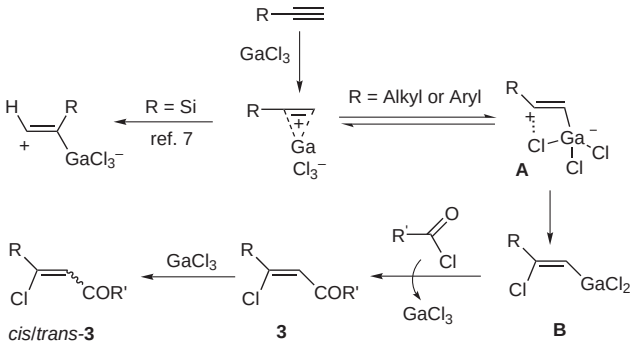
Table 1 Synthesis of β-Chlorovinyl Ketones via the $GaCl_3$-Catalyzed Chloroacylation of Alkynes[a,6]



1 **2** **3**

Entry	R^1	R^2	Time (h)	Yield (%)[b] of **3** *cis*/*trans* ratio[c]
1	*n*-Pent	Ph	2	**3a** (65)
2	*n*-Pent	*n*-Pent	2	**3b** (61)
3	*n*-Pent	*n*-Pent	2	**3c** (58)
4	*n*-Hex	*n*-Pent	2	**3d** (62)
5	*n*-Hex	Ph	2	**3e** (66)
6	Me[d]	*n*-Pent	2.5	**3f** (62) (50:50)
7	Et[d]	*n*-Pent	2.5	**3g** (57) (69:31)
8	Et[d]	*n*-Bu	2.5	**3h** (55) (55:45)
9	Ph	$BrCH_2CH_2$	1.5	**3i** (52) (88:12)
10	Ph	Ph	1.5	**3j** (61) (89:11)
11	*p*-Tol	Ph	1.5	**3k** (62) (87:13)
12	Et[d]	*n*-Pent	5	**3g** (55) (62:38)
13	Et[d]	*n*-Bu	5	**3h** (59) (52:48)
14	Ph	$BrCH_2CH_2$	5	**3i** (58) (83:17)
15	Ph	Ph	5	**3j** (58) (82:18)
16	*p*-Tol	Ph	5	**3k** (55) (84:16)

[a] All reactions were carried out using **1** (0.6 mmol), **2** (0.5 mmol) and $GaCl_3$ (0.1 mmol) in CH_2Cl_2 (5 mL) at r.t.
[b] Isolated product yield after chromatography.
[c] The *cis*/*trans* ratios of **3** were determined by NMR spectroscopy.
[d] Acid chloride (1 mmol) was used.



Scheme 2

In summary, we have reported a simple and efficient protocol for the synthesis of β-chlorovinyl ketones. The catalysis of $GaCl_3$ may produce organogallium intermediates, which have received much less attention in organic synthesis than organoaluminum compounds.[1] The activation of unsaturated bonds by $GaCl_3$, synthetic applications of organogallium compounds, and the reaction mechanism are being studied further in our laboratory.

Acknowledgment

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References and Notes

(1) For a review, see: Amemiya, R.; Yamaguchi, M. *Eur. J. Org. Chem.* **2005**, 5145.
(2) (a) Yamaguchi, M.; Tsukagoshi, T.; Arisawa, M. *J. Am. Chem. Soc.* **1999**, *121*, 4074. (b) Arisawa, M.; Akamatsu, K.; Yamaguchi, M. *Org. Lett.* **2001**, *3*, 789. (c) Arisawa, M.; Amemiya, R.; Yamaguchi, M. *Org. Lett.* **2002**, *4*, 2209. (d) Kobayashi, K.; Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc.* **2002**, *124*, 8528. (e) Yonehara, F.; Kido, Y.; Morita, S.; Yamaguchi, M. *J. Am. Chem. Soc.* **2001**, *123*, 11310. (f) Arisawa, M.; Akamatsu, K.; Yamaguchi, M. *Org. Lett.* **2001**, *3*, 789.
(3) (a) Pohland, A. E.; Benson, W. R. *Chem. Rev.* **1966**, *66*, 161. (b) Luo, F. T.; Lai, J. H.; Shaeh, J. C. *Acad. Sin.* **1987**, *34*, 23. (c) Martin, G. J.; Kirschleger, B. *Sci. Chim.* **1974**, *279*, 363. (d) Luo, F. T.; Hsieh, L. C. *Tetrahedron Lett.* **1994**, *35*, 9585. (e) Hua, R.; Onozawa, S.; Tanaka, M. *Chem. Eur. J.* **2005**, 3621. (f) Doyle, M. P.; Devia, A. H.; Bassett, K. E.; Terpstra, J. W.; Mahapatro, S. N. *J. Org. Chem.* **1987**, *52*, 1619. (g) Badrieh, Y.; Kayyal, A.; Blum, J. *J. Mol. Catal.* **1992**, *75*, 161.
(4) (a) Martens, H.; Janssens, F.; Hoornaert, G. *Tetrahedron* **1975**, *31*, 177. (b) Benson, W. R.; Pohland, A. E. *J. Org. Chem.* **1964**, *29*, 385. (c) Cavalchi, B.; Landini, D.; Montanari, F. *J. Chem. Soc. C* **1969**, *9*, 1204. (d) Sandermann, W.; Bruns, K. *Chem. Ber.* **1962**, *95*, 1863.
(5) (a) Amemiya, R.; Suwa, K.; Toriyama, J.; Nishimura, Y.; Yamaguchi, M. *J. Am. Chem. Soc.* **2005**, *127*, 8252. (b) Yonehara, F.; Kido, Y.; Sugimoto, H.; Morita, S.; Yamaguchi, M. *J. Org. Chem.* **2003**, *68*, 6752.
(6) All reagents were obtained commercially except $GaCl_3$. The $GaCl_3$ used was prepared as follows: Gallium (3.5 g) was dissolved in concd HCl (100 mL) under reflux and excessive HCl was removed under reduced pressure. To the reaction mixture was added $SOCl_2$ (35 mL) and excessive $SOCl_2$ was removed under reduced pressure (ca. 20 mm Hg by rotary evaporation then 5 mm Hg by a pump). The residue was used directly for our reaction with 80% purity.
$GaCl_3$-Catalyzed Acylation of Alkynes; General Procedure: To a solution of $GaCl_3$ (20 mol%) and acid chloride (0.6 mmol) in CH_2Cl_2 (5 mL) was added alkyne (0.5 mmol) under nitrogen. The reaction was stirred at r.t. and filtered through a short celite pad, washed with Et_2O, concentrated by vacuo, and purified by chromatography on silica gel with *n*-hexane–EtOAc (10:1) as the eluent.
(*Z*)-1-Chloro-1-phenyloct-1-en-3-one (3a): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66–7.69 (m, 2 H), 7.38–7.44 (m, 3 H), 6.79 (s, 1 H), 2.67–2.71 (t, *J* = 7.2 Hz, 2 H), 1.66–1.70 (t, *J* = 7.4 Hz, 2 H), 1.31–1.37 (m, 4 H), 0.89–0.92 (m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.0, 142.3, 137.4, 130.5, 128.6, 127.2, 123.8, 44.4, 31.3, 23.6, 22.4, 13.9. MS (EI): *m*/*z* = 239 (7.2) [M + 3], 238 (4.6) [M + 2], 237 (21.6) [M + 1], 236 (3.85) [M$^+$]. IR (neat): 1695, 1591 cm^{-1}.
(*Z*)-4-Chlorononon-3-en-2-one (*Z*-3f): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.24 (s, 1 H), 2.42–2.45 (t, *J* = 7.8 Hz, 2 H), 2.37 (s, 3 H), 1.61–1.64 (m, 2 H), 1.30–1.35 (m, 4 H), 0.89–0.92

(m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.6, 147.4, 125.0, 41.2, 31.4, 30.6, 26.9, 22.2, 13.8. MS (EI): *m*/*z* = 176 (1.25) [M + 2], 174 (2.68) [M^+]. IR (neat): 1710, 1610 cm^{-1}. **(*E*)-4-Chlorononon-3-en-2-one (*E*-3f)**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.44 (s, 1 H), 2.90–2.94 (t, *J* = 7.8 Hz, 2 H), 2.20 (s, 3 H), 1.59–1.62 (m, 2 H), 1.30–1.34 (m, 4 H), 0.87–0.91 (m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 157.0, 125.7, 35.8, 31.9, 30.9, 27.3, 22.3, 13.9. MS (EI): *m*/*z* = 176 (0.96) [M + 2], 174 (1.33) [M^+]. IR (neat): 1697, 1600 cm^{-1}.

(7) Yadav, J. S.; Reddy, B. V. S.; Eeshwaraiah, B.; Gupta, K. M.; Biswas, K. S. *Tetrahedron Lett.* **2005**, *46*, 1161.
(8) Yamaguchi, M.; Kido, Y.; Hayashi, A.; Hirama, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1313.