ORGANIC LETTERS

2004
Vol. 6, No. 23
4323−4325

Efficient Synthesis of 1-Adamantanecarboxaldehyde by the $GaCl_3$-Mediated Carbonylation of Adamantane under Mild Reaction Conditions

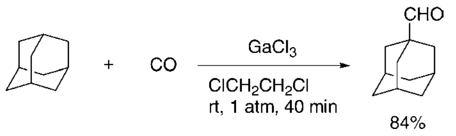
Masayuki Oshita and Naoto Chatani*

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

chatani@chem.eng.osaka-u.ac.jp

Received September 11, 2004

ABSTRACT

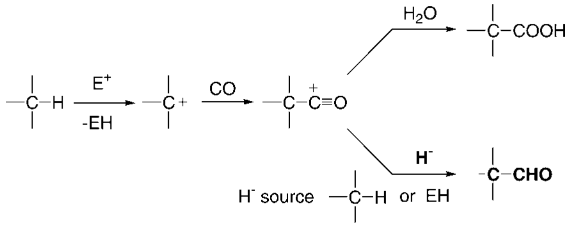


The reaction of adamantane (1) with CO (1 atm) in 1,2-dichloroethane at room temperature in the presence of $GaCl_3$ results in formylation to give 1-adamantanecarboxaldehyde (2) in up to 84% yield.

The Koch−Haaf reaction is a well-known and useful method for preparing carboxylic acids from olefins or alcohols, carbon monoxide (CO), and H_2O in the presence of a strong acid.[1] Saturated alkanes can also be used as substrates in this carboxylation reaction.[2] The carboxylation of saturated alkanes can be achieved by using superacidic media such as $HF-SbF_5$, which abstracts a hydride from an alkane to give a carbocation (Scheme 1). The resulting carbocation reacts with CO to generate acylium cations, which then undergo hydrolysis to give carboxylic acids. Acylium cations can also be used to produce aldehydes by abstraction of a hydride from an alkane or an EH, which is formed in the first step (Scheme 1). There are, however, only a few examples of the synthesis of aldehydes via the reaction pathway described above, presumably because of the instability of aldehydes compared to carboxylic acids under the strongly acidic reaction conditions used.[3] Other reasons would be the lack of a hydride source to react with the acylium cation when the reaction is carried out under strongly acidic conditions or when a strong electrophile (E^+) is used because no hydride source exists or the EH cannot function as a hydride source, respectively.

The first isolation of aldehydes by the superacid-mediated carbonylation reaction of saturated alkanes was reported by Olah.[4] Thus, the carbonylation of adamantane (**1**) in superacidic media such as CF_3SO_3H, $B(OSO_2CF_3)_3-HSO_3CF_3$ and $SbF_5-HSO_3CF_3$ was demonstrated to yield a small amount (up to 21% yield) of 1-adamantanecarboxaldehyde (**2**) in

Scheme 1. Carbonylation of Saturated Alkanes



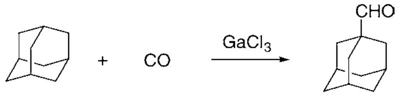
---

(1) Bahrmann, H. In *New Syntheses with Carbon Monoxide*; Falbe, J., Ed.; Springer-Verlag: Berlin, 1980; pp 372−413. *Carbonylation*; Colquhoun, H. M., Thomson, D. J., Twigg, M. V., Eds.; Plenum Press: New York, 1991.

(2) Yoneda, N.; Takahashi, Y.; Fukuhara, T.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2819. Delavarenne, S.; Simon, M.; Fauconet, M.; Sommer, J. *J. Am. Chem. Soc.* **1989**, *111*, 383. Souma, Y.; Tsumori, N.; Willner, H.; Xu, Q.; Mori, H.; Morisaki, Y. *J. Mol. Catal. A* **2002**, *189*, 67 and references therein.

10.1021/ol0481636 CCC: $27.50

Table 1. $GaCl_3$-Mediated Formylation of Adamantane (**1**)



1 (1 mmol)

2

entry	reaction conditions	yields (%)[a] **2**	**1**
1	$GaCl_3$ 1 mmol, 1,2-DCE 1 mL, CO 10 atm, 80 °C, 12 h	47	1
2	$GaCl_3$ 1 mmol, 1,2-DCE 1 mL, CO 1 atm, 80 °C, 12 h	0	0
3	$GaCl_3$ 1 mmol, 1,2-DCE 1 mL, CO 10 atm, rt, 12 h	63	20
4	$GaCl_3$ 1 mmol, 1,2-DCE 1 mL, CO 1 atm, rt, 1 h	55	40
5	$GaCl_3$ 1 mmol, 1,2-DCE 0.5 mL, CO 1 atm, rt, 40 min	77	15
6	$GaCl_3$ 1.5 mmol, 1,2-DCE 0.5 mL, CO 1 atm, rt, 40 min	84	1
7	$GaCl_3$ 1 mmol, CH_2Cl_2 0.5 mL, CO 1 atm, rt, 40 min	76	15
8	$GaCl_3$ 1 mmol, cyclohexane 0.5 mL, CO 1 atm, rt, 40 min	34	55
9[b]	$GaCl_3$ 1 mmol, 1,2-DCE 0.5 mL, CO 1 atm, rt, 40 min	19	68
10	$AlCl_3$ 1 mmol, 1,2-DCE 0.5 mL, CO 1 atm, rt, 40 min	75	25
11	$GaBr_3$ 1 mmol, 1,2-DCE 0.5 mL, CO 1 atm, rt, 40 min	58	6
12	$AlBr_3$ 1 mmol, 1,2-DCE 0.5 mL, CO 1 atm, rt, 40 min	60	22

[a] GC yield. [b] Methylcyclopentane (2 mmol) was added.

addition to the usual main product, 1-adamantanecarboxylic acid (60−75%). Olah subsequently reported that $AlCl_3$ can also be used to mediate the formylation of **1** in CH_2Cl_2 but that the carboxylic acid was still the major product and the yield of the aldehyde was low (maximum of 21%).[5] More recently, Akhrem reported that **2** is formed in nearly quantitative yield when $CH_2Br_2/2AlBr_3$ is used as an electrophile precursor (E^+) to abstract a hydride from **1** with methylcyclopentane as the hydride source.[6] In many of the cases reported so far, more than equimolar amounts of acids compared to the substrates are necessary for the reaction to proceed effectively.

Meanwhile, $GaCl_3$,[7,8] a mild Lewis acid compared to $AlCl_3$, is also known to generate carbocations from tertiary alkanes, similar to $AlCl_3$. Yamaguchi reported on $GaCl_3$-catalyzed reactions of alkanes with aromatics and proposed that the reaction is initiated by hydride abstraction from the alkane by $GaCl_3$.[8] Accordingly, it would be expected that $GaCl_3$ would effectively promote the carbonylation of adamantane. Herein, we report on the $GaCl_3$-mediated reaction of adamantane with CO leading to 1-adamantanecarboxaldehyde. The reaction does not require excess $GaCl_3$, and a hydride source is not required for the reaction to proceed.

It was interesting to discover that $GaCl_3$ functions as a promoter of the formylation of adamantane. Thus, the reaction of adamantane (**1**, 1 mmol) and $GaCl_3$ (1 mmol) in 1,2-dichloroethane (1 mL) under 10 atm of CO at 80 °C for 12 h gave 1-adamantanecarboxaldehyde (**2**) in 47% GC yield with the nearly complete consumption of adamantane (entry 1, Table 1). The report by Akhrem[6] that the formylation of adamantane could be achieved, even at room temperature under 1 atm of CO, inspired us to carry out the reaction under milder reaction conditions. However, when the CO pressure was lowered to 1 atm at 80 °C, **1** was completely consumed with none of the desired aldehyde **2** being detected (entry 2). On the other hand, a reaction at room temperature at 10 atm of CO resulted in the formation of the aldehyde in moderate yield with 20% of unreacted **1** being recovered (entry 3). Moreover, we could successfully lower the CO pressure to 1 atm when the reaction was conducted at room temperature, although the conversion was not as high (entry 4). After a series of experiments, we found that the yield could be improved by decreasing the amount of solvent used to 0.5 mL and by shortening the reaction time to 40 min. Thus, the conversion was increased by 85%, giving **2** in 77% (entry 5). Furthermore, when 1.5 mmol of $GaCl_3$ was used, **1** was fully consumed and **2** was produced in a yield of 84% (entry 6).

A systematic examination of the solvents used revealed that dichloromethane is also appropriate for the reaction, while the use of cyclohexane gave a lower yield (entries 7

---

(3) Takeuchi, K.; Akiyama, F..; Miyazaki, T.; Kitagawa, I.; Okamoto, K. *Tetrahedron* **1987**, *43*, 701. Olah, G. A.; Prakash, G. K. S.; Marinez, E. R. *Angew. Chem., Int. Ed.* **2000**, *39*, 2547 and references therein.

(4) Farooq, O.; Marcelli, M.; Prakash, G. K. S.; Olah, G. A. *J. Am. Chem. Soc.* **1988**, *110*, 864.

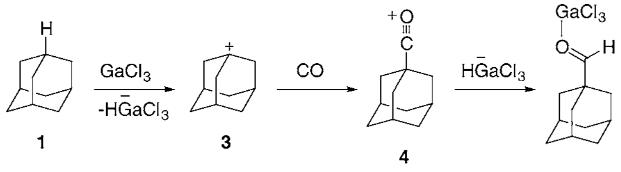
(5) Olah, G. A.; Wang, Q. *Synthesis* **1992**, 1090.

(6) Akhrem, I.; Churilova, I.; Bernadyuk, S.; Vol'pin, M. *Tetrahedron Lett.* **1996**, *37*, 5775. Akhrem, I. S.; Churilova, I. M.; Bernadyuk, S. Z.; Vol'pin, M. E. *Russ. Chem. Bull.* **1997**, *46*, 491. Akhrem, I. S. *Russ. Chem. Bull.* **2003**, *52*, 2606.

(7) Recently, $GaCl_3$ has been found to show a unique catalytic activity. Chatani, N.; Inoue, H.; Kotsuma, T.; Murai, S. *J. Am. Chem. Soc.* **2002**, *124*, 10294. Viswanathan, G. S.; Li, C.-J. *Synlett* **2002**, 1553. Amemiya, R.; Fujii, A.; Arisawa, M.; Yamaguchi, M. *J. Organomet. Chem.* **2003**, *686*, 94. Bez, G.; Zhao, C.-G. *Org. Lett.* **2003**, *5*, 4991. Chatani, N.; Oshita, M.; Tobisu, M.; Ishii, Y.; Murai, S. *J. Am. Chem. Soc.* **2003**, *125*, 7812. Usugi, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Org. Lett.* **2004**, *6*, 601. Amemiya, R.; Nishimura, Y.; Yamaguchi, M. *Synthesis* **2004**, 1307. Amemiya, R.; Fujii, A.; Yamaguchi, M. *Tetrahedron Lett.* **2004**, *45*, 4333.

(8) Yonehara, F.; Kido, Y.; Morita, S.; Yamaguchi, M. *J. Am. Chem. Soc.* **2001**, *123*, 11310. Yonehara, F.; Kido, Y.; Sugimoto, H.; Morita, S.; Yamaguchi, M. *J. Org. Chem.* **2003**, *68*, 6752.

Scheme 2. Possible Reaction Mechanism



and 8). We also examined the effect of methylcyclopentane, which was used as a hydride source by Akhrem.[6] However, the addition of methylcyclopentane led to a significant deterioration in the yield of the desired product (entry 9). We next investigated the effect of Lewis acids other than $GaCl_3$. Although Olah reported the $AlCl_3$-mediated formylation of adamantane at CO pressures as high as 70 atm, our optimal reaction conditions, requiring room temperature and 1 atm of CO afforded the desired aldehyde **2** in much higher yields than that reported by Olah (entry 10). Among some other Lewis acids examined, $GaBr_3$ and $AlBr_3$ gave lower yields than the analogous chloride Lewis acids (entries 11 and 12). $InCl_3$ and $ZrCl_4$ did not promote the formylation at all. In an attempt to use methylcyclohexane as a starting material, no formylation product was observed.

In a possible reaction mechanism, $GaCl_3$ initially abstracts a hydride from adamantane to generate the 1-adamantyl cation **3** (Scheme 2). The cation **3** reacts with CO, and the resulting acylium cation **4** abstracts a hydride from the gallium hydride species, formed in the first step, to give 1-adamantanecarboxaldehyde. The rate-determining step is assumed to be the first hydride abstraction to form the 1-adamantyl cation **3**. This is supported by the fact that the effects of CO pressure on the efficiency of the reaction are negligible. We hypothesize that the hydride source in the final step is the gallium hydride species, and not adamantane. On the other hand, in the Akhrem reaction system, methylcyclopentane was used as a hydride source. This difference in hydride source might be attributed to differences in the reactivity of the hydride abstraction reagents used. Akhrem's reagent is so reactive and highly electrophilic that hydride abstraction occurs irreversibly. In contrast, $GaCl_3$ is less electrophilic, and consequently the generated gallium hydride species ($HGaCl_3^-$) can easily release hydride to **4**. It is also noteworthy that the formylation of adamantane proceeded only in the presence of a normal Lewis acid, such as $GaCl_3$, although superacidic conditions have frequently been employed for this transformation.

In conclusion, we describe the $GaCl_3$-mediated carbonylation of adamantane to 1-adamantane-carbaldehyde under mild reaction conditions such as room temperature and an atmospheric pressure of CO of 1.[9] The reaction requires only 1 equiv of $GaCl_3$ and does not require a hydride source.

Acknowledgment. This work was supported, in part, by grants from Ministry of Education, Culture, Sports, Science and Technology, Japan. M.O. expresses special thanks for the Center of Excellence (21COE) program "Creation of Integrated EcoChemistry of Osaka University".

OL0481636

---

(9) **Typical Procedure.** A 8 mL screw-cap vial with a rubber septum was charged with $GaCl_3$ (1.0 M in methylcyclohexane, 1 mmol, 1 mL) by means of a syringe, and the methylcyclohexane was removed in vacuo. The residue was dissolved in 1,2-dichloroethane (0.5 mL), and adamantane (**1**) (1 mmol, 136 mg) was added. A syringe needle was introduced through the rubber septum, and the vial was placed in a 50 mL stainless autoclave. The system was flushed with 10 atm of CO three times and finally was pressurized to 1 atm. After 40 min, the vial was removed from the autoclave and the reaction mixture was treated with a saturated aqueous Na_2CO_3. The solution was extracted with Et_2O three times. The combined organic layer was then washed with H_2O, dried over $MgSO_4$, and evaporated to dryness under reduced pressure. The column chromatography of the residue on SiO_2 (hexane/Et_2O = 10/1) gave 1-adamantanecarboxaldehyde (**2**) as a white solid (116 mg, 70% yield): ^1H NMR ($CDCl_3$) δ 1.60−1.83 (c, 12H), 2.02−2.15 (c, 3H), 9.31 (s, 1H); MS, *m*/*z* (relative intensity, %) 164 (M^+, 2.9), 135 (100), 107 (12), 93 (29), 79 (41), 67 (21), 55 (14).