Tetrahedron Letters 49 (2008) 5322–5323

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Zinc(0)/dimethylformamide-mediated synthesis of symmetrical carboxylic anhydrides from acid chlorides

Audrey Serieys[a], Candice Botuha[a,b], Fabrice Chemla[a,b,*], Franck Ferreira[a,b,*], Alejandro Pérez-Luna[a,b]

[a] UPMC Univ Paris 06, UMR 7611, Laboratoire de Chimie Organique, Institut de Chimie Moléculaire (FR 2769), case 183, 4 place Jussieu, F-75005 Paris, France
[b] CNRS, UMR 7611, Laboratoire de Chimie Organique, Institut de Chimie Moléculaire (FR 2769), case 183, 4 place Jussieu, F-75005 Paris, France

ARTICLE INFO

Article history:
Received 4 June 2008
Accepted 16 June 2008
Available online 19 June 2008

Keywords:
Carbenoids
Carboxylic anhydrides
Reductive insertion
Vilsmeier iminiums
Zinc

ABSTRACT

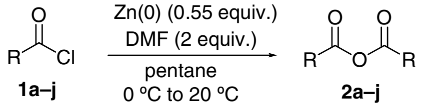
The high yielding synthesis of symmetrical carboxylic anhydrides from acid chlorides mediated by zinc dust in the presence of dimethylformamide is presented. A mechanism involving the reductive insertion of zinc(0) into the C–Cl bond of a Vilsmeier-type iminium intermediate as the crucial step is also proposed.

© 2008 Elsevier Ltd. All rights reserved.

A panoply of methods has been reported in the literature for the synthesis of carboxylic anhydrides.[1] Generally, these are prepared by dehydration of carboxylic acids with powerful acylating or dehydrating agents. For instance, among the very recent publications thionyl chloride,[2] sulfonyl chlorides,[3] phosgene equivalents,[4] phophoranes,[5] pyridazin-3(2*H*)-ones,[6] imidazolinium chlorides,[7] dinitrogen tetroxide,[8] 1,3,5-triazines,[9] trichloroacetonitrile/triphenylphosphine,[10] and carbodiimides[11] have been used. Alternatively, carboxylic anhydrides can be prepared by the reaction of acid chlorides with carboxylates,[12] or by the direct reaction of acid chlorides with carboxylic acids in the presence of a base,[13] a solid-phase 4-vinylpyridine co-polymer,[13c] a polymer-supported cobalt phosphine complex,[13d] and palladium(II) or cobalt(II) chlorides.[14] Carboxylic anhydrides have also been recently prepared from acid chlorides by reaction with a base and water,[13c,15] under ultrasound basic media,[16] and under basic phase-transfer conditions using ammonium chlorides.[17]

In this Letter, we would like to report the zinc(0)/dimethylformamide-triggered preparation of various symmetrical carboxylic anhydrides from the corresponding acid chlorides. Under the optimized conditions, acid chlorides **1a–j** (1 equiv) were added dropwise at 0 °C to a stirred suspension of zinc dust (0.55 equiv) in a mixture of anhydrous dimethylformamide (2 equiv) and pentane (Table 1).[18,19] The resulting suspension, with a clear colorless supernatant, was allowed to warm to 20 °C. It was then maintained under vigorous stirring at this temperature until the disappearance of all the zinc (2–20 h) and the formation of a dark orange gummy mixture. In all the cases, symmetrical carboxylic anhydrides **2a–j** were obtained in good to excellent yields (66–95%) as analytically pure products after trituration of the dark orange gum with 3% Et_2O in pentane and filtration of the reaction mixture through flash silica gel.

Table 1
Zinc(0)/dimethylformamide-mediated conversion of acid chlorides **1a–j** into carboxylic anhydrides **2a–j**



1a–j → **2a–j**

Entry	R	Anhydride[a]	*t* (h)	Yield[b] (%)
1	Pent	**2a**	20	71
2	*i*-Bu	**2b**	20	69
3	*t*-Bu	**2c**	16	89
4	Cyclopropyl	**2d**	3	77
5	Cyclobutyl	**2e**	2	84
6	Cyclopentyl	**2f**	2	66
7	Cyclohexyl	**2g**	2	92
8	C_6H_5	**2h**	2	75
9	4-MeOC_6H_4	**2i**	2	67
10	4-ClC_6H_4	**2j**	2	95

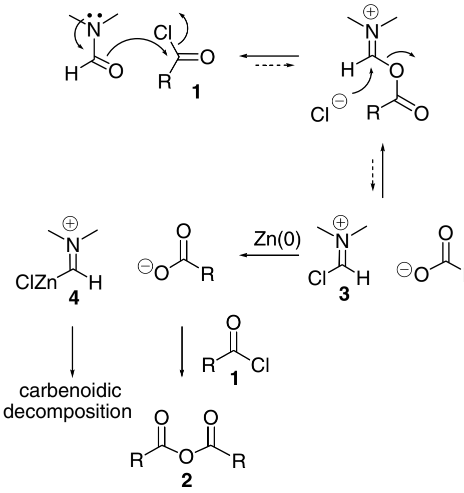
[a] All new compounds were fully characterized by IR, ^1H, and ^{13}C NMR.
[b] Yields in pure symmetrical carboxylic anhydrides.

Interestingly, both zinc and dimethylformamide were demonstrated to play a crucial role in this reaction, since no reaction

---

[*] Corresponding authors. Tel.: +33 1 44 27 55 71; fax: +33 1 44 27 75 67 (F.F.).
E-mail addresses: fabrice.chemla@upmc.fr (F. Chemla), franck.ferreira@upmc.fr (F. Ferreira).

0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.06.073



Scheme 1. Postulated mechanism for the zinc(0)/dimethylformamide-mediated formation of carboxylic anhydrides from acid chlorides.

occurs without one of these two reagents. In order to explain this, we have envisioned that the reaction is driven by the zinc(0)-mediated reduction of a Vilsmeier-type species generated in situ from acid chlorides **1** and dimethylformamide.[20] We have then postulated that the initial steps of the mechanism might correspond to the activation of 1 equiv of acid chloride **1** through the nucleophilic attack of dimethylformamide leading to the *reversible*[21] formation of the Vilsmeier-type iminium salt **3** with a carboxylate anion as the counter ion (Scheme 1).

The fact that no reaction occurs without zinc(0) suggests that these initial steps are equilibria which are very little displaced in the sense of the formation of **3**. In the following step, the *irreversible* zinc(0)-mediated reduction of iminium salt **3**,[22,23] resulting in the observed disappearance of zinc(0), might give carbenoid **4** with a carboxylate counter ion. Carbenoid **4** might then undergo carbenoidic reactions[24] resulting in the formation of the dark orange gum. This reduction, which might drive all the initial equilibria in the sense of the formation of **4**, could be a zinc insertion analogous to those previously described by one of us for the preparations of enol esters[25] and thiosulfonic *S*-esters,[26] the key steps of which involve, respectively, the insertion of zinc(0) into the C–Cl bond of acid chlorides and the S–Cl bond of thiosulfonic acid chlorides. Finally, the corresponding symmetrical carboxylic anhydride **2** is obtained by the condensation of the carboxylate counter ion of carbenoid **4** with another equivalent of acid chloride **1**.

In conclusion, we have disclosed an easy and straightforward high yielding preparation of various symmetrical carboxylic anhydrides by reaction of acid chlorides with zinc dust in the presence of dimethylformamide. In order to confirm the postulated mechanism, further studies will be undertaken to prove the formation of carbenoid **4**. The extension of this method to the synthesis of unsymmetrical carboxylic anhydrides is currently under investigations in our group and will be reported in due course.

References and notes

1. Ogliaruso, M. A.; Wolfe, J. F. *Synthesis of Carboxylic Acids, Esters and Their Derivatives*; John Wiley & Sons: New York, 1991; pp 198.
2. Kazemi, F.; Kiasat, R. *Phosphorous, Sulfur, and Silicon* **2003**, *178*, 2287.
3. Kazemi, F.; Sharghi, H.; Nasseri, M. A. *Synthesis* **2004**, 205.
4. Kocz, R.; Roestamadji, J.; Mobashery, S. *J. Org. Chem* **1994**, *59*, 2913.
5. Kawamura, Y.; Sato, Y.; Horie, T.; Tsukayama, M. *Tetrahedron Lett.* **1997**, *38*, 7893.
6. (a) Park, Y.-D.; Kim, J.-J.; Kim, H.-K.; Cho, S.-D.; Kang, Y.-J.; Park, K. H.; Lee, S.-G.; Yoon, Y.-J. *Synth. Commun.* **2005**, *35*, 371; (b) Kim, J.; Park, Y.-D. ; Lee, W. S.; Cho, S.-D. ; Yoon, Y.-J. *Synthesis* **2003**, 1517.
7. Isobe, T.; Ishikawa, T. *J. Org. Chem.* **1999**, *64*, 6984.
8. Kim, Y. H.; Kim, K.; Park, Y. J. *Tetrahedron Lett.* **1990**, *31*, 3893.
9. Kamiñski, Z. J.; Kolesiñska, B.; Malgorzata, M. *Synth. Commun.* **2004**, *34*, 3349.
10. Kim, J.; Jang, D. O. *Synth. Commun.* **2001**, *31*, 395.
11. Clarke, P. A.; Kayaleh, N. E.; Smith, M. A.; Baker, J. R.; Bird, S. J.; Chan, C. *J. Org. Chem.* **2002**, *67*, 5226.
12. (a) Hajipour, A. R.; Mazloumi, Gh. *Synth. Commun.* **2002**, *32*, 23; (b) Liang, Y.; Jwo, J.-J. *J. Mol. Catal. A* **2001**, *170*, 57; (c) Ferris, A. F.; Emmons, W. D. *J. Am. Chem. Soc.* **1953**, *75*, 232; (d) Pasha, M. A.; Rizwana, S. *Indian J. Chem. Sect. B* **2005**, *44*, 420.
13. (a) Fukuoka, S.; Takimoto, S.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 4711; (b) Rambacher, P.; Mäke, S. *Angew. Chem.* **1968**, *80*, 487; (c) Fife, W. K.; Zhang, Z. *Tetrahedron Lett.* **1986**, *27*, 4933; (d) Leadbeater, N. E.; Scott, K. A. *J. Org. Chem.* **2000**, *65*, 4770.
14. (a) Wang, J.-X.; Hu, Y.; Cui, W.-F. *Synth. Commun.* **1994**, *24*, 3261; (b) Srivastava, R. R.; Kabalba, G. W. *Tetrahedron Lett.* **1992**, *33*, 593.
15. Dhimitruka, I.; SantaLucia, J., Jr. *Org. Lett.* **2006**, *8*, 47.
16. Hu, Y.; Wang, J.-X.; Li, S. *Synth. Commun.* **1997**, *27*, 243.
17. (a) Jászay, Z.; Petneházy, I.; Toke, L. *Heteroat. Chem.* **2004**, *15*, 447; (b) Wang, J.-X.; Hu, Y.-L.; Cui, W.-F. *J. Chem. Res. (S)* **1990**, 84; (c) Plusquellec, D.; Roulleau, F.; Lefeuvre, M.; Brown, E. *Tetrahedron* **1988**, *44*, 2471.
18. *Typical procedure: Under* argon, to a suspension of zinc dust (360 mg, 5.50 mmol) in pentane (10 mL) and anhydrous DMF (1.55 mL, 20.00 mmol) was added dropwise at 0 °C the acid chlorides **1a**–**j** (10 mmol). The resulting mixture was warmed to room temperature and stirred between 2 and 20 h depending on the acid chloride (see Table 1). The mixture was then filtered over a pad of flash silica gel (5 × 3 cm) eluting with 3% Et_2O in pentane (500–700 mL). Removal of the solvents in vacuo furnished the corresponding pure symmetrical carboxylic anhydrides **2a**–**j**.
19. *Data for cyclopentanecarboxylic anhydride* **2f**: ^{1}H NMR (400 MHz, C_6D_6) δ 1.20–1.27 (m, 4H), 1.41–1.48 (m, 4H), 1.53–1.60 (m, 4H), 1.77–1.86 (m, 4H), 1.49–2.57 (m, 2H); ^{13}C NMR (50.3 MHz, C_6D_6) δ 26.5, 30.1, 45.5, 172.8; IR (ATR diamond) 1740 (s), 1807 (s), 2872 (m), 2956 cm^{-1} (m).
20. For early work concerning the formation of acid halides from carboxylic acids and imidoyl halides, see: (a) Bosshard, H. H.; Mory, R.; Schmid, M.; Zollinger, Hch. *Helv. Chim. Acta* **1959**, *42*, 1653; (b) Colson, A. *Bull. Soc. Chim. Fr.* **1897**, *17*, 59.
21. Barrett, A. G. M.; Braddock, D. C.; James, R. A.; Koike, N.; Procopiu, P. A. *J. Org. Chem.* **1998**, *63*, 6273.
22. For the titanium(0)-mediated reduction of an iminium chloride, see: Betschart, C.; Seebach, D. *Helv. Chim. Acta* **1987**, *70*, 2215.
23. For related reductions of acid cyanides, see: (a) Baek, H. S.; Lee, S. J.; Yoo, B. W.; Ko, J. J.; Kim, S. H.; Kim, J. H. *Tetrahedron Lett.* **2000**, *41*, 8097; (b) Baruah, B.; Boruah, A.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **1997**, *38*, 7603.
24. For carbenoids derived from Vilsmeier reagents, see: (a) Cheng, Y.; Goon, S.; Meth-Cohn, O. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1619; (b) Böhme, H.; Sutoyo, P. *Tetrahedron Lett.* **1981**, *22*, 1671.
25. Chemla, F.; Normant, J. F. *Tetrahedron* **1997**, *53*, 17265.
26. (a) Chemla, F.; Karoyan, P. *Org. Synth.* **2002**, *78*, 99; (b) Chemla, F. *Synlett* **1998**, 894.