## **RSC** Advances

## COMMUNICATION

View Article Online View Journal

## Homogeneous catalytic hydrogenation of perfluoro methyl esters<sup>†</sup>‡

Cite this: DOI: 10.1039/c3ra43410a

Received 5th July 2013, Accepted 8th July 2013 Dario Lazzari,\*<sup>a</sup> Maria Cristina Cassani,\*<sup>b</sup> Maurizio Bertola,<sup>a</sup> Francisco Casado Moreno<sup>a</sup> and Damiano Torrente<sup>a</sup>

DOI: 10.1039/c3ra43410a

www.rsc.org/advances

The first example of perfluoroalkyl methyl ester  $R_fC(O)OMe$  ( $R_f = C_3F_7$ ,  $C_5F_{11}$ ) reduction by homogeneous catalytic hydrogenation with the ruthenium catalyst Ru-MACHO<sup>TM</sup> is herein reported. The hydrogenation process leads to the corresponding perfluorinated alcohols thus replacing sodium borohydride that has so far represented the state of art in perfluoro ester reduction.

The existing concern towards long perfluorinated alkyl chains owing to their bioaccumulation, toxicity and environmental persistence is making more and more important the availability of fluorinated building blocks with shorter perfluorinated carbon chains. In general, the reduction of the perfluorinated chain lengths on one hand decreases the toxicity and bioaccumulation potential but, on the other, leads to inferior performances in the applications where a large content of fluorine atoms is mandatory. Therefore, the synthetic strategies adopted by academic and industrial research groups working in this field are not simply consisting in a shortening of the fluorocarbon chains but also include a complete molecule redesign and a common approach is to replace a single long chain with branched structures containing short fluorocarbon alkyl groups.<sup>1</sup> In this context the need for short fluorinated alcohols is becoming a pressing request for several industries in the development of new fluorinated additives, surfactants and reagents for surface treatment.<sup>2</sup> While a telomerisation approach delivers only alcohols with an even number of carbon atoms, alcohols with an odd number of fluorinated carbons can be synthesised *via* reduction of perfluor-oesters.

The production of fluorinated alcohols of the type  $R_fCH_2OH$ where  $R_f = C_3F_7$  and  $C_5F_{11}$  is part of the core competence of Miteni S.p.A.<sup>3</sup> They are obtained from reduction of the corresponding perfluoro methyl esters whose preparation is depicted in Scheme 1. In the first step the butanoyl and hexanoyl chlorides undergo an halide exchange with anhydrous HF, then, by Electrochemical Fluorination (ECF),<sup>4</sup> the acyl fluorides are transformed in the perfluoro acyl derivatives  $CF_3(CF_2)_nC(O)F$ (under n.c.: n = 2, gas; n = 4 liquid) that after methanolysis leads to the formation of the perfluoromethyl esters.

The traditional method reported in the literature for the reduction of perfluoro esters to alcohols of formula  $R_fCH_2OH$  is based on the use of  $NaBH_4$ .<sup>5</sup> The yields of hydrogenation are in the range of 80%, and although sodium borohydride is a versatile reagent, its hazardous nature, complex postreaction workup procedures, and high level of residual waste are matters of concern in industrial operations. Moreover the postreaction

Table 1 Reduction of C<sub>3</sub>F<sub>7</sub>C(O)OMe<sup>a</sup>

Entry	$T/^{\circ}\mathbf{C}$	$pH_2$ (bar)	Cat. (mol%)	Yield <sup>b</sup>	TON
1	40	10	0.1	99	990
2	40	10	0.05	89	1780
3	40	10	0.045	65	1444
4	20	10	0.05	17	340
5	60	10	0.05	97	1940
6	60	10	0.025	89	3560
7	60	10	0.0125	74	5920
8	60	10	0.005	46	9200
9	80	10	0.0125	66	5280
$10^c$	100	30	0.05	_	_
$11^d$	50	10	0.005	43	8600
$12^e$	60	10	0.005	36	7200

<sup>*a*</sup> Reaction conditions: MeOH,  $pH_2 = 10$  bar, 23 h, ester/NaOCH<sub>3</sub> molar ratio = 0.25, in a 100 mL autoclave. <sup>*b*</sup> Determined by GC analysis (internal standard: decane). <sup>*c*</sup>  $pH_2 = 30$  bar, 5 h. <sup>*d*</sup> Perfluorobutanol. <sup>*e*</sup> Isopropyl alcohol.

<sup>&</sup>lt;sup>a</sup>Miteni S.p.A., Località Colombara 91, I-36070 Trissino (VI), Italy.

E-mail: dario.lazzari@miteni.com; Fax: +39 0445 499507; Tel: +39 0445 499560 <sup>b</sup>Dipartimento di Chimica Industriale "Toso Montanari", Viale Risorgimento 4, I-40136 Bologna, Italy. E-mail: maria.cassani@unibo.it; Fax: +39 051 2093694; Tel: +39 0512093700

<sup>&</sup>lt;sup>†</sup> Electronic supplementary information (ESI) available: Experimental details, characterisation data, <sup>1</sup>H and <sup>13</sup>C NMR spectra. See DOI: 10.1039/c3ra43410a

<sup>‡</sup> Typical procedure for hydrogenation of a perfluorinated methyl ester in methanol (Table 1, entry 6): a 100-mL stainless steel autoclave equipped with a Teflon-coated stirring bar and previously filled with nitrogen (three purging cycles) was charged with methanol (7.0 g, 0.22 mol), NaOCH<sub>3</sub> (0.62 g, 0.011 mol),  $C_3F_7C(O)OMe$  (10.0 g, 0.044 mol) and Ru-Macho (0.007 g, 0,011 mmol). The autoclave was closed and purged three times with nitrogen. Successively the vessel was purged three times with hydrogen gas then the mixture was stirred (500 rpm), heated up to 60 °C and pressurized with hydrogen (10 bar). After stirring for 23 h, the system was cooled to 25 °C, and then the hydrogen gas released. The mixture was analyzed by GC.



workup generates boric acid and borates that according to the IUCLID Dataset published by the European Commission, in high doses show significant developmental toxicity and teratogenicity in rabbits, rats, and mouse fetuses as well as cardiovascular defects, skeletal variations, mild kidney lesions.<sup>6,7</sup>

Replacing hydride reductions with hydrogenations enables companies to implement simple and convenient processes. For this purpose, catalysts which work under mild conditions would have significant industrial advantages. The catalytic hydrogenation of perfluoroalkyl esters to fluoroalkyl alcohols is a very exotic research area and to the best of our knowledge very few examples have been recently reported on this topic.<sup>8</sup> In particular in the hydrogenation ( $pH_2 = 50$  bar, 140 °C, 24 h) of CF<sub>3</sub>(CF<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>Me reported by Clarke *et al.*, the ruthenium catalyst bearing a chiral tridendate amine functionalized phosphine (0.5%) must be activated by a three-fold excess (1.5%) of LiHBEt<sub>3</sub>.<sup>8a</sup>

Our first attempts were done carrying out the hydrogenation reaction under heterogeneous conditions: several systems such as Pd, Pt and Ru on a variety of supports (activated carbon, alumina, titania) were tested with, at least under relatively harsh experimental conditions, negligible or no results.§ In view of these findings we have therefore decided to focus our efforts on homogenous catalytic hydrogenation and we considered the ruthenium(II) tri-chelated complex carbonylchlorohydrido[bis(2-(diphenylphosphinoethyl)amino]ruthenium(II), a commercial catalyst known as Ru-MACHO produced in bulk by the Takasago Company. This catalyst is active in the hydrogenation of esters<sup>9</sup> although no information were available regarding his activity in the hydrogenation of perfluorinated methyl esters. The hydrogenation of fully fluorinated methyl esters  $CF_3(CF_2)_n C(O)OMe$  (n = 2,  $R_f = C_3F_7$ ; n = 4,  $R_f = C_5F_{11}$ ) was carried out in autoclave† under a variety of reaction conditions in the presence of Ru-MACHO and NaOMe in methanol (Scheme 2).

A set of catalytic entries have been proposed with the aim of investigating the influence of the catalyst loading, solvent, temperature and reaction set-up on the reaction output. Table 1 summarizes the results collected by varying the catalyst loading, temperature and solvents for the reduction of  $C_3F_7C(O)OMe$ . The reduction carried out in methanol at 40 °C,  $pH_2 = 10$  bar using a cat. loading of 0.1 mol% led to the formation of alcohol with a 99% yield (GC, IS)† in an highly reproducible manner (entry 1).



Scheme 2 Hydrogenation of perfluorinated methyl esters with Ru-MACHO.

By decreasing the catalyst loading by half (0.05 mol%) the yields decreases of *ca.* 10% but the TON is nearly doubled whilst a further reduction of the cat. loading leads to a significant decrease of the yield (entries 2 and 3 respectively). The reaction temperature also has a significant influence as demonstrated in the entries 4 to 10 with the optimal working conditions temperatures found at 60 °C and turn over frequencies higher than those generally reported for this catalyst.<sup>9b</sup> At higher temperature we observed a drastic reduction of the catalyst performances even in the presence of an H<sub>2</sub> pressure of 30 bar (entry 10). We also performed the hydrogenation in different solvents such perfluorobutanol (PFB) and isopropanol alcohol (IPA) (entries 11, 12) with similar results whilst in THF we constantly observed a significantly lower catalytic activity (data not reported).

The reduction of  $C_5F_{11}C(O)OMe$ , carried out in the same conditions ( $pH_2 = 10$  bar), led to the corresponding alcohol although in lower yields. Contrary to what observed in the previous case, we found that the hydrogenation reaction is particularly sensitive to the ester/NaOMe molar ratio. As shown in Table 2 entry 1, when the hydrogenation is carried out at 40 °C with a cat. loading of 0.05 mol% and an ester/NaOMe molar ratio equal to 0.25 the alcohol is obtained with just a 10% yield that raises to nearly 50% when the ester/NaOMe molar ratio is doubled.

Once again we found that the reaction temperature has a significant impact on the final outcome (entry 6) with the best conditions found in the temperature range 40–60  $^{\circ}$ C as described in entries 3 and 4.

Table 2 Reduction of C<sub>5</sub>F<sub>11</sub>C(O)OMe<sup>a</sup>

Entry	$T/^{\circ}\mathbf{C}$	Cat. (mol%)	ester/NaOMe molar ratio	Yield <sup>b</sup>	TON
1	40	0.05	1/0.05	10	200
1	40	0.05	1/0.25	10	200
2	40	0.05	1/0.50	48	960
3	40	0.065	1/0.50	81	1246
4	60	0.075	1/0.50	86	1146
5	60	0.041	1/0.50	9	220
6	80	0.059	1/0.50	17	288

<sup>*a*</sup> Reaction conditions: MeOH,  $pH_2 = 10$  bar, 23 h, in a 100 mL autoclave. <sup>*b*</sup> Determined by GC analysis (internal standard: decane).

Communication

In conclusion, in this communication we have shown that the ruthenium catalyst Ru-MACHO is an active catalyst for the hydrogenation of perfluorinated methyl esters under *very mild* conditions and represents a valid alternative to the use of metal hydrides.

M.C.C. wishes to thank the University of Bologna and the Ministero dell'Università e della Ricerca (MUR) (project: "New strategies for the control of reactions: interactions of molecular fragments with metallic sites in unconventional species", PRIN 2007) for financial support.

## Notes and references

 $\$  Under the following conditions: 10% Ru on Carbon with hydrogen pressures up to 50 bar and temperature up to 120  $^\circ$ C a 1% conversion (GC) was observed.

- (a) P. Kirsch, Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications, Wiley-VCH, Verlag, 2nd edn, 2013; (b)
  R. Berger, G. Resnati, P. Metrangolo, E. Weber and J. Hulliger, Chem. Soc. Rev., 2011, 40, 3496; (c) W. R. Dolbier Jr., J. Fluorine Chem., 2005, 126, 157; (d) M. Cametti, B. Crousse, P. Metrangolo, R. Milani and G. Resnati, Chem. Soc. Rev., 2012, 41, 31; (e) J.-M. Vincent, Chem. Commun., 2012, 48, 11382.
- 2 (a) S. Schellenberger, J. Pahnke, R. Friedrich and G. Jonschker, *Europ. Coat. Jnl.*, 2012, 11, 32; (b) R. J. Farn, *Chemistry and Technology of Surfactants*, Blackwell Publishing, 2006, pp. 228–229; (c) A. Rao, Y. Kim, C. M. Kausch, V. M. Russell and R. R. Thomas, *Langmuir*, 2006, 22, 4811.
- 3 Miteni S.p.A. (http://www.miteni.com) is part of I.C.I.G. (International Chemical Investors Group, http://www. ic-investors.com/) an industrial group composed of 19 chemical companies, operating worldwide in base chemicals, fine chemicals and polymers.
- 4 (a) J. H. Simons, *Fluorine Chemistry*, ed. J. H. Simons, Academic Press, New York, 1950, vol. 1; (b) S. Nagase, *Fluorine Chem. Rev.*,

1967, 1, 77; (c) G. Siegemund, W. Schwertfeger, A. Feiring, B. Smart, F. Behr, H. Vogel and B. McKusick, *Fluorine Compounds, Organic in Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, 2005; (d) F. G. Drakesmith, *Electrofluorination of Organic Compounds, Topics in Current Chemistry*, Springer, Berlin-Heidelberg, 1997, vol. 193; (e) J. H. Simons, *J. Electrochem. Soc.*, 1949, **95**, 47; (f) L. Conte and G. P. Gambaretto, *J. Fluorine Chem.*, 2004, **125**, 139.

- 5 (a) W. V. Childs, Phillips Petroleum Company, US 4,156,791, 1979; (b) S. A. Fontana, C. A. P. Tonelli and P. Gavezotti, Solvay Specialty Polymers Italy S.p.A., WO 2012168156, 2012; (c) R. D. Chambers, *Fluorine in Organic Chemistry*, Blackwell Publishing, 2004.
- 6 (a) European Chemicals Bureau; IUCLID Dataset, Boric acid (10043-35-3) (2000 CD-ROM edition). Available from: http://esis.jrc.ec.europa.eu/; (b) Y. Ishii, N. Fujizuka, T. Takahashi, K. Shimizu, A. Tuchida, S. Yano, T. Naruse and T. Chishiro, *Clin. Toxicol.*, 1993, 31, 345; (c) A. Restuccio, M. E. Mortensen and M. T. Kelley, *Am. J. Emerg. Med.*, 1992, 10, 545.
- 7 In August 2008, the EU decided to amend its classification as reprotoxic category 2 and to apply the risk phrases R60 (may impair fertility) and R61 (may cause harm to the unborn child).
- 8 (a) M. L. Clarke, M. B. Diaz-Valenzuela and A. M. Z. Slawin, Organometallics, 2007, 26, 16; (b) A. Ishii, T. Ootsuka, M. Imamura, T. Nishimiya and K. Kimura, WO 2013018573, 2013, in Japanese; (c) A. Ishii, T. Ootsuka, T. Ishimaru and M. Imamura, WO 2012105431, 2012, in Japanese.
- 9 (*a*) W. Kuriyama, T. Matsumoto, Y. Ino, O. Ogata and N. Saeki, Takasago Int. Co., WO 2011048727, 2011; (*b*) W. Kuriyama, T. Matsumoto, O. Ogata, Y. Ino, K. Aoki, S. Tanaka, K. Ishida, T. Kobayashi, N. Sayo and T. Saito, *Org. Process Res. Dev.*, 2012, 16, 166; (*c*) D. Spasyuk, S. Smith and D. G. Gusev, *Angew. Chem., Int. Ed.*, 2012, 51, 2772; (*d*) Z. Han, L. Rong, J. Wu, L. Zhang, Z. Wang and K. Ding, *Angew. Chem., Int. Ed.*, 2012, 51, 13041; (*e*) D. Spasyuk, S. Smith and d. G. Gusev, *Angew. Chem., Int. Ed.*, 2013, 52, 2538.