



A facile method for the preparation of hexafluoroisopropanol functionalized derivatives using hexafluoroacetone trihydrate via a carbonyl-ene reaction

Madabhushi Sridhar^{a,*}, Chinthala Narsaiah^a, Beeram C. Ramanaiah^a, Vishnu M. Ankathi^a,
Rajesh B. Pawar^b, Shrinandan N. Asthana^b

^a Fluoroorganics Division, Indian Institute of Chemical Technology, Hyderabad 500 007, India

^b High Energy Materials Research Laboratory, Sutarwadi, Pune 411 021, India

ARTICLE INFO

Article history:

Received 30 October 2008

Revised 8 December 2008

Accepted 11 December 2008

Available online 16 December 2008

Keywords:

Hexafluoroisopropanol functionalized derivatives

Carbonyl-ene reaction

Alkenes

Hexafluoroacetone trihydrate

Molecular sieves

Microwave reaction

ABSTRACT

Hexafluoroacetone trihydrate was shown to undergo an efficient carbonyl-ene reaction with a variety of alkenes in the presence of molecular sieves under microwave heating and conventional heating producing hexafluoroisopropanol functionalized derivatives in high yields.

© 2009 Published by Elsevier Ltd.

Hexafluoroisopropanol (HFIP) functionality is a very strong hydrogen bond donor,¹ and molecules appended with this group often exhibit interesting properties.² Hexafluoroisopropanol functionalized derivatives are widely in use in micro electromechanical system (MEMS)-based chemical sensors,³ chemical preconcentrators for micro analytical detection techniques⁴ and analytical and purification applications.⁵

In addition, these compounds are also useful as chemical amplification resists for 157 nm lithography,⁶ and as pharmaceuticals.⁷

One of the general methods for the preparation of HFIP functionalized derivatives is the carbonyl-ene reaction of anhydrous hexafluoroacetone (AHFA) with an alkene having allylic hydrogens. However, this method has the following drawbacks: AHFA is a highly toxic gas (bp $-26\text{ }^{\circ}\text{C}$) and is expensive; yields are often very low and form a mixture of products; and special equipment is required for handling AHFA. Because of these disadvantages, the development of a more simple and convenient alternative approach for this reaction is desired.

Hexafluoroacetone trihydrate (HFAT) is a widely available and inexpensive chemical. Since HFAT is a liquid (bp $106\text{--}108\text{ }^{\circ}\text{C}$) at room temperature, it is highly convenient for handling and storage.

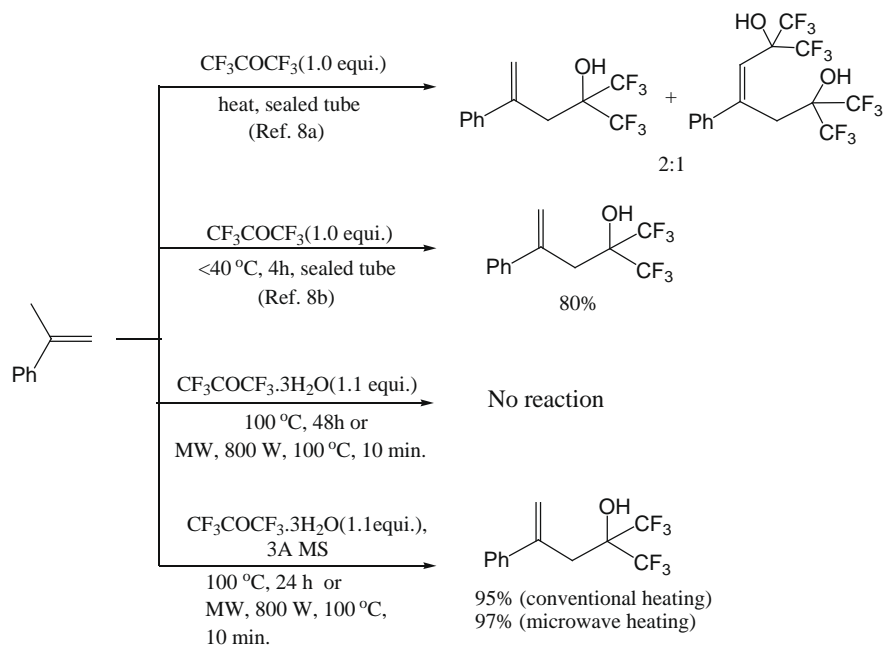
Unlike AHFA, HFAT is highly unreactive with alkenes and its carbonyl-ene reactions are not known in the literature.

In the course of our recently initiated activity on the development of novel HFIP functionalized derivatives for sensor applications, we discovered that HFAT also gives an efficient carbonyl-ene reaction with alkenes having allylic hydrogens upon heating in the presence of a solid such as molecular sieves, silica gel or alumina, giving HFIP functionalized derivatives in high yields. The results of the typical carbonyl-ene reactions of AHFA and HFAT with α -methylstyrene are shown in Scheme 1.

AHFA is a strong electrophile and the mechanism of its carbonyl-ene reaction was known to involve a four-member, cyclic dipolar addition transition state.^{8b} HFAT is, however, not a strong electrophile and the mechanism of its carbonyl-ene reaction is not clear. In a control experiment, no AHFA was generated when HFAT was heated with molecular sieves. This shows that the involvement of AHFA in the formation of observed products in the present study is a remote possibility.

The carbonyl-ene reaction of HFAT with α -methylstyrene was studied with a variety of solids such as molecular sieves (3 Å, 4 Å and 5 Å MS), silica gel, alumina, calcium oxide and montmorillonite K10 clay and also with water-tolerant Lewis acid catalysts, namely, La(OTf)₃, Eu(OTf)₃, Gd(OTf)₃ and Yb(OTf)₃, under microwave heating (800W, $100\text{ }^{\circ}\text{C}$, 10 min). In this study, molecular

* Corresponding author. Tel.: +91 40 2719 1891; fax: +91 40 2716 0387.
E-mail address: smiict@iict.res.in (M. Sridhar).



Scheme 1.

Table 1
Solid surface mediated carbonyl-ene reaction of hexafluoroacetone trihydrate with α -methylstyrene

S. no.	Solid catalyst	Isolated yield of HFA adduct
1	3 Å MS ^a	92
2	4 Å MS ^a	82
3	5 Å MS ^a	79
4	Silica gel	75
5	Alumina	57
6	CaO	No reaction
7	K10 clay ^b	0
8	Ln(OTf) ₃ ^b Ln = La, Eu, Gd, Yb	0

^a Powder.

^b Only oligomers of α -methylstyrene were obtained.

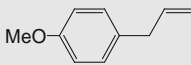
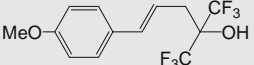

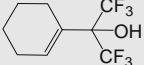
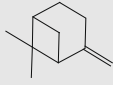
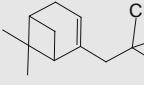
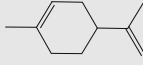
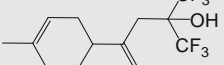

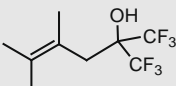
sieves (3 Å, 4 Å and 5 Å MS) and silica gel were found to be highly promising in promoting the reaction and alumina was found to be moderately active. The order of efficiency of these solids in catalyzing the carbonyl-ene reaction is 3 Å MS > 4 Å MS > 5 Å MS > silica gel > alumina. Calcium oxide was found to be ineffective in catalyzing the reaction. With K10 clay and lanthanide triflates, oligomers of α -methylstyrene are essentially formed in the reaction. The representative results are shown in Table 1.

In our further study, we have investigated the carbonyl-ene reactions of HFAT with a variety of alkenes under microwave irradiation (800 W, 100 °C, 10 min) and also under conventional heating in an oil bath at 100 °C.⁹ In this study, the microwave-assisted reactions were found to proceed very rapidly (in 10 min) giving the HFIP functionalized derivatives in 62–97% yields. On the other

Table 2
Carbonyl-ene reactions of hexafluoroacetone trihydrate with alkenes

Entry	Alkene	Adduct	Conventional heating	Microwave Heating
			Yield ^a (%) (reaction time, h)	Yield ^a (%) (reaction time, min)
1			95 (24)	97 (10)
2			82 (24)	93 (10)
3			78 (24)	92 (10)
4			56 (28)	62 (10)

Table 2 (continued)

Entry	Alkene	Adduct	Conventional heating	Microwave Heating
			Yield ^a (%) (reaction time, h)	Yield ^a (%) (reaction time, min)
5			68 (28)	88 (10)
6			63 (28)	94 (10)
7			64 (28)	85 (10)
8			73 (28)	89 (10)
9			60 (28) ^b	67 (10)

^a Isolated yields. Yields are based on alkene. All products gave satisfactory ¹H NMR, IR and mass spectral data.

^b This reaction was carried out in a sealed pressure tube.

hand, the reactions under conventional heating also gave the products in comparable yields (56–95%), but the reaction times were comparatively very long (>24 h). The results obtained in this study are presented in Table 2.

In summary, the present work describes a simple, efficient and economical method for the preparation of hexafluoroisopropanol functionalized derivatives with high selectivity by a carbonyl-ene reaction of hexafluoroacetone trihydrate with alkenes having allylic hydrogens under microwave heating and also under conventional heating. This work is the first study on the carbonyl-ene reactions of hydrated hexafluoroacetone using simple solid catalysts, which are inexpensive, easily recoverable and recyclable.

Acknowledgement

C.N., B.C.R. and V.M.A. are thankful to the Director, IICT, for providing financial support in the form of project JRF.

References and notes

- (a) Maiti, N. C.; Zhu, Y.; Carmichael, I.; Serianni, S. S.; Anderson, V. E. *J. Org. Chem.* **2006**, *71*, 2878–2880; (b) Berrien, J. F.; Ourevitch, M.; Morgant, G.; Ghermani, N. E.; Crousse, B.; Bonnet-Dolphon, D. *J. Fluorine Chem.* **2007**, *128*, 839–843.
- Vuluga, D.; Legros, J.; Crousse, B.; Bonnet-Delpon, D. *Chem. Commun.* **2008**, 4954–4955.
- (a) Andrew, M.; Abraham, M. H.; Grate, J. W. *Chemtech* **1994**, 27–37; (b) Grate, J. W. U.S. Patent 5,756,631, 1998; Houser, E. J.; McGill, R. A. U.S. Patent 7,132,294, 2006.
- Voiculescu, I.; Zaghoul, M.; Narasimhan, N. *Trends Anal. Chem.* **2008**, *27*, 327–343.
- McGill, R. A. *J. Fluoropolym. Sci. Technol.* **2001**, *14*, 583–593.
- Ito, H.; Wallraff, G. M.; Fender, N.; Brock, P. J.; Larson, C. E.; Truong, H. D.; Breyta, G.; Miller, D. C.; Sherwood, M. H.; Allen, R. D. *J. Fluoropolym. Sci. Technol.* **2001**, *14*, 583–593.
- Dehmlow, H.; Kuhn, B.; Masciadri, R.; Panday, N.; Ratni, H.; Wright, M.B. U.S. Patent 7,253,282, 2005.
- (a) Urry, W. H.; Niu, J. H. Y.; Lundted, L. G. *J. Org. Chem.* **1968**, *33*, 2302–2310. and references cited therein; (b) Adelman, R. *J. Org. Chem.* **1968**, *33*, 1400–1410; (c) Kobayashi, Y.; Nagai, T.; Kumadaki, I. *Chem. Pharm. Bull.* **1984**, *32*, 5031–5035.
- Typical experimental procedure for solid surface mediated carbonyl-ene reaction of hexafluoroacetone trihydrate with alkenes under microwave heating is as follows: α -Methylstyrene (0.5 g, 4.2 mmol), hexafluoroacetone trihydrate (1.01 g, 4.6 mmol) and 3 A MS (0.5 g, powder) were taken in a 10 ml pressure tube and subjected to microwave heating (CEM discover, 800 W, 100 °C, 16 psi) for 10 min. Next, the reaction mixture was diluted with dichloromethane (5 ml) and filtered. The molecular sieves were rinsed with dichloromethane (2 × 5 ml) and the combined extracts were concentrated and purified by normal column chromatography to obtain the corresponding addition product, 1,1,1-trifluoro-4-phenyl-2-(trifluoromethyl)pent-4-ene-2-ol in the form of colourless oil (1.38 g, 97%).
Procedure for reaction under conventional heating: The reaction mixture was taken as described above into a 25 ml round-bottomed flask fitted with a condenser and a calcium chloride guard tube. The mixture was heated on an oil bath at 100 °C for 24 h and after completion of the reaction (TLC) it was extracted with dichloromethane following the procedure above. The extract was concentrated under reduced pressure. Purification of the crude by normal column chromatography afforded the corresponding addition product (1.35 g) in 97% yield. The product obtained gave the following spectral data: ¹H NMR (300 MHz, CDCl₃): δ 2.8 (1H, s, exchange with D₂O), 3.3 (2H, s), 5.38 (1H, s), 5.6 (1H, s), 7.3–7.6 (5H, m); ¹³C NMR (75 MHz, CDCl₃): δ 35.6, 121.0, 125.2, 127.0, 129.0, 130, 140.9; ¹⁹F NMR (282 MHz, CDCl₃): δ -77, IR (neat, cm⁻¹): 3540, 3061, 1628, 1494, 1447, 1393, 1207, 1149, 107, 988, 778, 669; EIMS (*m/z*, %): 284 (M⁺, 35), 221 (15), 197 (15), 177 (15), 147 (20), 128 (20), 115 (100), 103 (35), 91 (70); exact mass observed for C₁₂H₁₀F₆O: 284.065 (calcd: 284.063).