Pergamon

Tetrahedron Letters 42 (2001) 759–761

TETRAHEDRON
LETTERS

$Yb(OTf)_3/FeCl_3$ mediated facile conversion of alcohols, ketals and acid sensitive ethers into diphenylmethyl (DPM) ethers[†]

G. V. M. Sharma,* T. Rajendra Prasad and A. K. Mahalingam

Discovery Laboratory, Organic Chemistry Division III, Indian Institute of Chemical Technology, Hyderabad 500 007, India

Received 11 October 2000; revised 9 November 2000; accepted 15 November 2000

Abstract—10 mol% $Yb(OTf)_3$ or $FeCl_3$ have been developed as efficient reagents for the conversion of alcohols into diphenylmethyl (DPM) ethers. Similarly, $FeCl_3$ has also been advantageously utilised to successfully convert ketals and acid sensitive ethers into DPM ethers. © 2001 Elsevier Science Ltd. All rights reserved.

Selective and efficient protection[1] of functional groups play a prominent role in a multi-step synthesis. The triphenylmethyl, diphenylmethyl, benzyl and phenyl groups are frequently used for the protection of alcohol, amino and carboxylic acid functional groups. The diphenylmethyl (DPM) group was found as a part structure in a few New Chemical Entities (NCEs)[2] showing therapeutic activity. Conventionally DPM protection is carried out by using DPMCl or DPMBr in the presence of base,[3] DPM diazomethane, tri-DPM phosphate–trifluoroacetic acid[4] or diphenylmethanol in the presence of conc. H_2SO_4.[5] The disadvantages encountered with the existing methods include compatibility towards acid and base sensitive groups. Hence, there is still a need to identify new reagents and better methods for the preparation of DPM ethers. In continuation of our interest in the development of new reagents[6] and new methods[7–10] for masking and unmasking functional groups, herein, we describe our results on the use of diphenylmethanol (A) in the presence of $Yb(OTf)_3$ or $FeCl_3$ for the conversion of alcohols, and $FeCl_3$ mediated one-pot conversion of ketals and acid sensitive ethers, into DPM ethers (Eq. (1)).

$$\mathrm{ROH} \xrightarrow[\mathrm{Yb(OTf)_3/FeCl_3\ (10\ mol\%),\ CH_2Cl_2}]{\mathrm{Ph_2CHOH\ (\mathbf{A})}} \mathrm{RODPM} \qquad (1)$$

Initially, alcohol **1** was subjected to reaction with A and 10 mol% $Yb(OTf)_3$ in CH_2Cl_2 at room temperature for 0.5 h to give **1a** in 87% yield. Similarly, $FeCl_3$ (10 mol%) also induced the formation of ether **1a** in 88% yield in 0.5 h from **1**. Having established 10 mol% $Yb(OTf)_3$ and $FeCl_3$ as efficient reagents for the conversion of alcohols into DPM ethers, the protocol was extended to a variety of alcohols (Table 1). Unlike the case of **1**, the alcohol group in **2**, containing acid sensitive acetonides, on reaction with $FeCl_3$ gave **2a** in 86% yield, while $Yb(OTf)_3$ gave **2a** in 92% yield. Likewise, the secondary alcohol group in menthol (**3**) gave **3a** in 88 and 86% yields with $FeCl_3$ and $Yb(OTf)_3$, respectively. Alcohol **4** underwent facile protection with $Yb(OTf)_3$ to give the DPM ether **4a** (80%) in 0.5 h, which indicates that the acid sensitive acetonide in **4** can withstand the reaction conditions. However, with $FeCl_3$ compound **4** underwent deprotection and gave a complex mixture of products.

Selective etherification of symmetrical diol **5** with $FeCl_3$ afforded the mono protected ether **5a** (60%) along with di-ether **5b** (20%). Similarly, reaction of the unsymmetrical diol in **6** with $FeCl_3$ furnished **6a** (60%) and **6b** (20%); however, a better selectivity was observed with $Yb(OTf)_3$ where **6a** was obtained in 78% yield with a decrease in the formation of di-ether **6b** (10%).

After establishing $Yb(OTf)_3$ and $FeCl_3$ as two new and better reagents for the conversion of alcohols into DPM ethers, $FeCl_3$ has been advantageously utilised for the one-pot preparation of DPM ethers from ketals and acid sensitive ethers. Accordingly, TBDPS ether **7** underwent desilylation and protection in 1 h to give **1a** in 81% yield, while the THP ether **8** furnished **1a** in 85% yield in 2 h. The acetonide group in ester **9** was hydrolysed and concomitantly converted into mono-ether **9a** (52%) and di-ether **9b** (14%), while the ester functionality was found to remain intact under the

---

Keywords: $Yb(OTf)_3$; $FeCl_3$; diphenylmethanol; diphenylmethyl (DPM) ethers.

* Corresponding author. E-mail: esmvee@iict.ap.nic.in

[†] IICT Communication No. 4657.

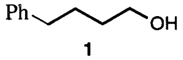
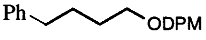
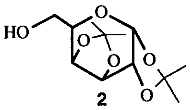
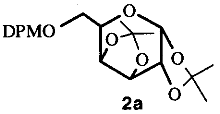
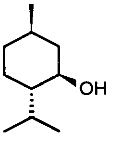
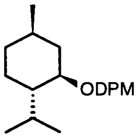
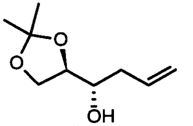
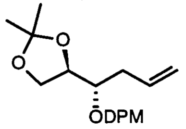
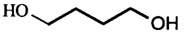
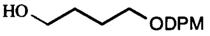
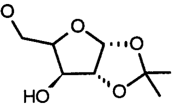
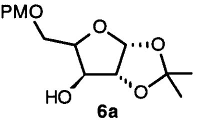
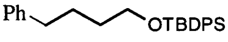
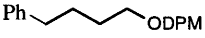
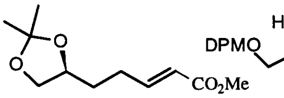
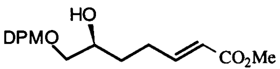
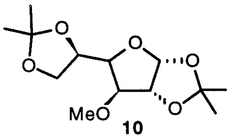
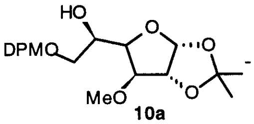
0040-4039/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(00)02108-0

reaction conditions. However, the acetonide **10** underwent facile hydrolysis and resulted in the exclusive formation of mono protected ether **10a** (72%).

Thus, in conclusion, the present protocol demonstrated that: (a) 10 mol% of $Yb(OTf)_3$ or $FeCl_3$ are efficient reagents for the conversion of alcohols into DPM ethers; (b) secondary acetonides in compounds such as **2** and **6** and ester functionality in **9** survive the $FeCl_3$ conditions; (c) $Yb(OTf)_3$ is demonstrated to be the reagent of choice and has no effect on acetonides; and (d) $FeCl_3$ has been very advantageously used for the one-pot conversion of acid sensitive substrates into DPM ethers in good yields. Thus, the present protocol, making use of diphenylmethanol instead of its derivatives, in the presence of either $Yb(OTf)_3$ or $FeCl_3$ should be of great use in synthetic chemistry, particularly in carbohydrate chemistry.

Typical experimental procedure: $FeCl_3$ method: A mixture of alcohol/ketal (1 mmol), diphenylmethanol (1 mmol) and $FeCl_3$ (0.1 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 0.5–2 h. The reaction mixture was diluted with CH_2Cl_2 (25 mL) and washed with water (2×10 mL), brine (10 mL), dried (Na_2SO_4), evaporated and the residue purified by column chro-

Table 1. $Yb(OTf)_3/FeCl_3$ mediated conversion of alcohols, ketals and acid sensitive ethers to DPM ethers

Starting materials	Products	$Yb(OTf)_3$		$FeCl_3$	
		Time(h)	Yield(%)	Time(h)	Yield(%)
 **1**	 **1a**	0.5	87	0.5	88
 **2**	 **2a**	0.5	92	0.5	86
 **3**	 **3a**	1	86	1	88
 **4**	 **4a**	0.5	80	-	-
 **5**	 **5a**	-	-	0.5	60
	5b diether				20
 **6**	 **6a**	1	78	0.75	60
	6b diether		10		20
 **7**	 **1a**	-	-	1	81
 **8**	 **1a**	-	-	2	85
 **9**	 **9a**	-	-	1.5	52
	9b diether	-	-		14
 **10**	 **10a**	-	-	1.25	72

matography (silica gel, ethyl acetate: pet. ether) to afford DPM ethers in 52–88% yields.

$Yb(OTf)_3$ method: A mixture of alcohol (1 mmol), diphenylmethanol (1 mmol) and $Yb(OTf)_3$ (0.1 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 0.5–1 h. The reaction mixture was filtered, evaporated and the residue purified by column chromatography (silica gel, ethyl acetate: pet. ether) to afford DPM ethers in 78–92% yields.

Spectral data for selected compounds: ^1H NMR (200 MHz, $CDCl_3$, TMS): **1a**: δ 1.58–1.83 (m, 4H, H-2, 2′, 3, 3′), 2.62 (t, 2H, $J=3.2$, 6.9 Hz, H-4,4′), 3.45 (t, 2H, $J=2.0$, 7.4 Hz, H-1,1′), 5.25 (s, 1H, $\mathrm{Ph_2\underline{CH}}$), 7.08–7.35 (m, 15H, ArH); FABMS: m/z 315 (M^+-1, 10%), 167 (100%), 91 (50%), 73 (45%); **3a**: δ 0.42 (d, 3H, $J=3.2$ Hz), 0.8–1.0 (m, 9H), 1.18–1.40 (m, 3H), 1.54–1.68 (m, 2H), 2.08–2.22 (m, 1H), 3.12 (dt, 1H, $J=3.7$, 10.3 Hz), 5.50 (s, 1H, $\mathrm{Ph_2\underline{CH}}$), 7.12–7.48 (m, 10H, ArH); FABMS: m/z 345 (M^++23, 18%), 321 (M^+-1, 25%), 167 (100%), 83 (18%), 69 (14%), 55 (15%); **9a**: δ 1.48–168 (m, 2H, H-5,5′), 2.24–2.44 (m, 2H, H-4,4′), 3.25–3.50 (m, 2H, H-7,7′), 3.70 (s, 3H, $-OCH_3$), 3.72–3.88 (m, 1H, H-6), 5.33 (s, 1H, $\mathrm{Ph_2\underline{CH}}$), 5.80 (d, 1H, $J=16.4$ Hz, H-2), 6.82–7.0 (m, 1H, H-3), 7.15–7.35 (m, 10H, ArH); FABMS: m/z 363 (M^++23, 10%), 339 (M^+-1, 12%), 167 (100%), 95 (25%), 81 (32%), 69 (52%), 55 (75%).

Acknowledgements

T. Rajendra Prasad and A. K. Mahalingam are thankful to CSIR, New Delhi (India), for financial support.

References

1. Greene, T. W.; Wuts, P. G. M. *Protecting Groups in Organic Synthesis*; John Wiley & Sons: New York, 1991; 2nd ed.
2. Hayashi, M.; *Drug Data Report* **1997**, 704–705 (JP 97077745).
3. Dobson, D.; Todd, A.; Gilmore, J. *Synth. Commun.* **1991**, *21*, 611–617.
4. Lapatsanis, L. *Tetrahedron Lett.* **1978**, *19*, 4697–4698.
5. Sugasawa, S.; Fujiwara, K. *Org. Synth. Coll.* **1963**, *4*, 72–73.
6. Sharma, G. V. M.; Mahalingam, A. K.; Rajendra Prasad, T. *Synlett.* **2000**, in press.
7. Sharma, G. V. M.; Ilangovan, A.; Mahalingam, A. K. *J. Org. Chem.* **1998**, *63*, 9103–9104.
8. Sharma, G. V. M.; Ilangovan, A. *Synlett.* **1999**, 1963–1965.
9. Sharma, G. V. M.; Mahalingam, A. K. *J. Org. Chem.* **1999**, *64*, 8943–8944.
10. Sharma, G. V. M.; Mahalingam, A. K.; Nagarajan, M.; Ilangovan, A.; Radha Krishna, P. *Synlett* **1999**, 1200–1202.