Pergamon

Tetrahedron Letters 43 (2002) 4593–4595

TETRAHEDRON
LETTERS

Iron-catalyzed solvent-free conversion of alcohols and phenols into diphenylmethyl (DPM) ethers[†]

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Received 27 March 2002; revised 8 May 2002; accepted 9 May 2002

Abstract—A catalytic amount of iron salts enables the solvent-free preparation of diphenylmethyl (DPM) ethers of alcohols and phenols at moderate temperatures. © 2002 Elsevier Science Ltd. All rights reserved.

The selective protection of alcohols is a common event in multi-step organic syntheses. The preparation of DPM ethers is one of the significant methods in view of their inexpensive nature and stability towards a variety of reagents.[1] Additionally, DPM ethers and DPM groups are found as a part of several pharmacologically active compounds.[2] There are several reagents available for the preparation of DPM ethers of alcohols which include the use of diphenylmethyl chloride or bromide in the presence of a base,[3] diphenylmethyl diazomethane or diphenylmethyl phosphate–trifluoroacetic acid,[4] diphenylmethanol in the presence of concentrated sulphuric[5] or *p*-toluenesulphonic acid,[6] xenon difluoride[7] and ytterbium triflate–ferric chloride ($FeCl_3$).[8] Although these methods are suitable for some synthetic operations, they require a high catalyst to substrate ratio, relatively long reaction times and involve the use of volatile organic solvents or large amounts of solid supports, which eventually result in the generation of substantial amount of wastes. Thus, there is a need for a solventless and catalytically efficient alternative for the protection of hydroxyl functionality as DPM ether. As a part of an ongoing research program to develop environmentally friendlier chemical transformations,[9] herein, we report an efficient iron-catalyzed solvent-free conversion of alcohols and phenols into DPM ethers.

The present protocol, in its entirety, simply involves mixing an alcohol or phenol with diphenylmethanol in the presence of a catalytic amount of an iron salt and warming the reaction mixture to afford the correspond-

Table 1. Catalytic effect of iron salts on the formation of DPM ether[a]

Entry	Benzhydrol (mmol)	Time (min)	Temperature (°C)	Yield % (isolated)
1	1	30	55	95
2	1	30	80	84[b]
3	10	30	55	83
4	50	60	80	48
5	100	120	80	37
6	100	120	80	41[c]
7	100	120	80	36[d]

[a] $Fe(NO_3)_3 \cdot 9H_2O$ (1 mmol).
[b] Product is benzophenone.
[c] $FeCl_3$ (1 mmol).
[d] $FeCl_2 \cdot 4H_2O$ (1 mmol).

Keywords: alcohols; phenols; diphenylmethyl ethers; iron nitrate nonahydrate; solvent-free.

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[†] Presented, in part, at the IUPAC CHEMRAWN XIV Conference on Green Chemistry: Toward Environmentally Benign Processes and Products, Boulder, Colorado, USA, 9–13 June, 2001.

PII: S0040-4039(02)00890-0

ing DPM ether. After completion of the reaction, the product is isolated by column chromatography using hexane–ethyl acetate mixture as eluent. Table 1 provides the details of DPM ether formation under various reaction conditions with benzhydrol as the substrate.[10] Longer reaction time and higher reaction temperature are required at elevated concentration of the substrates (entries 1, 3, 4 and 5). Ferrous or ferric chloride can also be used as catalysts for the preparation of ethers (entries 6 and 7). Ether preparation at a low substrate to catalyst ratio is preferable at a temperature ideally around 55°C, which prevents or reduces iron nitrate-catalyzed oxidation of alcohol to carbonyl compounds (entry 2).

A variety of hydroxylated compounds are converted to the corresponding DPM ethers via this procedure using $Fe(NO_3)_3 \cdot 9H_2O$ and the results are summarized in Table 2. The reactions are reasonably fast and the order of reactivity for various alcohols is, primary>secondary>tertiary. In the case of reactive alcohols such as benzylic or primary alcohols or phenols, the DPM ethers are formed in good yields with only a trace amount (<5%) of formation of self-condensed ether of diphenylmethanol,[10] which increases in amount for less reactive substrates, e.g. secondary alcohols (entry 3, Table 2) and *t*-butanol (entry 7, Table 2). Also, relatively higher temperatures or longer reaction times are required for solid alcohols.

The chemoselective feature of this solvent-free method is an attractive attribute as the ease of formation of diphenylmethyl ether of primary alcohols is more pronounced when compared to secondary or tertiary alcohols.

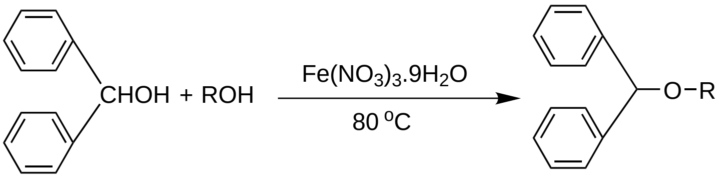
The preparation of DPM ether of benzyl alcohol is representative of the general procedure employed: iron(III) nitrate nonahydrate (1 mmol), diphenyl methanol (50 mmol) and benzyl alcohol (55 mmol) were mixed in a 50 mL round bottomed flask and stirred at 80°C. The progress of the reaction was monitored by TLC and GC–MS and upon completion of the reaction the product was purified via column chromatography using eluent, hexane–ethyl acetate (10:1 to 1:1) to afford pure product (89%). All the DPM ethers are known compounds and were characterized by spectral analyses (GC and NMR).

In conclusion, the present method describes an efficient and practical alternative to the preparation of DPM ethers of alcohols that, in contrast to most of the existing protocols, does not require any solvent or solid support or the use of distilled and/or dry reagents, and consequently minimizes the generation of toxic waste. The major advantages of this methodology are mild reaction conditions and faster reaction rates with high substrate to catalyst ratio. We believe this method will find useful application for the preparation of DPM ethers.

Acknowledgements

V.V.N. is a postgraduate research participant at the National Risk Management Research Laboratory administered by the Oak Ridge Institute for Science and Education through an interagency agreement between the US Department of Energy and the US Environmental Protection Agency.

Table 2. Iron-catalyzed preparation of diphenylmethyl ethers from alcohols[a]



Entry	Alcohol	Time (h)	Temperature (°C)	Yields % (isolated)
1	Methanol	1	70	88
2	1-Hexanol	2	80	85
3	3-Hexanol	4	80	39
4	Cyclohexanol	3	80	43
5	Cyclohexylmethanol	2	80	83
6	Phenol	2	80	71
7	*tert*-Butanol	2	80	<5
8	3-Methyl-2-butene-1-ol	2	80	76
9	Benzyl alcohol	1	80	89
10	4-Fluorobenzyl alcohol	1	80	90
11	2-Chlorobenzyl alcohol	1	80	87
12	3-Chlorobenzyl alcohol	1	80	75
13	4-Chlorobenzyl alcohol	1	80	90
14	Benzyl alcohol	1	80	88[b]

[a] $Fe(NO_3)_3 \cdot 9H_2O$ (1 mmol), diphenylmethanol (50 mmol) and alcohol (55 mmol).

[b] Ferrous chloride (1 mmol) is used as the catalyst.

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10. Dibenzhydryl ether: mp 106.5–107°C (lit. mp 107–107.5);[4a] ^{1}H NMR (250 MHz; $CDCl_3$, TMS), δ_H: 5.39 (s, Ph$\underline{C}$H), 7.2–7.37 (m, Ph); ^{13}C NMR δ_C 80.11, 127.36, 128.46, 142.30.