

ReBr(CO)₅ a good catalyst to prepare diphenylmethyl (DPM) ethers

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Abstract: Highly efficient Rhenium (I)-catalyzed C-O bond formation from the dehydration of primary benzyl and aliphatic alcohols. The reaction affords unsymmetrical benzyl ethers in good yield with high selectivity.

Keywords: Lewis acid, Benzylic alcohols, Williamson reaction, Ether formation.

Introduction

The development of efficient and practically useful Lewis acid catalysts for various organic transformations is of great importance [1]. Among these, dehydrative reactions can be used for a wide variety of transformations including etherifications, esterifications and especially protecting applications [2]. In other hand the correct choice of an efficient protecting group is often decisive for the completion of the successful synthesis of a complex molecule, for which the strategy should take into account the different requirements that are present in the molecule. Protection of a hydroxyl functionality as the benzyl ether is preferred as a permanent protective group.

Ether formation is an important reaction in organic synthesis, for both bulk and fine chemicals preparation. Generally, this route is more environmentally friendly than classical methods (Williamson and Ullmann) as the only byproduct is water, whereas the use of strongly basic alkoxides or phenoxides with alkyl or aryl halides in the Williamson method produces considerable amounts of salt byproducts. In fact alcohols are attractive electrophiles as they are cheap and readily available.

However, the cleavage of oxygen-carbon bonds poses a great challenge in organic chemistry, demanding harsh conditions due to the fact that hydroxide ions are poor leaving groups. In etherification reactions, a wide variety of catalysts have been employed including alumina, [3-4] phase transfer catalysts, [5-6] Lewis acids, [7-9] and several transition metal complexes [10-12]. However, many of these procedures require elevated temperatures or long reaction times. Thus, the introduction of a new and efficient method for this transformation under more convenient and general conditions would be welcome. Among these catalysts, Re compounds have a special position [13-14]. High-valent Rhenium complexes have been found to be efficient catalysts in catalytic organic synthesis. It should be noted that dehydrative etherification of benzylic alcohols has been investigated to a lesser extent than phenols, however, such catalytic reactions could be useful in synthetic chemistry, e.g. for protecting alcohols [15-23].

Results and discussion

Benzyl type protecting groups are among the most commonly used, due to their deprotection conditions orthogonal to other protecting and functional groups, and they have been applied to the protection of

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alcohols, thiols, amines, and acids. Diphenylmethanol protecting group is one of the important in this area [24-26]. In a recent paper, it has been reported that ReBrCO_5 was, among various metal Lewis acids, the best catalyst for the protection of alcohols as DPM ethers. In this letter, we would like to report on the

extension use of a heterogeneous ReBrCO_5 catalyst diphenylmethanol. We use the optimization condition of previous research again [27].

With old procedure in hand, we then evaluated its scope, focusing our attention to the other alcohols (Table 1).

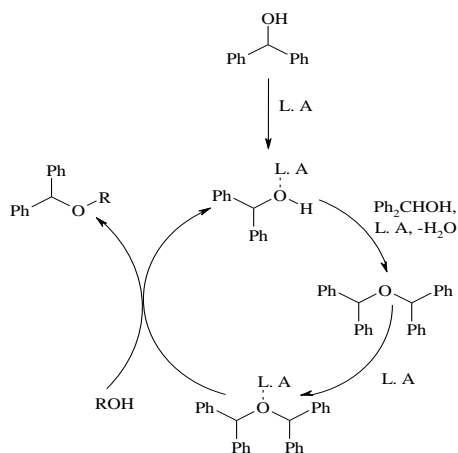
Table 1: Scope of the ReBrCO_5 catalyzed DPM ether formation^a.

Entry	ROH	Yield%	Product
a		95 ^a	
b		94	
c		93	
d		89	
e		90	
f		95	
g		91	

a: Yields are for isolated products

Mechanistic consideration:

According to the information available in the literature [28-29], It was found that all these reactions proceed via the symmetrical ether and the follow mechanism can be proposed (Scheme 1).



Scheme 1: Proposed mechanism for the Re (I) catalyzed substitution reaction of benzylic alcohols.

Conclusion

We have described effective Re (I) - catalyzed method for the synthesis of unsymmetrical ethers from alcohols. The results show that secondary benzylic alcohols can be efficiently mixed with primary and secondary aliphatic alcohols to provide the corresponding ethers in good to excellent yields. The use of a moderate excess of aliphatic alcohol allows the unsymmetrical ether to be prepared with a good yield and with no formation of the symmetrical ether. In addition, the water that builds up in the reaction does not compete as a hydroxylic reagent with the aliphatic alcohol, thus allowing a good conversion without the

use of dehydrating agents. As far as we are aware, the reaction developed herein represents is one of the few examples in which an alcohol acts as an electrophile in Rhenium chemistry.

Experimental

All compounds were obtained from *Sigma Aldrich* and used without further purification, uncorrected. ^1H , ^{13}C NMR spectra were recorded with a 300 MHz spectrometer; δ in ppm, J in Hz. Elemental analyses (C, H, N): *Heraeus CHN-O-Rapid* analyzer.

General procedure for the synthesis of compounds **3**:

A well dried round flask was charged with the catalyst, the substrate (1 mmol) was added and the flask was purged with nitrogen for 1 minute, then the nucleophile (8 mmol), and DCE (5 ml) were added. Then heated at 80 ° C for 8 hours. The solvent was removed under reduced pressure and the residue was separated by flash silica gel (Merck 230–400 mesh) column chromatography using *n*-hexane–EtOAc (7:1) mixture as eluent to get pure product **3**.

1-[(allyloxy)(phenyl)methyl]benzen (**3a**) [30]:

Colorless oil, 0.213 g, yield 95%. Anal Calcd. For $\text{C}_{16}\text{H}_{16}\text{O}$ (224.30): C, 85.68; H, 7.18; Found: C, 85.60; H, 7.12 %. ^1H NMR: 3.89 (2 H, d, $^3J = 3.5$ Hz, O-CH₂), 5.35 (2 H, m, =CH₂), 5.52 [1 H, s, O-CH (Ph₂)], 6.2 (1 H, m, O-CH=C), 7.25-7.42 (10 H, m, 10 CH); ^{13}C NMR: 70.1 (O-CH), 82.9 [O-CH(Ph₂)], 117.6 (CH), 120.6 (CH₂), 127.9 (4 CH), 129.1 (CH), 129.4 (4 CH), 142.0 (2 C).

1-[phenyl(propoxy)methyl]benzen (**3b**):

Colorless oil, 0.212 g, yield 94%. Anal. Calc. For $\text{C}_{16}\text{H}_{18}\text{O}$ (226.32): C, 84.91; H, 8.02; found: C, 85.3; H, 8.18. ^1H NMR: 1.0 (3 H, t, $^3J = 7.1$, CH₃), 1.55-1.62 (2 H, m, CH₂), 3.54 (2 H, t, $^3J = 6.5$, O-CH₂), 5.30 [1 H, s, O-CH (Ph₂)], 7.21-7.45 (10 H, m, 10 CH). ^{13}C -NMR: 14.2 (CH₃), 19.1 (CH₂), 69.2 (O-CH₂), 78.9 [O-CH (Ph₂)], 127.2 (4 CH), 127.6 (4 CH), 128.6 (2 CH), 143.0 (2 C).

1-[isopropoxy(phenyl)methyl]benzen (**3c**) [31]:

Colorless oil, 0.210 g, yield 93%. Anal Calcd. For $\text{C}_{16}\text{H}_{18}\text{O}$ (226.32): C, 84.91; H 8.02; Found: C, 84.85; H, 8.11. ^1H NMR: 1.19 (6 H, d, $J = 6$ Hz, 2 CH₃), 3.66 [1 H, hept., $J = 6$ Hz, O-CH(Me₂)], 5.39 [1 H, s, O-CH(Ph₂)], 7.25-7.45 (10H, m, 10 CH). ^{13}C -NMR: 22.9 (2 CH₃), 69.6 [O-CH(Me₂)], 80.5 [O-CH(Ph₂)], 127.7 (4 CH), 127.4 (2 CH), 128.7 (4 CH), 143.3 (2 C).

1-[butoxy(phenyl)methyl]benzene (**3d**) [27]:

Colorless oil, 0.213 g, yield 89%. Anal. Calc. For $\text{C}_{17}\text{H}_{20}\text{O}$ (240.35): C, 84.96; H, 8.39; found: C, 85.1; H, 8.25. ^1H NMR: 1.0 (3 H, t, $^3J = 7.5$, CH₃), 1.48-1.55 (2 H, m, CH₂), 1.70- 1.75 (2 H, m, CH₂), 3.54 (2 H, t, $^3J = 6.5$, O-CH₂), 5.42 [1 H, s, O-CH(Ph₂)], 7.29-7.45 (10 H, m, 10 CH). ^{13}C NMR: 14.2 (CH₃), 19.8 (CH₂), 32.3 (CH₂), 69.2 (O-CH₂), 83.9 [O-CH(Ph₂)], 127.2 (4 CH), 127.6 (4 CH), 128.6 (2 CH), 143.0 (2 C).

1-[(*z*)-3-hexenyloxy](phenyl)methyl]benzene (**3e**):

Colorless oil, 0.239 g, yield 89%. Anal Calcd. For $\text{C}_{19}\text{H}_{22}\text{O}$ (266.39): C, 85.67; H, 8.32; Found: C, 85.88; H, 8.49. ^1H NMR: 1.05 (3 H, t, $^3J = 7.3$ Hz), 1.89–2.09 (2 H, m, CH₂), 2.24–2.41 (2 H, m, CH₂), 3.54 (2 H, t, $^3J = 7.0$ Hz, O-CH₂), 5.38 [1 H, s, O-CH(Ph₂)], 5.39–5.54 (2 H, m, 2 CH), 6.86–6.93 (4 H, m, 4 CH), 7.21–7.29 (6 H, m, 6 CH). ^{13}C NMR: 14.4 (CH₃), 20.6 (CH₂), 28.1 (CH₂), 65.2 (O-CH₂), 82.8 [O-CH(Ph₂)], 113.7 (CH), 125.1 (CH), 127.7 (4 CH), 128.1 (2 CH), 134.9 (4 CH), 142.0 (2 C);

1-[benzyloxy(phenyl)methyl]benzene (**3f**) [32]:

White needles, mp 53-55 °C 0.260 g, yield 95%. Anal Calcd. For $\text{C}_{20}\text{H}_{18}\text{O}$ (274.37): C 87.56, H 6.61; Found: C, 87.69 H 6.73. ^1H NMR: 4.60 (2 H, s, O-CH₂Ph), 5.49 [1 H, s, O-CH(Ph₂)], 7.12–7.51 (15 H, m, 15 CH); ^{13}C NMR: 70.6 O-CH₂Ph), 82.6 [O-CH(Ph₂)], 127.4 (2 CH), 127.3 (4 CH), 127.8 (2 CH), 127.7 (4 CH), 128.7 (2 CH), 128.4 (CH), 138.7 (C), 142.1 (2 C).

1-[cyclopentylmethoxy](phenyl)methyl]benzene (**3g**):

colourless oil, 0.242 g, yield 91%. Anal calcd. for $\text{C}_{19}\text{H}_{22}\text{O}$ (266.39): C 85.67, H 8.32; Found: C, 85.88; H 8.45. ^1H NMR: 1.19–1.25 (4 H, m, 2 CH₂), 1.42–1.47 (4 H, m, 2 CH₂), 1.93–2.03 (1 H, m, CH), 3.57 (2 H, t, $^3J = 6.5$, O-CH₂), 5.45 [1 H, s, O-CH(Ph₂)], 6.90-7.18 (10 H, m, 10 CH). ^{13}C NMR: 27.4 (2 CH₂), 28.3 (2 CH₂), 39.8 (CH), 72.4 (O-CH₂), 83.1 [O-CH(Ph₂)], 125.3 (4 CH), 128.0 (2 CH), 129.1 (4 CH), 142.6 (2 C).

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