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# Deprotection of benzylic esters catalysed by anhydrous ferric chloride and rhenium carbonyl compounds

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**Abstract**—Anhydrous ferric chloride and $[Re(CO)_4Br]_2$ are shown to be useful reagents for the catalytic deprotection of benzylic esters. A suitable protecting group is $p$-$MeC_6H_4CH_2$ with a working temperature of 50°C for debenzylation.

Benzyl esters and -ethers are widely used as protecting groups for carboxylic acids and alcohols, respectively.[1] A common deprotection method is catalytic hydrogenolysis or transfer hydrogenation but these procedures can be problematic with certain multifunctional substrates. Therefore, a variety of alternative strategies are employed, including the use of Lewis acids, e.g. for ester deprotection, $AlCl_3$ for benzyl,[2] $p$-methoxybenzyl[3] and benzhydryl;[3] $BCl_3$ for benzyl,[4] and $BF_3$ for benzhydryl.[5] For deprotection of mono- and oligosaccharide benzyl ethers,[6c] anhydrous $FeCl_3$ has been used. Whilst the conditions for such processes are mild (e.g. from −50[3] to 40°C[5]) it should be noted that for ester[2–5] and ether[6] deprotection at least 1 mol equiv. and 8–16 mol equiv. of Lewis acid are required, respectively. There is a continuing requirement, particularly for industrial-scale processes, for methods in which the Lewis acid functions in a catalytic manner. We now illustrate the use of rhenium carbonyl species $[Re(CO)_5X; X = Cl, Br]$ and $[Re(CO)_4Br]_2$ in this context, along with a comparative study with anhydrous ferric chloride. Our interest in evaluating transition metal organometallics emanated from a report[7] of their successful application for catalytic mediation of Friedel–Crafts acylation (e.g.

**Table 1.** Deprotection of benzylic esters by rhenium carbonyl compounds and ferric chloride

| Entry | Substrate | Catalyst[a] | Reaction conditions | Yield of carboxylic acid (%) |
|---|---|---|---|---|
| 1 | $ClCH_2CO_2CH_2Ph$ | $[Re(CO)_5Cl]$[b] | Neat/160°C/3 h | Quantitative |
| 2 | $ClCH_2CO_2CH_2Ph$ | $[Re(CO)_5Br]$[b] | Decalin[c]/140°C/25 h | Quantitative |
| 3 | $ClCH_2CO_2CH_2Ph$ | $[Re(CO)_5Br]$[b] | Mesitylene[c]/130°C/2 h | Quantitative[d] |
| 4 | $ClCH_2CO_2CH_2C_6H_4Me$-$p$ | $[Re(CO)_5Br]$[b] | Mesitylene[c]/70°C/5 h | Quantitative[e] |
| 5 | $ClCH_2CO_2CH_2C_6H_4Me$-$p$ | $[Re(CO)_4Br]_2$[f] | Mesitylene[c]/50°C/24 h | Quantitative[e] |
| 6 | $PhCO_2CH_2Ph$ | $[Re(CO)_4Br]_2$[f] | Mesitylene[c]/90°C/18 h | Quantitative[d] |
| 7 | 3,5-$(O_2N)_2C_6H_4CO_2CH_2C_6H_4Me$-$p$ | $[Re(CO)_4Br]_2$[f] | Mesitylene[c]/90°C/24 h | 39[e] |
| 8 | $p$-$HOC_6H_4CO_2CH_2C_6H_4Me$-$p$ | $[Re(CO)_4Br]_2$[f] | Mesitylene[c]/90°C/72 h | 82[e] |
| 9 | 3,5-$(O_2N)_2C_6H_4CO_2CH_2C_6H_4Me$-$p$ | $FeCl_3$ | Mesitylene[c]/50°C/48 h | Quantitative |
| 10 | $p$-$HOC_6H_4CO_2CH_2C_6H_4Me$-$p$ | $FeCl_3$ | Mesitylene[c]/70°C/24 h | Quantitative |

[a] The catalyst concentration was 1 mol%.
[b] Purchased from Strem chemicals Inc.
[c] The substrate:solvent w/w ratio was ca. 1:2–4.
[d] 1,3,5-Trimethyl-2[(phenyl)methyl]benzene was also isolated, see Ref. 9.
[e] The co-products were mono, bis and tris [$p$-$MeC_6H_4CH_2$]-substituted mesitylenes in ca. 90:8:2 ratio (GC, MS and NMR analyses).
[f] See Ref. 10 for preparative procedure.

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in 0.05 mol% concentration for the reaction of toluene and benzoyl chloride).

An early experiment in this work (entry 1, Table 1) showed that benzyl chloroacetate was quantitatively deprotected by treating it with $[Re(CO)_5Cl]$ (1 mol%), albeit under forcing conditions; the product was polybenzyl $[C_6H_4CH_2]_n$ which was characterised by spectroscopic comparison (IR, $^1H$ NMR) with material prepared in our laboratory by oligomerization of benzyl alcohol in conc. $H_2SO_4$ or anhydrous HF.[8] Extensive trituration was necessary to extract oligomer-entrapped chloroacetic acid and an improved procedure is to use decalin as solvent (entry 2); in this medium, the suspension of polybenzyl was easily filtered and the carboxylic acid was isolated quantitatively after alkaline extraction.

Mesitylene was then used as a reactive solvent (cf. Ref. 2) to divert the incipient benzyl cation believed to be the source of polybenzyl. The working temperature for deprotection was not significantly decreased (entry 3), but *p*-methylbenzyl chloroacetate was quantitatively cleaved[9] by $[Re(CO)_5Br]$ and $[Re(CO)_4Br]_2$ at 70 and 50°C, respectively (entries 4 and 5); the latter bromine-bridged, binuclear compound dissociates in solution to create more readily a vacant coordination site which is believed to be necessary for catalytic activity in Friedel–Crafts reactions.[7] Dimeric $[Re(CO)_4Br]_2$ was also used to debenzylate benzyl benzoate and related esters (entries 6–8) but a higher temperature was required and the nitro group had a detrimental effect.

Having established the catalytic utility of $[Re(CO)_4Br]_2$ we then compared its behaviour with a conventional Lewis acid, viz. anhydrous ferric chloride. Surprisingly, in the light of previous accounts (see earlier) it proved to be an equally effective catalyst (1 mol%) for reactions outlined in entries 1–6 under identical conditions and more effective for those in entries 7 and 8 [quantitative deprotection at 50°C (48 h) and 70°C (24 h), respectively (see entries 9 and 10)].

A brief study of catalytic debenzylation of benzyl phenyl ether in mesitylene was conducted for comparison. Reaction was complete with anhydrous $FeCl_3$ (1 mol%) after 24 h at 50°C but very little reaction occurred using $[Re(CO)_4Br]_2$ under identical conditions.

In summary, anhydrous $FeCl_3$ and $[Re(CO)_4Br]_2$ are useful reagents for catalytic debenzylation of *p*-methylbenzyl-protected carboxylic acids. Furthermore, the latter may prove to be valuable for the selective catalytic deprotection of such esters that also contain a benzyl-protected OH group.

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9. Typical experimental procedure: benzyl chloroacetate (4.86 g, 26.0 mmol), 1,3,5-trimethylbenzene (10 mL) and bromopentacarbonylrhenium (1 mol%) were heated under a nitrogen atmosphere at 130°C for 2 h. The cooled reaction mixture was extracted with aq. $NaHCO_3$ (5×10 mL), the residual organic phase was dried ($MgSO_4$) and evaporated to afford 1,3,5-trimethyl-2[(phenyl)methyl]benzene[11] as an oil {$^1H$ NMR: $\delta$ ($CDCl_3$) 2.31 (s, 6H, 2×Me), 2.38 (s, 3H, Me), 4.12 (s, 2H, $CH_2$), 7.00 (s, 2H, Ar-H), 7.10–7.37 (m, 5H, Ar-H)}. The combined aqueous extract was acidified with dil. HCl and extracted with diethyl ether to give chloroacetic acid in quantitative yield.
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