Efficient acetylation and formylation of alcohols in the presence of $Zr(HSO_4)_4$

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Acetylation and formylation of alcohols with acetic and formic acids have been carried out in the presence of catalytic amounts of $Zr(HSO_4)_4$ under mild and heterogeneous conditions.

Keywords: acetylation, acetic acid, alcohols, formylation, formic acid, $Zr(HSO_4)_4$

The acetylation and formylation of hydroxy groups are two of the most widely used transformations in organic synthesis.[1,2] The acetylation of an alcohol is routinely carried out by acetic anhydride or acetyl chloride in the presence of pyridine or triethylamine as a catalyst.[3] In addition 4-(dimethylamino)pyridine,[4] iodine,[5] $CoCl_2$,[6] $TaCl_5$,[7] $Sn(OTf)_2$,[8] $In(OTf)_3$,[9] $Sc(OTf)_3$,[10] Bu_3P,[11] $MgBr_2$,[12] WO_3-ZrO_2,[13] $InCl_3$,[14] InI_3,[15] HBF_4-SiO_2,[16] yttria-zirconia based Lewis acid[17,18] and zirconium sulfophenyl phosphonate[19] have been applied for the acetylation of alcohols. However, some of these methods are not entirely satisfactory: triethylamine and pyridine have unpleasant odours and are not easy to remove; tributylphosphine is an irritant which is highly flammable and expensive; indium and scandium triflates are expensive catalysts; magnesium bromide gives low yields of the products over long reaction times. Therefore, introduction of new methods and catalysts for the preparation of acetates is still in demand.

Because of the possibility of the selective deprotection of a formyl group in the presence of other groups, formylation of the hydroxy group has attracted considerable attention, so that various methods and reagents have been reported for this purpose.[20-29] Although some of these methods produce good results, there are still serious limitations for the preparation of formates due to drastic reaction conditions, the use of uncommon reagents, the formation of undesirable or toxic by-products, the application of expensive catalysts for preparation of formylating agents and the thermal instability of the reagents. Due to the instability of the anhydride and acid chloride of formic acid, formylation of alcohols by formic acid is an important synthetic reaction.

In recent years there has been a tremendous upsurge of interest in chemical transformations performed under heterogeneous catalysis.[30] Moreover, using inexpensive and non-corrosive heterogeneous catalysts, chemical transformations proceed with better efficiency, higher purity of products, easier work-up and evident economic and ecological advantages, especially for industrial processes.

In our development of new methods for functional group transformations, we are especially interested in exploring the potential use of hydrogen sulfate salts.[31-33] Along these lines, we found that $Zr(HSO_4)_4$ can be used as an efficient reagent for the cleavage of C=N bonds in the presence of wet SiO_2.[34] In continuation of this study, we report the applicability of $Zr(HSO_4)_4$ in the catalytic acetylation and formylation of alcohols with acetic and formic acids under mild and heterogeneous conditions (Scheme 1).

Treatment of benzyl alcohol with CH_3CO_2H and $Zr(HSO_4)_4$ in *n*-hexane at room temperature provided the corresponding acetate in excellent yield (Table 1, entry 1). The acetylation reaction was extended to a variety of alcohols including benzylic alcohols carrying both electron-withdrawing and electron-releasing groups and aliphatic alcohols; good to high yields were obtained in all cases (Table 1).

$$R^1CO_2H + R^2OH \xrightarrow[n\text{-hexane, rt, } R^1 = H, Me]{Zr(HSO_4)_4} R^1CO_2R^2$$

Scheme 1

The formylation of alcohols with formic acid was performed in the presence of a catalytic amounts of $Zr(HSO_4)_4$ in *n*-hexane at room temperature and under completely heterogeneous conditions, to produce the desired ester in good to high yields (Table 1). Benzylic primary, hindered and unhindered secondary and sterically hindered tertiary alcohols were formylated without formation of any side products with 0.2 mol. equiv. of catalyst. It is generally known that diarylcarbinols can easily dimerise or dismutate in the presence of a Lewis acid catalyst. [35] We have observed that $Zr(HSO_4)_4$ can bring about the formylation of benzhydrol in high yields without dimerisation.

It is noteworthy that in the case of optically active alcohols the acetylation and formylation reactions proceeded well with complete retention of configuration (Table 1, entries 11, 24, 25).

To conclude, we have developed a new, efficient and excellent yielding method for the acetylation and formylation of alcohols. It should be noted that the easy and clean isolation procedure, and the high yields of the products make the proposed method attractive for large-scale applications. In addition an important point is that the reaction is heterogeneous which may be important in an industrial setting. We believe that our procedure provides an important addition to the existing methods.

Experimental

General: Chemicals were purchased from the Merck, Fluka, BDH and Aldrich Chemical Companies. $Zr(HSO_4)_4$ was synthesised by the previously reported method.[34] Products were separated and purified by different chromatography techniques, and were identified by the comparison of their mp, bp, IR, NMR and refractive index with those reported for authentic samples.[36-41] All yields refer to the isolated products. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica gel polygram SILG/UV 254 plates. Column chromatography was carried out on Merck Kieselgel 60H.

General procedure for the acetylation and formylation of alcohols: A mixture of the substrate (1 mmol), acid (1 mmol) and $Zr(HSO_4)_4$ (0.2 mmol) in *n*-hexane (5 ml) was stirred at room temperature for the specified time (Table 1). The reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the solid residue was washed with dichloromethane (10 ml). Evaporation of the solvent followed by column chromatography on silica gel gave the corresponding esters in from good to high yields. Representative data are presented:

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Table 1 Acetylation and formylation of alcohols at room temperature[a]

Entry	Alcohols	Esters	Time/h	Yield/%[b]
1	$C_6H_5CH_2OH$	$C_6H_5CH_2OAc$	1.5	95
2	$2\text{-}BrC_6H_4CH_2OH$	$2\text{-}BrC_6H_4CH_2OAc$	1.5	95
3	$4\text{-}ClC_6H_4CH_2OH$	$4\text{-}ClC_6H_4CH_2OAc$	1.5	92
4	$3\text{-}O_2NC_6H_4CH_2OH$	$3\text{-}O_2NC_6H_4CH_2OAc$	1.4	95
5	$2\text{-}MeC_6H_4CH_2OH$	$2\text{-}MeC_6H_4CH_2OAc$	1.3	90
6	$4\text{-}Me_3CC_6H_4CH_2OH$	$4\text{-}Me_3CC_6H_4CH_2OAc$	1.2	95
7	$C_6H_5CH(Me)OH$	$C_6H_5CH(Me)OAc$	1.3	87
8	$C_6H_5CH_2CH_2OH$	$C_6H_5CH_2CH_2OAc$	1.3	90
9	$C_6H_5CH_2CH_2CH_2OH$	$C_6H_5CH_2CH_2CH_2OAc$	3	80
10	$C_6H_5CH(Me)CH_2OH$	$C_6H_5CH(Me)CH_2OAc$	2.5	90
11	(-)-Menthol	(-)-Menthyl acetate	3	80
12	$C_6H_5CH_2OH$	$C_6H_5CH_2OCHO$	1.5	95
13	$2\text{-}BrC_6H_4CH_2OH$	$2\text{-}BrC_6H_4CH_2OCHO$	1.5	85
14	$4\text{-}ClC_6H_4CH_2OH$	$4\text{-}ClC_6H_4CH_2OCHO$	1.6	92
15	$3\text{-}O_2NC_6H_4CH_2OH$	$3\text{-}O_2NC_6H_4CH_2OCHO$	1.5	90
16	$2\text{-}MeC_6H_4CH_2OH$	$2\text{-}MeC_6H_4CH_2OCHO$	1	95
17	$4\text{-}Me_3CC_6H_4CH_2OH$	$4\text{-}Me_3CC_6H_4CH_2OCOH$	0.83	92
18	$C_6H_5CH(Me)OH$	$C_6H_5CH(Me)OCHO$	1.17	87
19	$C_6H_5CH(OH)C_6H_5$	$C_6H_5CH(OCHO)C_6H_5$	0.5	75
20	$C_6H_5CH(OCHO)C_6H_5$	$C_6H_5CH_2CH_2OCHO$	1.3	95
21	$C_6H_5CH_2CH_2CH_2OH$	$C_6H_5CH_2CH_2CH_2OCHO$	3.1	80
22	$C_6H_5CH(Me)CH_2OH$	$C_6H_5CH(Me)CH_2OCHO$	3	80
23	$C_6H_5CH_2CH(OH)CH_3$	$C_6H_5CH_2CH(OCHO)CH_3$	2	75
24	(-)-Menthol	(-)-Menthyl formate	3	75
25	(-)-Borneol	(-)-Bornyl formate	3.5	78
26	1-Adamantanol	1-Adamantanyl formate	3	75
27	2-Adamantanol	2-Adamantanyl formate	3	90

[a]Products were characterised by their physical constants, comparison with authentic samples and IR and NMR spectroscopy. [b]Isolated yield.

From Table 1:

Entry 9: Colourless liquid; IR: 3025, 2950, 1750, 1365, 1240, 1035, 745 and 700 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.96 (m, 2H), 2.05 (s, 3H), 2.69 (t, 2H, J = 7.6 Hz), 4.09 (t, 2H, J = 6.4 Hz), 7.17–7.31 (m, 5H).

Entry 11: Colourless liquid; $[\alpha]_D^{25} = -117.7$ (c 1.0, $CHCl_3$) {lit.[39] $[\alpha]_D^{20} = -80.5$ ° (c 8.0, benzene).

Entry 19: Colourless liquid; IR: 3032, 2929, 1727, 1495, 1454 and 1163 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.00 (s, 1H), 7.29–7.35 (m, 10 H), 8.22 (s, 1H).[40]

Entry 22: Colourless liquid; IR: 2967, 1724, 1495, 1454 and 1172 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.31 (d, 3H), 3.12 (sextet, 1H), 4.19–4.31 (m, 2H), 7.25–7.38 (m, 5H), 8.05 (s, 1H).[41]

We thank Guilan University Research Council for partial support of this work.

Received 6 June 2005; accepted 7 October 2005
Paper 05/3289

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