SYNTHETIC COMMUNICATIONS, 30(14), 2587–2592 (2000)

MAGNESIUM BROMIDE CATALYSED ACYLATION OF ALCOHOLS

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ABSTRACT

Magnesium bromide is an efficient catalyst for the acetylation and benzoylation of a variety of primary and secondary alcohols with the respective acid anhydrides at ambient temperature. Acetylation of tertiary alcohols requires subambient temperature to suppress competing dehydration. Coordinating solvents retard the acylation process.

The acylation of an alcohol is usually achieved by reaction with an acid anhydride or acid chloride in the presence of a base and several acyl transfer reagents have been employed to facilitate the process.[1] Recent investigations have focused on alternative reaction conditions and tributylphosphine,[2] cobalt chloride[3]

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and scandium triflate[4] have been successfully employed as acylation catalysts in the absence of a base. Herein, we describe preliminary results on the use of magnesium bromide as a catalyst for the acylation of alcohols with anhydrides.

The role of $MgBr_2$ as a Lewis acid is well known, especially in reactions of Grignard reagents, and other magnesium (II) salts have found application as Lewis acids in several synthetic transformations.[5] To the best of our knowledge, $MgBr_2$ has not been used as a catalyst for the acylation of alcohols.[6]

Initial investigations were conducted with menthol **(1)** as the substrate. Treatment of a CH_2Cl_2 solution of menthol with acetic anhydride (6 equiv.) in the presence of $MgBr_2$[7] (5 mol%) for 3h at ambient temperature generated menthyl acetate in 72% isolated yield. Acylation is very slow in the absence of $MgBr_2$ (ca. 10% conversion after 3h at ambient temperature). The rate of acylation is comparable in toluene or benzene but is considerably reduced in ether (60% isolated yield after 16h at ambient temperature). Use of acetonitrile as solvent also reduces the rate of acylation. The solvent of choice is CH_2Cl_2 and typically 5-10 mol% of $MgBr_2$ can be used. Benzoic anhydride can also be employed as the acylating species to yield the corresponding benzoates (Scheme 1, Table 1).

The reaction is applicable to a variety of substrates and the acetylation of 1-phenylethyl alcohol **(2)** is representative. The rate of acylation increases with increase in the amount of $MgBr_2$ employed (alcohol **4**, Table 1). Acetylation of the nitroalcohol **(7)** is of particular interest due to its tendency to undergo dehydration during acylation.[8] Treatment of **7** with $MgBr_2/Ac_2O$ affords the pure (^{1}H NMR) acetate in excellent yield (95%) thereby emphasizing the advantage of non-basic reaction conditions. Attempted acylation of the tertiary alcohols **9** and **10** with the $MgBr_2/Ac_2O$ system resulted in elimination at ambient temperature.

Conducting the acetylation of **9** at 0 °C reduced the rate of the elimination process, but no acetate was obtained (30% olefin plus unreacted **9** after 24 h by

Scheme 1

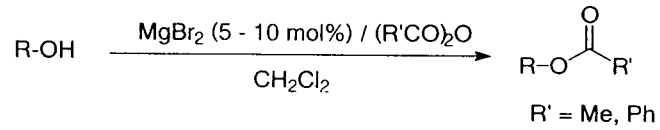
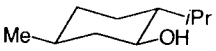
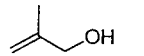
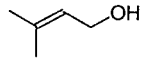
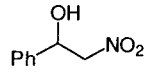
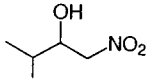
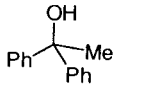
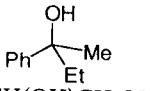


Table 1. $MgBr_2$ catalysed acylation of alcohols

Substrate	No.	Anhydride	mol% $MgBr_2$	Reacn. Time	Yield % ester
	**1**	Ac_2O	5	3 h	72
$PhCH(OH)CH_3$	**2**	Ac_2O	5	5 h	83
	**3**	Ac_2O	5	3 h	65
		Bz_2O	5	5 h	67
	**4**	Bz_2O	5	16 h	62
		Bz_2O	25	45 min	80
	**5**	Bz_2O	10	30 min	63
2,6-di*tert*butyl-4-methylphenol	**6**	Ac_2O	5	12 h	65
	**7**	Ac_2O	10	48 h	95[a]
	**8**	Ac_2O	5	45 min	93[a]
	**9**	Ac_2O	5	24 h[b]	- (30[d])
				12 h	- (90[d])
	**10**	Ac_2O	5	24 h[b]	60[c]
				5 h	- (83[d])
$PhCH(OH)CH_2OH$	**11**	Ac_2O	5	24 h	-
Benzoin	**12**	Ac_2O	5	72 h	30

a: yield of crude product (pure by ^{1}H NMR). b: reaction at 0 °C. c: GC yield. d: yield of olefin.

^{1}HNMR analysis of the crude product). However, acetylation of **10** was successful at lower temperature (<5% olefin from **10** at 0 °C and 60% conversion to the acetate).

Acylation of 1-phenylethane-1,2-diol **(11)** was unsuccessful, presumably due to irreversible complexation of $MgBr_2$ by the substrate, thereby reducing its Lewis acidity. Interestingly, this does not seem to be a difficulty with the other alcohol substrates although they are present in large excess during the initial stages of the reaction. Similarly, nitroalcohols **7** and **8** are acetylated quite efficiently, although they are potential chelators of $MgBr_2$. In comparison, the acetylation of benzoin **(12)** proceeds at a much slower rate, presumably due to steric reasons and/or complexation with $MgBr_2$.

In conclusion, magnesium bromide has been demonstrated to be a useful catalyst for the acylation of a variety of alcohols. The mildness of the procedure is exemplified by the successful acetylation of nitroalcohol substrates which are prone to dehydration. Current efforts focus on an asymmetric modification of these reactions and application to other acylating agents.

Experimental

1-Phenylethyl acetate:[9] To a solution of acetic anhydride (0.48 ml, 25 mmol) and magnesium bromide (46 mg, 0.25 mmol) in dichloromethane (5 ml) at ambient temperature is added 1-phenylethyl alcohol (0.6 ml, 5 mmol). The mixture is stirred at ambient temperature for 5h and then diluted with dichloromethane (20 ml). The solution is washed with water (2 x 10 ml), dried (Na_2SO_4) and concentrated to give the crude acetate which is purified by flash column chromatography on silica gel to furnish 680 mg (83%) of 1-phenylethyl acetate. Data: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.34 (s, 5H, Ar*H*), 5.88 (q, *J* = 7, 1H, C*H*OAc), 2.07 (s, 3H, COCH_3), 1.53 (d, *J* = 7, 3H, CH_3). IR (neat): 3020, 1850, 1750, 1510, 1470, 1390, 1250, 1220, 1140, 1070, 1040, 960, 910, 880 cm^{-1}.

Acknowledgments

Financial assistance from the Council of Scientific and Industrial Research (Senior Research Fellowships to MGM and ANR) is gratefully acknowledged. We thank Mr. Tejas U. Gokhale for technical assistance. This is NCL Communication No. 6473.

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Received in the UK 8/3/99

SYNTHETIC COMMUNICATIONS, 30(14), 2593–2597 (2000)

A SHORT SYNTHESIS OF *trans*-CYCLOPENTANE-1,2-DIAMINE

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Abstract. A convenient and rapid synthesis of the title compound is described, requiring three steps with no chromatographic purification; the key procedure is a double Curtius rearrangement.

Vicinal diamines have important applications in many fields of chemistry.[1] One particularly successful example is the commercially available C_2 symmetrical *trans*-cyclohexane-1,2-diamine, which has been widely used as a tool in organic synthesis.[2] In contrast, much less work has been done with the lower homologue, *trans*-cyclopentane-1,2-diamine, **1**, which we required recently in gramme quantity. Indeed, synthetic routes to this compound are scarce. The original method of preparation[3] involves cyclopentane-1,2-dione dioxime as an intermediate and, despite recent improvements,[4-6] remains long and inefficient. A shorter method described by Tamm[7] suffers from the need to use hydrazoic acid under drastic conditions. A synthesis starting from *trans*-cyclopentane-1,2-diol,

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