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Acylation of alcohols with acetic anhydride Catalyzed by $TaCl_5$: Some implications in kinetic resolution

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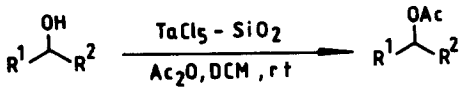
Abstract : $TaCl_5$ and $TaCl_5$-Silica gel have been effectively used as Lewis acid catalysts for acetylation of alcohols. Also $TaCl_5$-Chiral ligands have been used for kinetic resolution of 2° alcohols albeit in low ees.

Acetylation of alcohols under basic conditions using stoichiometric amounts of base viz., Et_3N and pyridine is well established.[1] Some procedures have also been developed wherein Lewis acid catalysts $CoCl_2$,[2] $Sc(OTf)_3$,[3] TMSOTf,[4] Bu_3P[5] are involved in combination with Ac_2O. The latest procedure reported involves Montmorillonite K-10 and KSF as catalysts.[6] It is needless to mention that all these procedures developed are important steps towards development of new chiral reagents and catalysts for non enzymatic kinetic resolution of 2° alcohols, wherein some progress has already been made. The important ones include chiral N-benzoyl imides,[7] chiral (dimethyl amino) pyridines,[8] chiral phosphines[9] and iron complexes.[10] In this direction, our group has already identified $TaCl_5$ and $TaCl_5$-SiO_2 as effective Lewis acid catalysts for tetrahydro pyranation of alcohols, thioacetalization of carbonyl compounds[11] and the imidation of anhydrides.[12] In continuation, this letter describes for the first time $TaCl_5$-SiO_2 and $TaCl_5$ as effective Lewis acid catalysts for acetylation of alcohols with Ac_2O (eq 1) and further some implications in kinetic resolution of 2° alcohols catalyzed by $TaCl_5$ in combination with some chiral ligands (vide supra).



Equation 1

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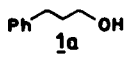
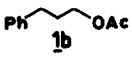
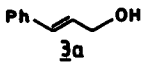
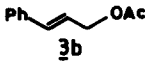
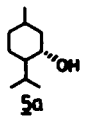
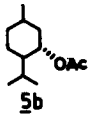
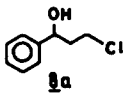
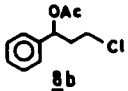
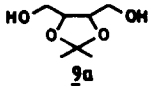
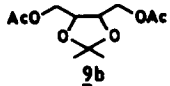
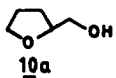
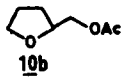
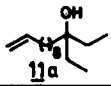
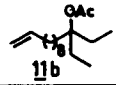
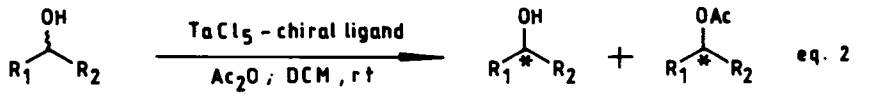
Table 1. Acetylation of alcohols catalyzed by $TaCl_5$ and $TaCl_5$-silicagel

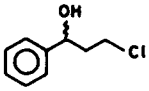
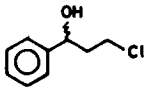
Entry	Substrate	Product	Catalyst	Yield%
1	 1a	 1b	$TaCl_5$-SiO_2	88
2	"	"	$TaCl_5$	70
3	 2a	 2b	$TaCl_5$-SiO_2	80
4	 3a	 3b	$TaCl_5$-SiO_2	80
5	$PhCH_2OH$ 4a	$PhCH_2OAc$ 4b	$TaCl_5$	77
6	 5a	 5b	$TaCl_5$-SiO_2	79
7	 6a	 6b	$TaCl_5$-SiO_2	81
8	 7a	 7b	$TaCl_5$-SiO_2	78
9	 8a	 8b	$TaCl_5$-SiO_2	74
10	 9a	 9b	$TaCl_5$-SiO_2	76
11	 10a	 10b	$TaCl_5$-SiO_2	81
12	 11a	 11b	$TaCl_5$-SiO_2	40

Initally, treatment of 3-phenyl-propan-1-ol with Ac_2O and $TaCl_5$-SiO_2 in anhydrous CH_2Cl_2 at ambient temperature provided the corresponding acetate in 88% yield (Table-1, entry 1). Further, a series of alcohols (Table-1) were acetylated in comparable yields without any difficulty. As expected, $TaCl_5$-SiO_2 acted as a more efficient Lewis Acid than $TaCl_5$ alone. It is evident from the table that 1°, 2°, allylic and benzylic alcohols behaved uniformly well (Table-1, entries 1,3,4 and 5). Also phenol and naphthol yielded corresponding acetates in 81% and 78% yields respectively (Table-1, entries 7 and 8). The only limitation has been that the 3° alcohols were acetylated with simultaneous elimination which poses a severe restriction to this class of alcohols (Table-1, entry 12). Encouraged by these results, further extrapolation of $TaCl_5$ in combination with two chiral ligands namely



eq. 2

Table 2 Enantioselective acylation of 2°- alcohols

Entry	Substrate	Ratio of $TaCl_5$ and ligand in mole %	Recovered alcohol[a]	Conversion %	ee (%)
1		15 : 15(A)		60	25
2	"	5 : 5 (B)	"	50	16
3		10 : 10 (A)		50	18
4	"	5 : 10(A)	"	55	40
5		10 : 10 (A)		70	<10

[a]The absolute stereochemistry of the recovered alcohol is determined based on sign of rotation (The chiral alcohols are available from M/s. Aldrich chemical company. inc.)

(-)2,3-O-iso propylidene-1,1,4,4-tetra phenyl-L-threitol (A) and α,α-Diphenyl-D- prolinol (B) were attempted (Table 2). To a premixed solution of $TaCl_5$ and A, when Ac_2O and phenyl-1-ethanol were added and monitored , at approximately 60% conversion, phenyl-1-ethanol was recovered, which was 25% enantiomerically enriched. Two other alcohols studies also responded with low ee's (See Table-2). Change of chiral ligand to B did not yield any better results. However when the ratio of $TaCl_5$ to ligand A was increased from 1:1 to 1:2, 40% ee of L-tetralol (Table-2, entry 4) was obtained.[13]

In conclusion, it is pertinent to mention that even though effective kinetic resolution was not achieved using $TaCl_5$-chiral ligands, an efficient catalytic cycle however has been developed for acetylation of alcohols in very high yields. Variations in the metal halide part as well in the chiral ligands is currently actively persued in our laboratories in order to achieve better ee's in kinetic resolution.

General procedure for the acylation of alcohols:

Alcohol (10 mmol) and Ac_2O (15 mmol) were added to a stirred solution of $TaCl_5$ (10 mol%) or $TaCl_5$-SiO_2 (5 mol%) in anhydrous CH_2Cl_2 (20 ml). The mixture was stirred at room temperature under a nitrogen atmosphere. The reaction upon completion (TLC) was diluted with water (15 ml) and extracted with CH_2Cl_2 (3x20 ml). Combined organic layers were washed with brine and dried over Na_2SO_4. The solvent was removed and the crude product was column chromatographed on a silica gel column to afford pure acetate ester.

General procedure for enantioselective acylation of racemic 2°-alcohols:

To a stirred solution of $TaCl_5$ (Table-2) in anhydrous CH_2Cl_2 was added the chiral ligand (A or B) (as shown in Table-2) and stirred at ambient temperature for 6 h. The reaction mixture was cooled to 0^0 C and premixed alcohol (Table-2) and Ac_2O (0.7 eq) in CH_2Cl_2 (5 ml) were added together over 10 min. The reaction was allowed to stir at room temperature for 40 h (approximately 50-60% conversion by TLC) and worked up by adding cold water (10ml) and extracted with CH_2Cl_2. The recovered alcohol after column chromatography was analysed using standard procedures.

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13. Further increase in $TaCl_5$ to chiral ligand ratio has not shown any improvement in ees.