

Acylation of alcohols with acetic anhydride Catalyzed by TaCl₅ : Some implications in kinetic resolution

S. Chandrasekhar*, T. Ramachander and Mohamed Takhi

Indian Institute of Chemical Technology, Hyderabad 500 007, India.

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Abstract : TaCl₅ and TaCl₅-Silica gel have been effectively used as Lewis acid catalysts for acetylation of alcohols. Also TaCl₅-Chiral ligands have been used for kinetic resolution of 2° alcohols albeit in low ees.

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Acetylation of alcohols under basic conditions using stoichiometric amounts of base viz., Et₃N and pyridine is well established.¹ Some procedures have also been developed wherein Lewis acid catalysts CoCl₂,² Sc(OTf)₃,³ TMSOTf,⁴ Bu₃P⁵ are involved in combination with Ac₂O. 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 phosphines⁹ and iron complexes.¹⁰ In this direction, our group has already identified TaCl₅ and TaCl₅-SiO₂ as effective Lewis acid catalysts for tetrahydro pyranation of alcohols, thioacetalization of carbonyl compounds¹¹ and the imidation of anhydrides.¹² In continuation, this letter describes for the first time TaCl₅-SiO₂ and TaCl₅ as effective Lewis acid catalysts for acetylation of alcohols with Ac₂O (eq 1) and further some implications in kinetic resolution of 2° alcohols catalyzed by TaCl₅ in combination with some chiral ligands (vide supra).

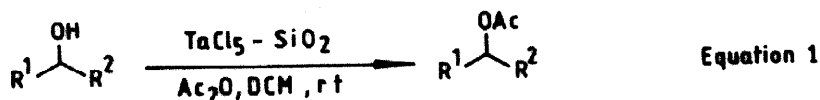
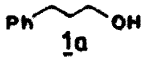

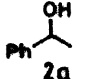
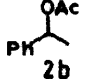
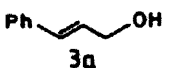
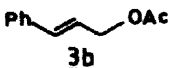
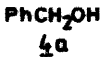
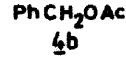
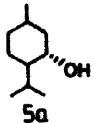
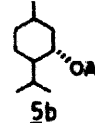


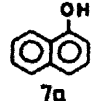
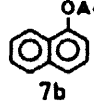
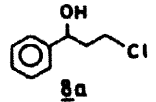
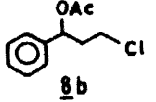
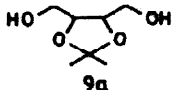
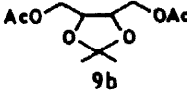
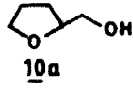
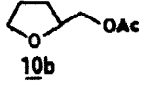
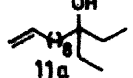
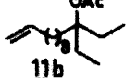


Table 1. Acetylation of alcohols catalyzed by TaCl₅ and TaCl₅-silicagel

Entry	Substrate	Product	Catalyst	Yield %
1			TaCl ₅ - SiO ₂	88
2	"	"	TaCl ₅	70
3			TaCl ₅ - SiO ₂	80
4			TaCl ₅ - SiO ₂	80
5			TaCl ₅	77
6			TaCl ₅ - SiO ₂	79
7			TaCl ₅ - SiO ₂	81
8			TaCl ₅ - SiO ₂	78
9			TaCl ₅ - SiO ₂	74
10			TaCl ₅ - SiO ₂	76
11			TaCl ₅ - SiO ₂	81
12			TaCl ₅ - SiO ₂	40

Initially, treatment of 3-phenyl-propan-1-ol with Ac₂O and TaCl₅-SiO₂ in anhydrous CH₂Cl₂ 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, TaCl₅-SiO₂ acted as a more efficient Lewis Acid than TaCl₅ 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 TaCl₅ in combination with two chiral ligands namely

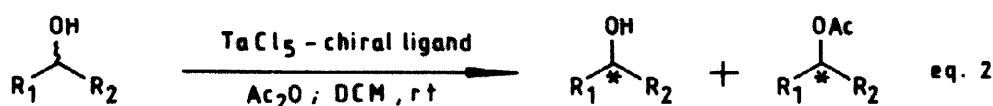

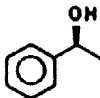

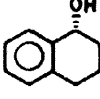
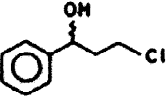
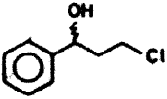


Table 2 Enantioselective acylation of 2°-alcohols

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

^aThe 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-isopropylidene-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 TaCl₅ and A, when Ac₂O 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 TaCl₅ 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 TaCl₅-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 pursued in our laboratories in order to achieve better ee's in kinetic resolution.

General procedure for the acylation of alcohols:

Alcohol (10 mmol) and Ac₂O (15 mmol) were added to a stirred solution of TaCl₅ (10 mol%) or TaCl₅-SiO₂ (5 mol%) in anhydrous CH₂Cl₂ (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 CH₂Cl₂ (3x20 ml). Combined organic layers were washed with brine and dried over Na₂SO₄. 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°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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