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Short communication

Niobium pentachloride: An efficient catalyst for the selective acetylation of amines and thiols under mild conditions

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Abstract

A variety of amines and thiols were reacted smoothly with acetic anhydride to give the corresponding acetylated products in excellent yields catalysed by niobium pentachloride. All the reactions were performed at room temperature while using dichloromethane as solvent.

Keywords: Thiols; Amines; Niobium pentachloride; Acetic anhydride; Acetylation

1. Introduction

The acetylation of amines and thiols is a common and often used transformation in synthetic organic chemistry. It can be carried out by either basic or acidic conditions. The most common and inexpensive regent used to perform the acetylation is the activated carboxylic acid derivative acetic anhydride in the presence of amine bases like triethylamine, pyridine, 4-diaminopyridine (DMAP), and 4-pyrrolidino pyridine (PPY) [1], etc. Besides the above catalysts, protic or Lewis acids are also known to catalyze this transformation such as p-toluene sulphonic acid, $COCl_2$, $TiCl_4/AgClO_4$, $RuCl_2$, Iodine, $ZnCl_2$, K-10, $MgBr\text{-}R_3N$ [2], metal triflates such as $Cu(OTf)_3$, $Sn(OTf)_3$, $Sc(NTf_2)_3$ [3], and Zeolites HZSM-360 [4]. The main drawback of the reagents is that in addition to their lack of generality, they have to be applied in stoichiometric amounts or even in large excess to effect complete conversion of the substrate. Therefore, the introduction of a new and efficient method for this transformation under more convenient and general conditions is still in demand. Niobium pentachloride is well known in the literature as mild and efficient catalyst for various organic transformations [5]. In our previous report [6], we have demonstrated the acetylation of various alcohols and phenols successfully in excellent yields with acetic anhydride catalyzed by niobium pentachloride at room temperature (Scheme 1).

2. Experimental

2.1. General methods

Melting points were recorded on a Buchi R-535 apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR 240-c spectrophotometer. ^1H NMR spectra were recorded on a Gemini-200 spectrometer in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV. All the product's physical and spectroscopic data were compared with those reported in the literature. TLC was performed on 0.25 mm E. Merck precoated silica gel plates (60 F_{254}). Starting materials and reagents used in the reactions were obtained commercially from Aldrich, Lancaster, Acros, Fluka and were used without purification, unless otherwise indicated.

2.2. General procedure

To a stirred mixture of substrate (2 mmol) in dichloromethane (10 mL) was added acetic anhydride (3 mmol) followed by addition of catalyst niobium pentachloride (0.2 mmol) at room temperature. The progress of the reaction was monitored by thin layer chromatography. After complete conversation of starting material, as indicated by TLC, the reaction mixture was diluted by adding dichloromethane (20 mL) and given water washes twice followed by brine wash. The organic layer was dried over sodium sulfate and concentrated under reduced pressure to obtain the pure products.

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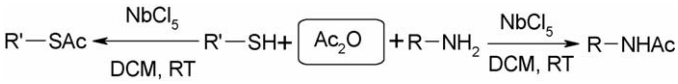


Scheme 1.

2.2.1. Spectral data for selected products

2.2.1.1. ***2d***. ^{1}H NMR ($CDCl_3$): 2.17 (s, 3H), 7.18 (d, 1H, J = 7.5 Hz), 7.32 (s, 1H), 8.10 (d, 1H, J = 7.5 Hz), 8.30 (br s, NH).

2.2.1.2. ***2e***. ^{1}H NMR ($CDCl_3$): 2.20 (s, 3H), 3.90 (s, 3H), 6.77–6.83 (m, 1H), 6.92–7.05 (m, 2H), 7.78 (br s, NH), 8.35 (d, 1H, J = 7.0 Hz). EIMS *m/z* (%). 165 (m^+ 31), 122 (18), 107 (12), 91 (41), 76 (100), 51 (29).

2.2.1.3. ***2f***. ^{1}H NMR ($CDCl_3$): 1.90 (s, 3H), 2.78–2.85 (m, 2H), 3.40–3.41 (m, 2H), 5.95 (br s, 1H), 7.15–7.32 (m, 5H); EIMS *m/z* (%). 163 (m^+ 18), 120 (25), 103 (10), 91 (100), 76 (15), 65 (31), 51 (10).

2.2.1.4. ***2j***. ^{1}H NMR ($CDCl_3$): 0.18–0.22 (m, 2H), 0.45–0.55 (m, 2H), 0.88–1.01 (m, 1H), 1.98 (s, 3H), 3.05–3.12 (m, 2H), 6.20 (br s, 1H).

2.2.1.5. ***2k***. ^{1}H NMR ($CDCl_3$): 0.80 (t, 3H, J = 6.5 Hz), 1.12 (d, 3H, J = 6.0 Hz), 1.40–1.50 (m, 2H), 1.95 (s, 3H), 3.80–3.95 (m,1H), 5.80 (br s, 1H).

2.2.1.6. ***2l***. ^{1}H NMR ($CDCl_3$): 1.30 (s, 9H), 1.85 (m, 3H), 5.54 (br s, 1H).

2.2.1.7. ***2m***. ^{1}H NMR ($CDCl_3$): 2.42 (s, 6H), 7.15 (d, 2H, J = 7.5 Hz), 7.25 (d, 2H, J = 7.5 Hz). EIMS *m/z* (%). 182 (m^+ 27), 139 (41), 124 (12), 108 (100), 92 (11), 76 (28), 51 (21).

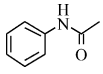
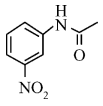
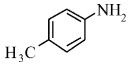
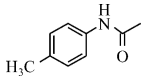
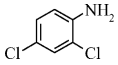
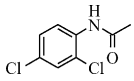
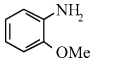
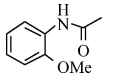
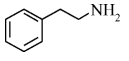
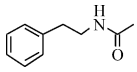
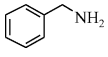
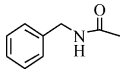
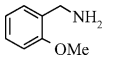
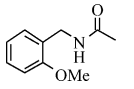
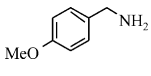
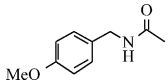
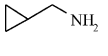
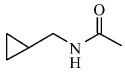
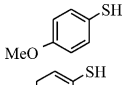
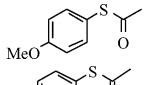
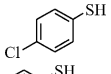
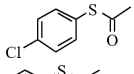
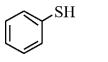
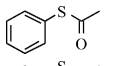
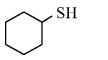
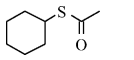
2.2.1.8. ***2n***. ^{1}H NMR ($CDCl_3$); 2.40 (s, 3H), 7.25–7.41 (m, 4H). EIMS *m/z* (%). 186 (m^+ 20), 143 (38), 108 (21), 76 (100), 51 (19).

3. Results and discussion

As part of our continuing interest in the development of new synthetic methodologies [7], herein, we wish to report an efficient method for the acetylation of various amines and thiols using acetic anhydride and niobium pentachloride at room temperature. For instance the treatment of aniline (entry **a**), with acetic anhydride in the presence of niobium pentachloride (10 mol.%) in dichloromethane at room temperature, afforded the acetylated compound in 95% yield. The reaction was completed within 1.0 h. The obtained product was very clean and further purification was not required.

In a similar manner, various substituted aromatic and aliphatic amines were acetylated very smoothly under mild reaction conditions while giving the products in very good yields. Accordingly, thiols also underwent acetylation very smoothly with acetic anhydride in the presence of niobium pentachloride at the same reaction conditions within short period of reaction time to obtain the acetylated products in excellent yields. All the reactions were performed by adding the acetic anhydride (1.5 equiv) to the substrate at room temperature in dichloromethane with high efficiency. This method is very mild and compatible with various functional groups such as nitro (entry **b**), methyl (entry **c**), chloro (entries **d** and **n**) and methoxy (entries **e**, **h**, **l**, **m**) groups present in the substrate. In view of the emerging importance and economic utility of catalytic reactions, we have studied niobium pentachloride as a true catalyst. It has been observed that acetylation of aryl amines containing electron-donating groups in the aromatic ring facilitate the reaction when

Table 1
Nioblum(V) Chloride an efficient catalyst for acetylation of amines and thiols

Entry	Substrate	Product[a]	Reaction Time (h)	Yield (%)[b]
a			1.0	95
b			1.5	90
c			1.0	93
d			1.5	90
e			1.5	92
f			2.0	88
g			1.5	90
h			2.0	87
I			1.5	91
j			2.0	86
k			2.0	87
l			2.0	85
m			1.0	93
n			1.5	90
o			2.0	94
p			1.0	89

[a] All the products characterized by ^{1}H NMR, IR and mass spectroscopy.
[b] Yields were isolated and unoptimized.

compared with electron withdrawing group containing systems. The same observation was found between aromatic amines and aliphatic amines. In all cases, the reactions were carried out at room temperature and the reactions were completed within 1–2 h of the reaction time. However, the aryl amines gave better yields (90–95%) as compared to aliphatic amines (85–88%). The results are summarized in Table 1.

4. Conclusion

In conclusion, the present methodology describes a simple, convenient and efficient procedure for the selective acetylation of various aliphatic as well as aromatic amines and thiols using a catalytic (10 mol.%) amount of niobium pentachloride. The notable features of this procedure are mild reaction conditions, cleaner reaction profiles, improved yields, enhanced reaction rates and simplicity in operation, which makes it a useful process for the acetylation of amines and thiols. The highly catalytic nature of niobium pentachloride and its wide applicability should make this protocol an attractive alternative over existing methods.

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