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A New Mild Method for the Synthesis of Esters and Benzenethiol Esters by Activation of Pyridine-2-thiol or Benzothiazol-2-thiol Esters by Methyl Iodide

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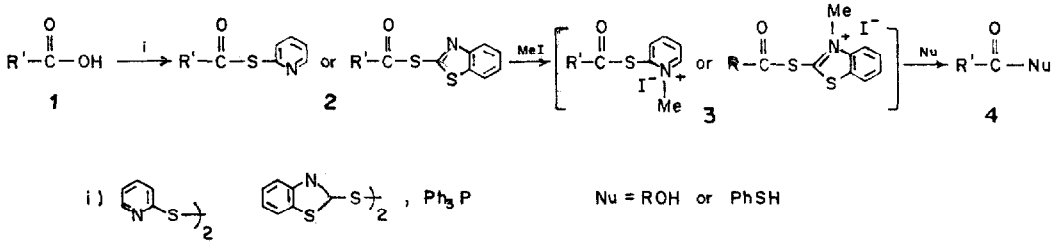
Abstract: *Activation of in-situ generated pyridine-2-thiol or benzothiazol-2-thiol esters by methyl iodide at room temperature in presence of alcohols and benzenethiol yields the corresponding esters and thiol esters.*

Formation of an ester is one of the most well-established fundamental reaction which is widely used in organic synthesis[1]. Although a number of useful methods have been presented to activate the carboxylic group toward facile esterification, only a few mild and efficient methods are available for preparation of bulky esters[2] and benzenethiol esters[3b], specially by use of equimolar amounts of the reactants[3]. In recent years thiol esters(2-pyridyl[2c,3a]alkyl and benzene[3b,4]) have gained importance in the synthesis of various natural products and thiophilic metal ions are used for their activation. A great need still exists for efficient methods to prepare hindered esters in high yields under mild conditons. Our recent synthesis of complex carbohydrates indicated that pyridyl-2-thio group is a good leaving group when activated by methyl iodide[5], this result prompted us to extend its utility toward the synthesis of esters.

We now report a mild and convenient one-pot method, where in-situ generated pyridine-2-thiol or benzothiazol-2-thiol esters 2 on activation by methyl iodide at RT in presence of diverse alcohols and benzenethiol give rise to esters and benezenethiol esters 4 in good yields (**Table 1**). Activation of thiol esters 2 with methyl iodide gives rise to a highly reactive intermediate 3 which undergoes a fast nucleophilic displacement to give esters 4 (***Scheme 1***).



Scheme 1

The mildness and efficiency of this method is shown by the use of various bulky reactants and functional groups sensitive to acid (**entries 9,10,14 and 17**) and base (***entries 14 and 17***).

In conclusion,this new mild esterification method complements the known methods,but has advantages over the thiophilic metal-ion promoted esterification in the sense that even thiol esters can be prepared by this mode of activation.

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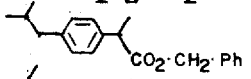
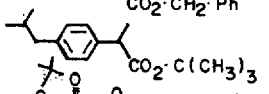
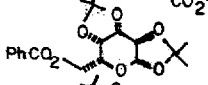
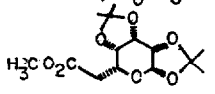
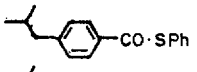
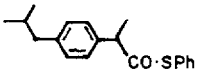
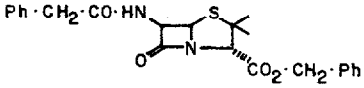
Table 1: Esterification of carboxylic acids with nucleophiles

Entry	Ester $R^1.CO.Nu$	Time(hr)	Isolated Yield %
1	$Ph.CH_2.CO_2.CH_2.Ph$	2	97
2	$Ph.CH_2.CO_2.C(CH_3)_3$	4	79
3	$O\text{-}CH_3.C_6H_4.CO_2CH_2.Ph$	3	96
4	$O\text{-}CH_3.C_6H_4.CO_2.C(CH_3)_3$	24	75
5	$H_2C{=}CH.(CH_2)_8.CO_2.CH_2.Ph$	2	85
6	$H_2C{=}CH.(CH_2)_8.CO_2.C(CH_3)_3$	6	68
7		2.5	89
8		3.5	74
9		20	86
10		22	95
11	$O\text{-}CH_3\text{-}C_6H_4.CO_2.SPh$	11	75
12	$CH_2{=}CH.(CH_2)_8.CO_2.SPh$	3.5	79
13	$Ph.CH_2.CO_2.SPh$	3	84
14	$Ph.CH(NH.CO_2.CH_2Ph)CO_2.SPh$	24	74
15		24	75
16		3	76
17		4	68

Typical experimental procedure: A suspension of carboxylic acid 1(1 mmol), Ph_3P(1.2 mmol), 2',2'-dipyridyl disulphide or 2',2'-dibenzothiazolyl disulphide (1.2 mmol) and 4A molecular sieves(100mg)in dry methylene chloride (20 ml)(EtOAc or $CHCl_3$) was stirred at room temperature for 30 minutes. Then the nucleophile (1.2 mmol) and methyl iodide (4-6 mmol in 1 ml CH_2Cl_2) were added and stirring continued at room temperature until the reaction is complete (t.l.c). Solvent was removed and the residue chromatographed (SiO_2)to obtain the desired ester 4 and characterised by their p.m.r. and i.r. spectra.

REFERENCES:

(1) For excellent reviews, see: (a) S.Masamune, G.S.Bates and J.W.Corcoran, Angew.Chem.Int.Ed.Engl, 1977, 16, 585.(b) K.C.Nicolaou, Tetrahedron 1977, 33, 683.(c) T.G.Back, ibid.1977, 33, 3041.(d) E.Haslam, ibid, 1980, 36, 2409.(e) S.Kim, Org.Prep.& Proce.Int, 1988, 20, 147. (2)(a) S.Takimoto, J.Inanaga, T.Katsukim and M.Tamaguchi, Bull.Chem. Soc. Jpn. 1976, 49, 2335.(b) T.Mukaiayama and H.Ko, Chem.Lett. 1976, 267.(c) S.Kim and J.I.Lee, J.Org. Chem. 1984, 49, 1712. (3)(a) H.Gerlach and A.Thalman, Helv.Chim.Acta. 1974, 57, 2661.(b) S.Masamune, Y.Hayase, W.Schilling, W.K.Chan and G.Bates, J.Am.Chem.soc., 1977,99, 6756. (5) G.Venugopal Reddy, V.R.Kulkarni and H.B.Mereyala, Tetrahedron Lett., 1989, accepted.

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