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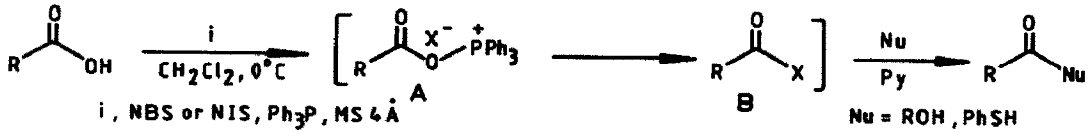
A Novel, General Route to the Synthesis of Carboxylic Acid Esters and Thiolesters

K. Sucheta, G.S.R. Reddy, D. Ravi and N. Rama Rao*
Birla Institute of Scientific Research, Malakpet, Hyderabad - 500 036, India.

Abstract: Carboxylic acids were conveniently esterfied with alcohols and thiols by the use of triphenylphosphine and N-bromo/Iodo succinimide to afford the corresponding esters and thiol esters.

Conversion of carboxylic acids to their corresponding esters and thiol esters is a well established fundamental organic reaction[1]. It's wide use in organic synthesis has instigated many researchers to develop elegant synthetic methods[2-6].

We, here in this letter, report a mild, general method for the convenient conversion of carboxylic acids to their corresponding esters by using triphenylphosphine and N-bromo/iodo succinimides. Thus, several acids were smoothly esterfied with diverse alcohols, thiols and obtained the esters and thiol esters in high yield (**scheme 1**).



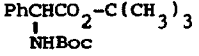
Scheme 1

The reaction of carboxylic acid with triphenylphosphine and N-halo succinimide leads to highly reactive intermediates **A** and / or **B** which further undergoes a smooth and fast nucleophilic displacement with the respective alcohol / thiol in the presence of pyridine to afford the corresponding esters and thiol esters. The efficacy of this methodology was further pro-ved by the synthesis of hindered and thiol esters in good yield.

In conclusion, the present method of esterification, not only complements but also offers advantages over the known methods in the sense that even thiol esters can also be made in high yields which are of great importance in the synthesis of natural products.

The application of this methodology for the synthesis of macrolactones is in progress and will be published elsewhere.

Table 1: Esterfication of carboxylic acids with alcohols and thiols

Entry	**Ester**	**Time(h)**	**Isolated % Yield**
1	$\mathrm{PhCH_2CO_2\text{-}CH_2Ph}$	1.0	98
2	$\mathrm{PhCH_2CO_2}$-Cyclohexyl	1.5	82
3	$\mathrm{PhCH_2CO_2\text{-}C(CH_3)_3}$	4.0	72
4	$\mathrm{PhCO_2\text{-}CH(CH_3)_2}$	1.0	93
5	$\mathrm{PhCO_2\text{-}C(CH_3)_3}$	6.0	72
6	$\mathrm{PhCO_2}$-Cyclohexyl	2.0	85
7	$\mathrm{3,5\text{-}(O_2N)_2\text{-}C_6H_4CO_2\text{-}C(CH_3)_3}$	3.0	79
8	$\mathrm{PhCH{=}CHCO_2\text{-}C(CH_3)_3}$	3.5	76
9	$\mathrm{PhCO_2}$-tetrahydropyran-2-methyl	1.5	89
10	$\mathrm{(CH_3)_3CO_2\text{-}CH_2Ph}$	8.5	83
11	$\mathrm{(CH_3)_3CO_2\text{-}C(CH_3)_3}$	12.0	63
12	 $\mathrm{Ph\underset{\displaystyle NHBoc}{\underset{\vert}{C}}HCO_2\text{-}C(CH_3)_3}$	10.0	69
13	PhCOSPh	1.0	82
14	$\mathrm{PhCH_2COSPh}$	1.5	87
15	$\mathrm{PhCH{=}CHCOSPh}$	2.5	87

Typical experimental procedure: To a stirred solution of N-bromosuccinimide(1.1mmol) in dry dichloromethane(25ml), and molecular sieves 4Å (100mg) at 0°C was added dropwise a solution of triphenylphosphine(1.1mmol) in dichloromethane where the clear solution developed orange colour. Acid(1mmol) was added at the same temperature and stirred for 30 minutes at room temperature. Pyridine(1.1mmol) and nucleophile(1.2mmol) were then added and stirred at room temperature until the reaction was complete(monitored by TLC). The organic layer was washed with water, dried over $\mathrm{Na_2SO_4}$, eluted with hexane over silicagel to afford the desired ester/thiol ester and were characterised by their pmr and ir spectra.

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REFERENCES:

(1) Greene, T.W. Protective Groups in organic synthesis; John Wiley, New York, 1981. (2) For excellent reviews, see: Nicolaou, K.C. Tetrahedron, 33(1977)683, b) Back,T.G. ibid, 33(1977)3041. (c) Haslam, E. ibid, 36(1980)2409. (d) Kim,S. Org.Prep & Proc.Int. 20(1988)147. (e) Masamune,S. and Corcoran, J.W. Angew.Chem.Int.End.Engl, 16(1977)585. (3) (a) Ravi,D. and Mereyala, H.B. Tetrahedron Lett. 30(1989)6089. (b) Gerlach,H. and Thalman, A. Helv.Chim.Acta 57(1974)2661. (4) Masamune, S., Hayase, Y., Schilling, W., Chan, W.K. and Bates,G. J.Am.Chem.Soc. 99(1977)6756. (5) Banerger, A. and Sengupta, S. J.Org.Chem. 48(1983)3106. (6) (a) Brook, M.A. and Chan, T.M. Synthesis,(1983)201 (b) Folmer, J.J. and Weinreb, S.M. Tetrahedron lett. 34(1993)2737.

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