Scholars Research Library

Der Pharma Chemica, 2014, 6(5):365-369
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

An Efficient and Practical Protocol for the Esterification of Aromatic Carboxylic Acids with Alcohols in presence of POCl3

Prashant Patila* and Atul chaskarb*

[a]*The Institute of Science, Madam Cama Road, Mumbai, India*
[b]*Institute of Chemical Technology, Matunga, Mumbai*

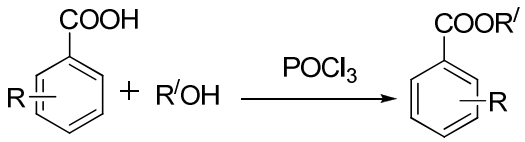
ABSTRACT

Functional group tolerant, an efficient and practical protocol has been developed for esterification of carboxylic acid with alcohol in presence of POCl3. The products were accomplished in quantitative yields at relatively low temperature.

Keywords: Aromatic carboxylic acid, alcohol, POCl3, esterification.

INTRODUCTION

Esterification is a privileged reaction in the myriad of organic synthesis owing to their enormous potential applications in synthesis of various building blocks of synthetic importance[1]. The carboxylic group can be converted to corresponding ester by reacting it with an alcohol in the presence of various homogeneous as well as heterogeneous catalysts. These subsumes conc. Sulphuric acid, hydrogen chloride, thionyl chlodide[2], alkyl chloroformate and Et_3N[3], phenyl dichlorophosphate[4], DCC and aminopyridine[5], SiO_2/$NaHSO_4$[6], amberlyst 15[7], USY zeolite[8], MoO_3/ZrO_2[9], $MgSO_4$/H_2SO_4[10], salycilic resin/$FeCl_3$[11], SiO_2[12], celite/CsF[13], dowex 50WX2[14], beta zeolite[15], Kaolinite clay[16], H_3PO_4/TiO_2-ZrO_2[17], etc. Besides the practical utility of heterogeneous catalysts, solubility of HPA in polar solvents and rapid catalyst deactivation of SiO_2, zeolites limit their use. Similarly though some catalysts have higher reactivity, the high operation temperature always gives a mixture of products. Generally, the use of stoichiometric amounts of multiple reagents limit the application of modern coupling reagents for esterification reaction[18,19]. All these and some more limitations encountered with many of the synthetic protocols triggered our interest to develop a new method that would function at room temperature for the synthesis of bioactive heterocyclic compounds. Here we wish to report our new, mild, clean and chemoselective protocol in presence of $POCl_3$. The methyl, ethyl and n-butyl esters prevailed in quantitative yields at room temperature whereas, isopropyl esters were obtained at reflux temperature. As compared to previously reported method[2] our method required less time.



R = OH, NH_2, COOH
R/ = CH_3, C_2H_5, *n*-C_4H_9, $CH(CH_3)_2$

Scheme 1. Esterification of carboxylic acid in presence of $POCl_3$

MATERIALS AND METHODS

All commercial reagents were used as received without purification and all solvents were of reagent grade. The reaction progress was monitored by TLC using on 0.25 mm E-Merck silica gel 60 F_{254} precoated plates, which were visualized with UV light. Melting points of products were taken in open capillaries on a Veego apparatus and are uncorrected. Infrared spectra were recorded on a Simadzu spectrophotometer in a KBr disc, and the absorption bands are expressed in cm^{-1}. ^1H NMR spectra were recorded on a Bruker 400 MHz spectrometer in $CDCl_3$. Chemical shifts (δ) are mentioned in (parts per million) ppm relative to TMS.

4.2. General procedure

$POCl_3$ (1.2 mmol) was added dropwise in the ice cold solution of benzoic acid (1 mmol) in methanol (5 mL), and the resultant solution was stirred at room temperature for 2 h. The reaction mixture was poured over crushed ice and then extracted using ethyl acetate. The combined organic solvent was washed with saturated solution of sodium bicarbonate, further dried over $MgSO_4$ and then concentrated under reduced pressure to get the product. For amino carboxylic acid the reaction mixture was first neutralised after pouring on crushed ice and then extracted using ethyl acetate.

4.3 Physical and Spectral Data

Methyl 4-chlorobenzoate

^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.91-7.95 (m, 2H), 7.35-7.39 (m, 2H), 3.87 (s, 3H).
^{13}C-NMR ($CDCl_3$, 100 MHz): δ 166.18, 139.35, 130.95, 128.69, 52.23.

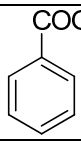
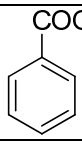
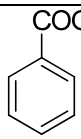
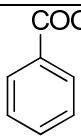
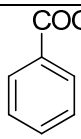
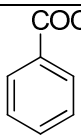
Ethyl 4-aminobenzoate

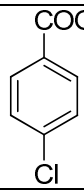
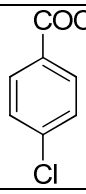
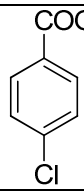
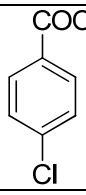
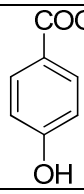
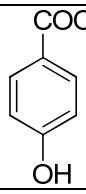
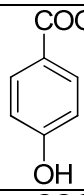
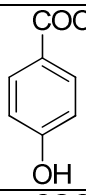
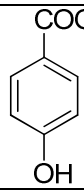
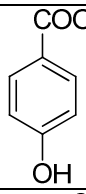
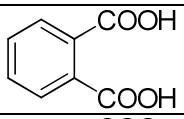
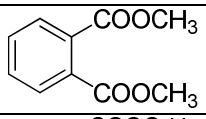
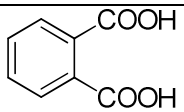
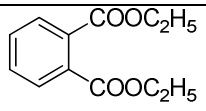
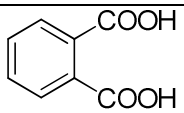
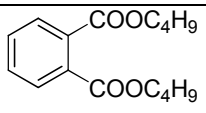
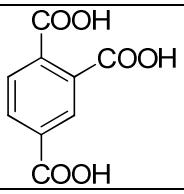
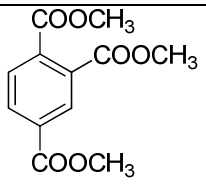
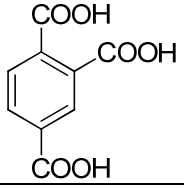
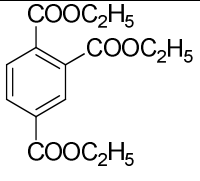
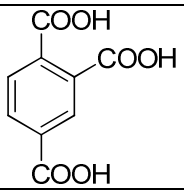
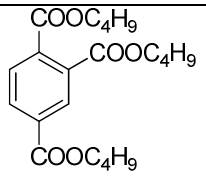
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.81-7.83 (d, *J* = 8.8 Hz, 2H), 6.59-6.61 (d, *J* = 8.8 Hz, 2H), 4.28-4.29 (q, 2H), 4.0 (bs, 2H, NH_2), 1.31-1.34 (t, 3H).
^{13}C-NMR ($CDCl_3$, 100 MHz): δ 166.77, 150.86, 131.54, 119.97, 113.77, 60.31, 14.42.

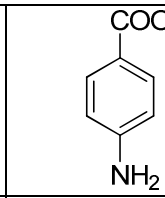
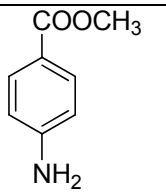
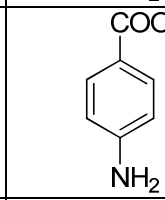
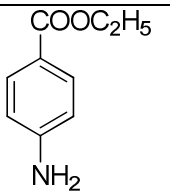
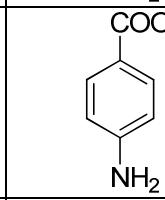
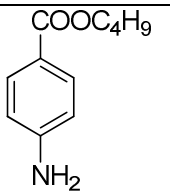
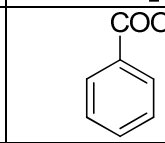
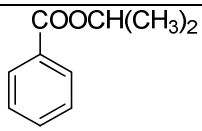
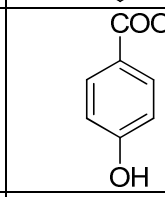
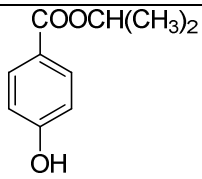
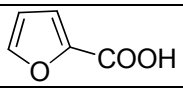
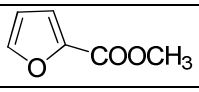
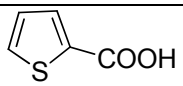
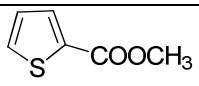
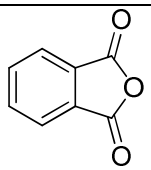
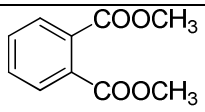
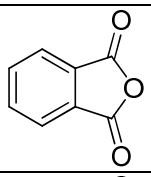
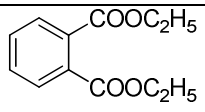
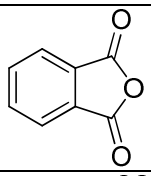
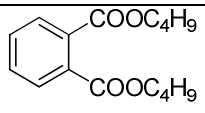
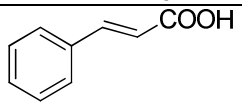
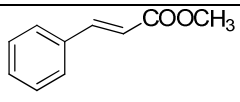
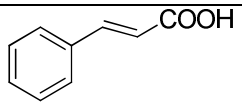
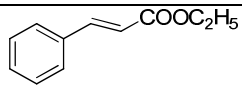
RESULTS AND DISCUSSION

The initial efforts were directed towards determination of the suitable reaction conditions. The reaction of benzoic acid and methanol in presence of $POCl_3$ was investigated and surprisingly, we observed quantitative conversion at room temperature. This result encouraged us to plan the esterification of mono-, di- and tri-carboxylic acids. Interestingly, the esterification with primary alcohols worked well at room temperature while for secondary alcohols higher temperature was required. The method has the ability to tolerate hydroxyl and amino functional groups as well as olefinic double bond; it shows that the reaction is chemoselective in nature. It is noteworthy that; our method offered good to high yields of esters of phthalic anhydride and heterocyclic carboxylic acids. The physical and spectral data of all the products are in agreement with literature reports.

Table 1. Esterification of Aromatic Carboxylic acids using $POCl_3$.[a]

Sr.No.	Acid	Alcohol	Product	Yield (%)[b]
1		CH_3OH		90
2		C_2H_5OH		90
3		*n*-C_4H_9OH		87

4		CH_3OH		90
5		C_2H_5OH		88
6		CH_3OH		75
7		C_2H_5OH		70
8		*n*-C_4H_9OH		68
9		CH_3OH		87
10		C_2H_5OH		83
11		*n*-C_4H_9OH		74
12		CH_3OH		60
13		C_2H_5OH		57
14		*n*-C_4H_9OH		55

15		CH_3OH		80
16		C_2H_5OH		76
17		*n*-C_4H_9OH		70
18		$(CH_3)_2CHOH$		72
19		$(CH_3)_2CHOH$		65
20		CH_3OH		61
21		CH_3OH		63
22		CH_3OH		90
23		C_2H_5OH		82
24		*n*-C_4H_9OH		67
25		CH_3OH		90
26		C_2H_5OH		87

[a]*Conditions: Monocarboxylic acid (1 mmol), alcohol (5 mL), $POCl_3$ (1.2 mmol), 2h.*
[b]*Isolated Yield*

CONCLUSION

Concluding word to our work, we have developed an expedient, inexpensive and practical protocol for the esterification of aromatic carboxylic acid with alcohol using $POCl_3$. We strongly believe that relatively low reaction temperature and good yield of product can make this protocol more attractive and applicable, too.

REFERENCES

[1] E. Haslam, *Tetrahedron*, **1980**, 36, 2409-2433.
[2] B. Hosangadi, R. Dave, *Tetrahedron Lett.*, **1996**, 37, 6375-6378.
[3] S. Kim, J. I. Lee, Y.C. Kim, *J.Org. Chem.* **1985**, 50, 560-565.
[4] M. Ueda, H. Oikawa, *J.Org. Chem.* **1985**, 50, 760-763.
[5] B. Neises, W. Steglich, *Angew. Chem. Int. Ed. Engl.* **1978**, 17, 522-524.
[6] B. Das, P. Venkataiah, P. Madhusudhan, *Synlett* **2000**, 1, 59-60.
[7] R.C. Anand, V. Milhotra, A. Milhotra, *J. Chem. Res (S)* **1999**, 6, 378-379.
[8] M. A. Wegman, J.M. Elzinga, E. Neeleman, F. van Rantwijk, R.A. Sheldon, *Green Chem.* **2001**, 3, 61-64.
[9] B. Manohar, V. R. Reddy, B. M. Reddy, *Synth. Commun.* **1998**, 28, 3183-3187.
[10] S. W. Wright, D. L. Hageman, A. S. Wright, L. D. McLure, *Tetrahedron Lett.* **1997**, 38, 7345-7348.
[11]Y. Huirong, L. B. C. Yingde, *Synth. Commun.* **1998**, 28, 1233-1238.
[12] L. Lami, B. Casal, L. Cuadra, J. Merino, A. Alvarez, E. RuizHitzky, *Green Chem.* **1999**, 1, 199-204.
[13] J. C. Lee, Y. Choi, *Synth. Commun*, **1998**, 28, 2021-2026.
[14] M. Saito, S. Fujisaki, Y. Ishii, T. Nishiguchi, *Tetrahedron Lett.*, **1996**, 37, 6733-6736.
[15] S. R. Kirumakki, N. Nagaraju, K.V.V.S.B.S.R. Murthy, S. Narayanan, *Appl. Catal. A: General* **2002**, 226, 175-182.
[16] D. Konwar, P. K. Gogoi, P. Gogoi, G. Borah, R. Baruah, N. Hazarika, R. Borgohain, *Ind. J. Chem. Technol.* **2008**, 15,75-78.
[17] R. J. Kalbasi, A. R. Massah, Z. Barkhordari, *Bull. Korean Chem.Soc.* **2010**, 31, 2361-2367.
[18] V. P. Fitzjarrald, R. Pongdee, (2007) *Tetrahedron Lett.* **2007**, 48, 3553-3557.
[19] N. Iranpoor, H. Firouzabadi, D. Khalili, S. Motevalli, *J. Org. Chem.* **2008**, 73, 4882-48887.