J. Chem. Research (S), 1998, 268–269†

1,3,4-Oxadiazolethiol as Acyl-transfer Reagent in Acylation of Amines: a One-pot Reaction†

B. N. Goswami,* N. Borthakur and A. C. Ghosh

Organic Chemistry Division, Regional Research Laboratory, Jorhat-785006, India

Amines are acylated using 5-(2,4-dichlorophenyl)-1,3,4-oxadiazolethiol in the presence of diethyl chlorothiophosphate (DCTP) in good yield.

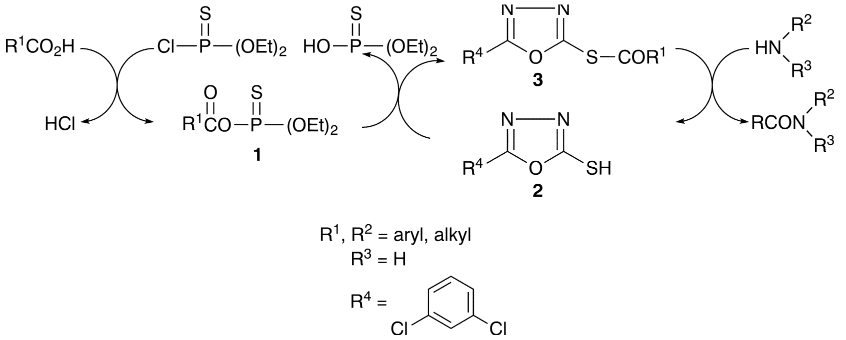
Activation of a carbonyl group under mild conditions is a challenging, current problem in organic synthesis. Triphenylphosphine,[1] diphenylphosphenyl azide,[2] *N*,*N*-bis-(2-oxo-3-oxazolidinyl)phosphorodiamidic chloride,[3] diethylphosphorobromidate,[4] phenyl *N*-phenyl phosphoramidochloridate,[5] 2-sulfanyl benzoxazole,[6] 3,6-diethyl-2-hydroxypyrazine,[7] 2-chloro-4,6-disubstituted-1,3,5-triazine[8] and other organophosphorus reagents[9,10] have been used as acyl-transfer reagents. All these methods require either expensive reagents or strong reaction conditions and tedious work-up procedures. For example, Hossain and Borthakur[9] used *O*,*O*-diethyl dithiophosphoric acid for the acylation of amines where the reaction was carried out by boiling under reflux a mixture of carboxylic acid, *O*,*O*-diethyl dithiophosphoric acid and a suitable amine in solvents such as toluene for several hours. In addition, some of these reactions are associated with undesired side products, such as urea derivatives. For example, carbodiimides[5] have been used as condensing agents in the synthesis of carboxamides from carboxylic acids and amines. The formation of *N*-acylureas and anhydrides as side products renders the isolation of the desired carboxamides difficult.

We report here that 5-(2,4-dichlorophenyl)-1,3,4-oxadiazolethiol[11] in the presence of diethyl chlorothiophosphate (DCTP) results in selective acylation of anilines in very good yield (>80%) at room temperature. The thiol transfers the acyl function from the acyl diethylthiophosphate **1** formed *in situ* by the reaction of carboxylic acid and diethyl chlorothiophosphate in the presence of triethylamine at room temperature. In the case of secondary amines, acylation could be accomplished only at an elevated temperature (80–85 °C).

Table 1 Preparation of amides $R^1CONR_2R^3$, **4** from amines

Entry	R^1	R^2	R^3	mp/bp (T/°C)	Yield (%)
1	Ph	Ph	H	163	90
2	Ph	oClC$_6$H$_4$	H	95	89
3	Ph	pCO$_2$HC$_6$H$_4$	H	278 (dec.)	83
4	Ph	p-MeOC$_6$H$_4$	H	158	86
5	Ph	o-OHC$_6$H$_4$	H	166	85
6	2,4-Cl$_2$C$_6$H$_3$	Ph	H	138	86
7	2,4-Cl$_2$C$_6$H$_3$	p-MeC$_6$H$_4$	H	162	87
8	2,4-Cl$_2$C$_6$H$_3$	p-BrC$_6$H$_4$	H	161	86
9	2,4-Cl$_2$C$_6$H$_3$	pCO$_2$HC$_6$H$_4$	H	277	81
10	2,4-Cl$_2$C$_6$H$_3$	oClC$_6$H$_4$	H	138	82
11	2,4-Cl$_2$C$_6$H$_3$	p-MeOC$_6$H$_4$	H	160	83
12	2,4-Cl$_2$C$_6$H$_3$	pClC$_6$H$_4$	H	158	80
13	Ph	Ph	Ph	179	80
14	Ph	Ph	Ph	Liquid	76

It is to be noted that the method has been applied to the reaction between anilines and benzoic acids. This is a one-pot reaction with a very simple work-up procedure. This efficient procedure for one-pot acylation of amines probably consists of two reactions; the formation of the active esters,[7] 5-(2,4-dichlorophenyl)-2-acyloxy-1,3,4-oxadiazole **3** from acyldiethyl thiophosphate **1** and 5-(2,4-dichlorophenyl)-1,3,4-oxadiazolethiol **2**, respectively, and their subsequent ammonolysis.



Scheme 1

Experimental

Mps were recorded in open capillaries in a Buchi apparatus and are uncorrected. IR spectra were recorded in a Perkin-Elmer 237 B spectrometer. The ^{1}H NMR spectra were recorded on a Varian T-60 (60 MHz) NMR spectrometer with Me$_4$Si internal standard. Mass spectra of the compounds were recorded on a Finnigan-MAT mass spectrometer. The purity of the compounds was checked by TLC using light petroleum–ethyl acetate (3:2) as eluent and the spots were visualised in iodine or KMnO$_4$ solution.

Preparation of Benzanilide **4**.—In a typical experiment benzoic acid (1.22 g, 0.01 mol), triethylamine (1.52 g, 0.015 mol) and DCTP (2.82 g, 0.01 mol) were mixed in 25 ml of acetonitrile. The reaction mixture became turbid owing to the formation of triethylamine hydrochloride. The mixture was then stirred magnetically for 3 h at room temperature. To this was added 5-(2,4-dichlorophenyl)-1,3,4-oxadiazolethiol (2.46 g, 0.015 mol) and the resultant mixture was kept overnight after stirring for 1 h. Then aniline (1.39 g, 0.015 mol) was added and stirred for another 0.5 h. After removal of the

---

*To receive any correspondence.

†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

solvent *in vacuo*, the residue was dissolved in dichloromethane (25 ml), washed successively with (10 × 3 ml) 10% KOH and 20 ml water and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a solid which was crystallised from ethanol. Yield 1.77 g (90%), mp 163 °C (lit. 164 °C), m/z 197 (M^+), ν_{max}/cm^{-1} (KBr) 3250 (NH), 1655 (C=O), δ_H (60 MHz, $CDCl_3$) 6.0–7.1 (m, Ar-H), 7.5 (br s, NH). The other compounds were prepared similarly. The acyl-carrier reagent **2** was recovered from the aqueous KOH layer (85%) for recycling. The course of the reaction is shown in Scheme 1 and the physical characteristics and yields of the acylated amines **4** so formed are shown in Table 1.

A control experiment was carried out in which benzoic acid (1.22 g, 0.01 mol), triethylamine (1.52 g, 0.015 mol) and DCTP (2.82 g, 0.01 mol) were taken in 25 ml of acetonitrile. The reaction mixture became turbid owing to the formation of triethylamine hydrochloride. This mixture was stirred magnetically for 3 h at room temperature. To this was then added aniline (1.39 g, 0.015 mol) and stirring continued for 2 h. Compound **4** did not form.

The authors thank the Director, Regional Research Laboratory, Jorhat for providing necessary facilities and Dr J. C. S. Kataky, for his keen interest in this work.

Received, 15th July 1997; Accepted, 14th January 1998
Paper E/7/05061E

References

1 S. Yamada and Y. Takenuchi, *Tetrahedron Lett.*, 1971, 3595.
2 T. Shioiri, K. Ninomiya and S. Yamada, *J. Am. Chem. Soc.*, 1972, **94**, 6203.
3 J. Diago-Meseguer, A. L. Palomo-Coll, J. R. Fernandez-Lizarbe and A. Zugaza-Bilbao, *Synthesis*, 1980, 547.
4 A. Gorecka, M. Leplawy and J. Zabrocki, *Synthesis*, 1978, 475.
5 R. Mestres and C. Palomo, *Synthesis*, 1982, 288.
6 M. Ueda, K. Seki and Y. Imai, *Synthesis*, 1981, 991.
7 A. Ohta, Y. Inagawa, Y. Okuwaki and M. Shimazaki, *Heterocycles*, 1984, **22**(10), 2369.
8 Z. J. Kaminski, *Tetrahedron Lett.*, 1985, **26**, 2901.
9 N. Hossain and N. Borthakur, *Indian J. Chem., Sect. B*, 1990, **29**, 1062.
10 S. H. Mashraqui, S. S. Nirantar and M. M. Biswas, *Indian J. Chem., Sect. B*, 1995, **34**, 1102.
11 B. N. Goswami, J. C. S. Kataky and J. N. Baruah, *J. Heterocyl. Chem.*, 1984, **21**, 205.
12 The compounds were characterised by mp, IR, ^1H NMR, MS and by comparison with authentic samples.