New reaction of dithiophosphoric acids with *O*-thioacylhydroxylamines. Nucleophilic substitution or single electron transfer process? †

Leszek Doszczak, Witold Przychodzeń, Dariusz Witt and Janusz Rachon*

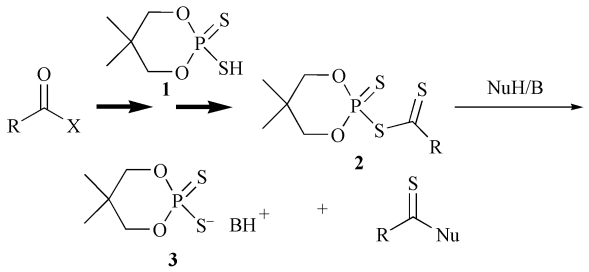
Department of Organic Chemistry, Faculty of Chemistry, Technical University of Gdańsk, ul. Narutowicza 11/12, 80-952 Gdańsk, Poland

Received (in Cambridge, UK) 15th April 2002, Accepted 5th August 2002
First published as an Advance Article on the web 30th August 2002

Disubstituted or sterically hindered hydroxylamines react with bulky *S*-thioacyl dithiophosphates yielding *O*-thioacylhydroxylamines. The reaction of *O*-thioacylhydroxylamines with dithiophosphoric acids yields acyl thiophosphoryl disulfides and ammonium dithiophosphates. The influence of radical traps on the reaction yield strongly suggests that radicals are involved in the mechanism of the process. The low redox potential of dithiophosphates, the observed photochemical stability of *O*-thioacylhydroxylamines and the influence of light on acyl thiophosphoryl disulfides yield imply involvement of a single electron transfer process in the investigated reaction.

Introduction

We have recently described[1,2] a convenient method of converting carboxylic acids into thioacyl dithiophosphates **2**, which are excellent thioacylating reagents (see Scheme 1). Thioacyl dithiophosphates **2** react much faster with nitrogen or sulfur nucleophiles than with oxygen ones. This kind of reactivity can find general application in the direct thioacylation of aminoalcohols and mercaptoalcohols having an unprotected hydroxy function. As we proved recently[3] thiohydroxamic acids (*N*-thioacylhydroxylamines) can also be obtained by direct thioacylation of hydroxylamines with thioacyl dithiophosphates **2**.



Scheme 1 *S*-Thioacyl dithiophosphates and their application as thioacylating agents.

However, when we treated *N*-isopropylhydroxylamine **4a** with thiopivaloyl dithiophosphate **2a**, to our surprise, from the reaction mixture[4,5] we isolated pivaloyl thiophosphoryl disulfide **5a** instead of the expected thiohydroxamic acid **6** (Scheme 2). In this paper, we would like to present the details of our research concerning this new reaction effecting the cleavage of the nitrogen–oxygen bond in the hydroxylamine moiety under the action of dithiophosphoric acid.

† Electronic supplementary information (ESI) available: ^{31}P NMR spectra of reaction mixtures formed from *O*-thiopivaloyl-*N*-(1-phenylethyl)hydroxylamine and dithiophosphoric acid in the presence of a radical trap; ^{1}H NMR spectrum of the reaction mixture formed after irradiation of *O*-thiopivaloyl-*N*-(1-phenylethyl)hydroxylamine in the presence of a radical trap and ^{1}H NMR spectra of the reaction mixtures formed after irradiation of *O*-thiopivaloyl-*N*-(1-phenylethyl)-hydroxylamine. For direct access see http://www.rsc.org/suppdata/p2/b2/b203619n/

Results and discussion

In order to explain the very unusual course of the reaction of *N*-isopropylhydroxylamine **4a** with thiopivaloyl dithiophosphate **2a**, we pondered over the difference between this and the other cases of hydroxylamine thioacylation. Both reagents have bulky substituents and, as we showed recently,[3] in the event of greater steric hindrance *O*-thioacylhydroxylamines **7** may be formed instead of the expected thiohydroxamic acids **6** (Scheme 3).

Hence, we made an assumption that *O*-thiopivaloyl-*N*-isopropylhydroxylamine **7a** was the intermediate and disulfide **5a** was formed on further reaction with the dithiophosphate anion. However, the question arose, why in this case it was impossible to isolate the respective *O*-thioacylhydroxylamine and an additional process took place. To answer this question we ran the reaction of another bulky hydroxylamine (*N*-*tert*-butylhydroxylamine **4b**; R′ = Bu^t, R″ = H) with pivaloyl dithiophosphate **2a**. Also in this case we isolated disulfide **5a** from the reaction mixture in 81% yield. Monitoring the reaction with ^{31}P NMR we found that after mixing the reagents, thioacyl dithiophosphate **2a** (δ_P 71 ppm) is consumed, though only dithiophosphate anion (δ_P 106 ppm) production can be observed (using ^{31}P NMR). It means that the formation of disulfide **5a** (δ_P 83 ppm) results from the following acidic work-up of the mixture. Therefore, we presumed that disulfide **5a** should be formed in the reaction of *O*-thioacylhydroxylamines with the dithiophosphoric acid. To verify this hypothesis we treated isolated *O*-thiopivaloyl-*N*-*tert*-butylhydroxylamine **7b** with two equivalents of dithiophosphoric acid **1**. From the reaction mixture we were able to isolate disulfide **5a** and *tert*-butylammonium dithiophosphate **3b** in very good yields (Scheme 4).

In order to check whether other hindered *O*-thioacylhydroxylamines reveal the same reactivity, we treated *O*-thiopivaloyl-*N*-(1-phenylethyl)hydroxylamine **7c** and *O*-thiopivaloyl-*N*-hydroxymorpholine **7d** with dithiophosphoric acid **1**. The formation of disulfide **5a** and the respective ammonium dithiophosphates **3** in each case shows that this kind of reactivity is typical for *O*-thioacylated hydroxylamines. Moreover, as we demonstrated, the reaction of *O*-thiopivaloyl-*N*-*tert*-butylhydroxylamine **7b** with other dithiophosphinic (dithio-

DOI: 10.1039/b203619n