Synthesis and reactivity of *O*-acyl selenophosphates†

Janusz Rachon,* Grzegorz Cholewinski and Dariusz Witt

Received (in Cambridge, UK) 17th February 2005, Accepted 21st March 2005
First published as an Advance Article on the web 12th April 2005
DOI: 10.1039/b502473k

The synthesis of several new *O*-acyl selenophosphates were investigated. The stability and reactivity of the products were studied and related to their structure.

O-acyl dithiophosphates are unstable and isomerise to *O*-thioacyl monothiophosphates and *S*-acyl monothiophosphates. Treatment of the above mixture with dithiophosphoric acid gives exclusively *S*-acyl dithiophosphates. These compounds have proved to be efficient, chemoselective thioacylating agents.[1] So far however, the mechanism of the isomerisation has remained undetermined.

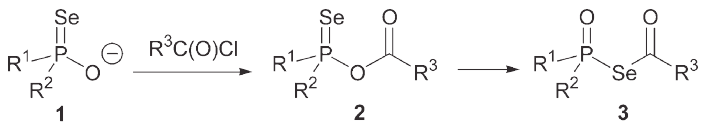
Organoselenium compounds play an important role in biological processes[2,3] and their synthesis has been intensively studied.[4]

The synthesis of the selenium analogues of mixed anhydrides, followed by an investigation of their thermodynamic stability and reactivity, may lead to new and interesting reagents.

To the best of our knowledge, *O*-acyl selenophosphates **2** have not been the subject of systematic studies. Nonetheless, the reaction of monoselenophosphoric acid salts **1** with acyl chlorides has been reported to yield *O*-acyl derivatives **2** exclusively,[5] even though monoselenophosphoric acid salts **1** are ambidentate nucleophiles.

We have synthesized a wide range of mixed anhydrides: *O*-acyl monoselenophosphates, monoselenophosphonates and monoselenophosphinites **2**, and also investigated their thermodynamic stability and reactivity (Scheme 1).

The results of our experiments are presented in Table 1. Syntheses of type **2** compounds were complete after 15 min at room temperature in THF solvent. Subsequently, we observed that some mixed anhydrides of type **2** isomerised to their *Se*-acyl derivatives **3**. The diagnostic ^{31}P NMR coupling constant $^{1}J_{P–Se}$ was useful for monitoring the isomerisation process.[6] The yield of isomerised product depended on the substituents at the P and C_{acyl} atoms (see Table 1). Cyclic derivatives **2a–b**, **2e–f** (entries 1, 2, 5 and 6) displayed higher degrees of isomerisation than acyclic derivatives **2k–n** (entries 11–14). Higher yields of *Se*-acyl derivatives **3** were observed for alkyl carboxylic acid mixed anhydrides **2b**, **2f** and **2l** (entries 2, 6, 12) than for aryl carboxylic acid mixed anhydrides **2a**, **2e** and **2k** (entries 1, 5, 11). The anhydrides containing electron-withdrawing (**2d**) and electron-donating (**2c**) groups attached to their carboxyl functionalities could not be isomerised to a corresponding **3** derivative, whereas this was seen for compounds **2a** and **2e**. This observation excludes the possibility that the isomerisation takes place *via* an ionic mechanism.



Scheme 1 The synthesis of mixed anhydrides of types **2** and **3**.

When a mixture of anhydrides **2h** and **2o** were stirred together at room temperature overnight, acyl group exchange was observed that lead to the formation of all possible anhydrides (**2g**, **2h**, **2o** and **2p**). Moreover, there was no isomerisation of these anhydrides either in the mixture or separately (Table 1, entries 7, 8, 15, and 16). When a mixture of **2b** and **2k** was stirred overnight, acyl exchange again occurred and anhydrides **2a**, **2b**, **2k**, and **2l** were formed. In this case however, isomerisation was observed in the mixture and derivatives **3a**, **3b**, **3k** and **3l** were formed respectively—similar to the behaviour of the separate anhydrides (Table 1, entries 1, 2, 11, and 12). As can be seen, the rapid acyl group exchange of type **2** compounds is responsible for the formation of crossover products **3a** and **3l**. The most interesting behaviour of all was observed for two mixtures; one of **2b** and **2o**, and the other of **2k** and **2p**. Upon acyl group exchange, all possible anhydrides were observed. However in these mixtures, only **3b** plus **3a** and **3k** plus **3l** were formed respectively. We can therefore conclude (i) acyl group exchange is more rapid than isomerisation and (ii) isomerisation of one type **2** anhydride cannot initiate the isomerisation of another (*i.e.* there is no entrainment effect).

In the next stage of the study we took further steps to verify our proposed isomerisation mechanism. Our working hypothesis assumed O–C(O) bond homolysis and formation of monoselenophosphoric and carbonyl radicals. Further recombination *via* selenium could thus afford the isomeric derivatives **3**.

We therefore performed the reactions of monoselenophosphoric acid salt **1a** with various chloroformates (Scheme 2 and Table 2, R^3 = alkoxy or aryloxy). ^{31}P NMR analysis of the crude reaction mixtures indicated that *Se*-alkoxycarbonyl-monoselenophosphates **5** were the major products together with traces of *O*-alkoxycarbonyl-monoselenophosphates **4**. This means that isomerisation is very rapid and occurs upon formation of the type **4** compound.

Surprisingly, in the reaction of salt **1a** with benzyl chloroformate, the *Se*-benzyl ester **6a** was obtained, probably *via* decarboxylation of **4a** or **5a**. **5a** was also detected and isolated from the reaction mixture (Table 2). The formation of **6a** in the mixture supports the hypothesis of O–C(O) bond homolysis. The benzyloxycarbonyl and monoselenophosphoric radicals can react together to give compound **5a**, or undergo decarboxylation to give a benzyl radical. This radical may then react with **4** or a monoselenophosphoric radical to afford **6a**. Decarboxylation of the benzyloxycarbonyl radical is very rapid,[7] meaning the

† Electronic Supplementary Information (ESI) available: Experimental conditions and characterisation of all presented compounds. See http://www.rsc.org/suppdata/cc/b5/b502473k/

*rachon@chem.pg.gda.pl

