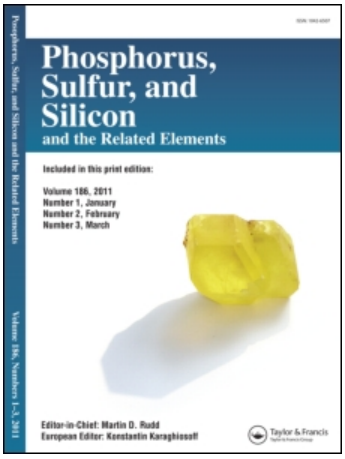

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Gerasimos M. Tsivgoulis[a]; Demetrios N. Sotiropoulos[a]; Panayiotis V. Ioannou[a]
[a] Department of Chemistry, University of Patras, Patras, Greece

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DECOMPOSITION OF ALKYLARSONIC ACIDS BY ACYLATING AGENTS

GERASIMOS M. TSIVGOULIS, DEMETRIOS N. SOTIROPOULOS and PANAYIOTIS V. IOANNOU†

Department of Chemistry, University of Patras, Patras, Greece

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Benzylarsonic acid is decomposed by palmitoyl chloride, slowly in the absence and rapidly in the presence of pyridine, giving benzyl chloride. Benzylarsonic acid is decomposed by palmitic anhydride in the presence, but not in the absence, of pyridine giving benzyl palmitate and benzyl pyridinium cation.

Key words: Alkylarsonic acids; acylating agents; decomposition.

INTRODUCTION

Aromatic arsonic acids, e.g. *p*-arsanilic acid, can be acylated with acyl chlorides without rupture of the, relatively strong,[1] C—As bond giving products of pharmaceutical interest.[2] Reactions of aliphatic arsonic acids with acylating agents, e.g. acyl halides or acid anhydrides, to the best of our knowledge have not been reported. Herein, we report on these reactions which bring about the decomposition of alkylarsonic acids under very mild conditions, giving products which depend on the nature of the acylating agent and the presence or absence of base.

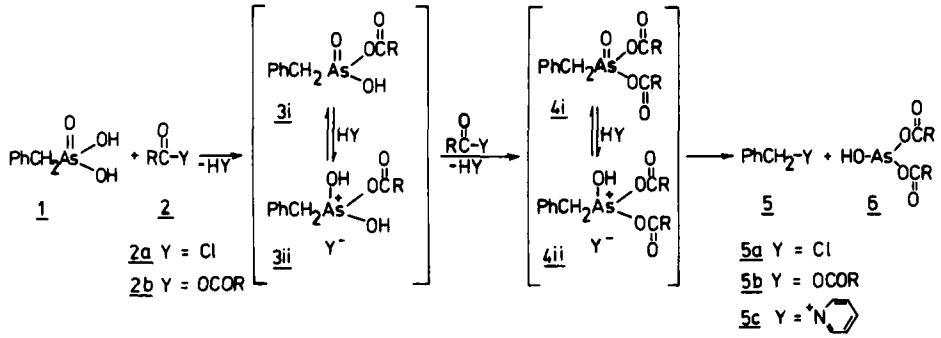
RESULTS AND DISCUSSION

In order to facilitate product identification by TLC, IR and ^{1}H-NMR we selected benzylarsonic acid (**1**) palmitoyl chloride (**2a**) and palmitoyl anhydride (**2b**). The C—As bond in this acid is weak, being ruptured by hot aqueous mineral acids much faster than in phenylarsonic or ethylarsonic acids.[1,3]

In Scheme 1 the origin of products is shown. Because in no case did we detect benzyl alcohol (TLC, ^{1}H-NMR) the reaction (1), which is analogous to the retro-Arbusov reaction

$$2PhCH_2As(O)(OCOR)_2 \longrightarrow 2PhCH_2OAs(OCOR)_2 \xrightarrow{H_2O} 2PhCH_2OH + As_2O_3 + 4RCOOH \quad (1)$$

observed in thermal treatment of alkanearsonic esters in the absence[4] and in the presence of alkyl halides,[5] does not take place under our conditions. We also did not detect As_2O_5 (magnesia mixture test). Intermediates **3ii** and **4ii** are plausible since compounds of the type $RAs^+(OR')_2(OR'')$ have been detected[5] and salts of the type $[RAs(OH)_3]X$ have been isolated.[1]



SCHEME 1

Benzylarsonic acid (**1**, 1 mmol) is decomposed slowly by palmitoyl chloride (**2a**, 2 mmol) (61% and 88% decomposition after 11 and 27 days, at room temperature, respectively) giving after working up benzyl chloride (**5a**) and arsenic trioxide. The slowness of the reaction is probably due to the very small solubility of **1** in dichloromethane and to the slow conversion of the modestly activated **3** to the activated, towards nucleophilic attack, **4**. Attack then by Cl^- at the benzylic carbon of **4** gives **5a** and **6** which hydrolyses according to equation (2) either by traces of water in the system or by the work up.

$$2HOAs(OCOR)_2 + H_2O \longrightarrow As_2O_3 + 4RCOOH \qquad (2)$$

That formation of **4** is required for the decomposition of arsonic acids was also shown by the experiment where 1 mmol of **1** reacted with 1 mmol of **2a** and 1 mmol of pyridine. In this case only 66% decomposition took place after 24 days reaction. Evidently shortage of **2a** did not allow rapid formation of **4ii**. When the amounts of **2a** and pyridine increased to 2 mmol each, then the decomposition of **1** was quite fast (78% and >99%, decomposition in 30 min and 30 days respectively). In all cases benzyl chloride (**5a**) was the sole organic product apart from palmitic acid.

Control experiment (1 mmol of **1** and 2 mmol of pyridinium hydrochloride) revealed <2% decomposition after 11 days at room temperature. A very mild activation towards nucleophilic attack may, in this case, occur *via* hydrogen bonding:

$$[PhCH_2As(OH)_2O \ldots H \ldots py]^+Cl^-$$

A stronger activation can result from complete protonation of **1** by e.g. hot aqueous hydrochloric acid and this explains its facile decomposition into benzyl chloride.[3] The hydrolysis of **1** by hot sulfuric acid is more complicated due to oxidizing properties of the acid.[1,3]

In contrast to palmitoyl chloride (**2a**) palmitic anhydride (**2b**) was virtually inert against benzylarsonic acid (**1**). Thus, <0.1% decomposition has been found after 9 days reaction of 1 mmol of **1** and 2 mmol of **2b**. In this case acylation to **3ii** and/or **4ii** did not occur to any great extent [as the anhydride (**2b**) was, by ^1H-

NMR, the sole organic species] and a free fatty acid is a very poor nucleophile. However, if 2 mmol pyridine was included then complete dissolution was observed after 5 days indicative of formation [no anhydride (**2b**) was seen by TLC and ^{1}H-NMR] and decomposition of **4i** to dichloromethane soluble products. Due to the equilibrium (3), **4ii** can be attacked by $RCOO^-$, by pyridine, or both. After 12 or

$$RCOO^-pyH^+ \rightleftharpoons RCOOH + py \quad (3)$$

25 days reaction, work up showed that 55% decomposition has taken place and benzyl palmitate (**5b**) (20%), benzyl pyridinium benzylarsonate (35%) and benzylarsonic acid (10%) were found.

Palmitic acid (2 mmol) alone or in the presence of pyridine (2 mmol) does not activate the arsonic acid (**1**) to any measurable extent for after 11 days reaction at room temperature <0.1% decomposition took place.

Reaction of propylarsonic acid (1 mmol) with palmitoyl chloride (2 mmol) and pyridine (2 mmol) lead to a 52% decomposition in 2 h, which is less than that found for benzylarsonic acid (**1**). These results are in accordance with the relative strengths of the C—As bonds in these alkylarsonic acids.

Decomposition of alkylarsonic acids *via* the formation of **4** seem to be much more facile than decomposition *via* protonation (ethylarsonic acid resists decomposition by hot aqueous hydrochloric acid[3]).

EXPERIMENTAL

Benzylarsonic[6] and propylarsonic[6] acids were prepared by the Meyer reaction. Palmitoyl chloride (b.p. 147–150°C/1 mmHg) was prepared from palmitic acid and redistilled thionyl chloride. Palmitic anhydride was prepared from palmitic acid and dicyclohexylcarbodiimide in dry carbon tetrachloride. Pyridine was distilled from sodium hydroxide and kept over activated A4 molecular sieves. Analytical reagent grade carbon tetrachloride and dichloromethane were dried over activated A4 molecular sieves.

TLC were run on microslides coated with Merck silica gel H. Proper controls were always cochromatographed. Developing solvents were for the fatty organic compounds ether/hexane 1:8 v/v and for arsonic acids methanol/conc. aq. ammonia 5:1 v/v. Visualization was effected by iodine vapors and by spraying with 35% sulfuric acid and charring. IR were run in KBr pellets on a Perkin Elmer model 577 spectrometer. ^{1}H-NMR were run on a Varian model T-60A, using CCl_4 or D_2O as solvents and TMS or DSS as internal standards.

Arsenic trioxide was determined titrimetrically with standard iodine solution.[7] Test for arsenic acid was done using magnesia mixture.

Reaction of arsonic acids with acylating agents in the absence and presence of pyridine. To a suspension of arsonic acid (1 mmol) in dry dichloromethane (5 ml) were added the acylating agent and pyridine and the system was stirred gently at room temperature. The quantities and reaction times are indicated in the results and discussion section. Filtration from unreacted arsonic acid and some arsenic trioxide (probably produced by traces of water, equation (2)) gave a clear organic phase which was treated with water (3 ml) to produce arsenic trioxide, *via* equation (2), which was removed by filtration. The organic and aqueous phases were then analysed. In the organic phase, apart from palmitic acid, benzyl cloride (**5a**) or benzyl palmitate (**5b**) were detected. Although benzyl alcohol is clearly separated from benzyl chloride (**5a**) in TLC and ^{1}H-NMR, it was not detected. The aqueous phase contained arsenic trioxide, traces of arsonic acid, and benzyl pyridinium benzylarsonate in the case of the reaction of **1** with **2b** in the presence of pyridine. The benzylarsonic acid can be precipitated by acidification, leaving the benzyl pyridinium peaks in the ^{1}H-NMR spectrum. Control experiments were run with pyridinium hydrochloride, palmitic acid and palmitic acid plus equivalent amount of pyridine.

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