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Silylation of *N*-(2-hydroxyphenyl)acetamide by methyl(organyl) dichlorosilanes: Structure and properties of resulting heterocycles

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ABSTRACT

The interaction of *N*-(2-hydroxyphenyl)acetamide with methyl(organyl)dichlorosilanes $RMeSiCl_2$ (R = Me, Vinyl, Ph) leads to the formation of 5-membered silaheterocyclic benzoxazasiloles **1a**-**3a**. According to data of NMR and FTIR spectra these compounds exist in equilibrium with 7-membered cyclic benzodioxazasilepines **1b**-**3b** which have the imidate structure. The structure of compound **1a** was proved by X-ray analysis. Compounds **1a**-**3a** are hydrolyzed to form silanols **4**–**6**. 3-Acetyl-2,2-dimethyl-2,3-dihydro-1,3,2-benzoxazasilole **1a** reacts with methanol and isopropanol and transforms into silanes **7** and **8**.

1. Introduction

N-(4-Hydroxyphenyl)acetamide, also known as paracetamol is one of the most popular and widely used drugs with analgesic and antipyretic properties [1]. Its chemical properties, pharmacological and clinical features have been extensively described over many decades. Recent investigations showed that its structural isomer, *N*-(2-hydroxyphenyl)acetamide, exhibits anti-inflammatory and antiplatelet activity [2]. Its toxicity is lower than that of aspirin and paracetamol [2e], that make possible its use for the prevention of cardiovascular disease and rheumatoid arthritis. The spectrum of the biological activity of *N*-(2-hydroxyphenyl)acetamide is rather wide and not completely understood. It was documented that this compound displayed the strong apoptotic activity in cells U87 GBM [3] and inhibited the growth of *Mycobacterium tuberculosis* H37Rv [4]. Probably, these encouraging results stimulated the search of more efficient methods of synthesis of *N*-(2-hydroxyphenyl)acetamide and an intensive study of its properties [5].

Silylation of compounds containing groups with the active hydrogen atom (N-H, O-H, S-H) is an important tool in chemistry [6]. Today, a silyl protecting groups are used widely in organic synthesis. Silylation of compounds results in reduced polarity, enhanced volatility, increased thermal stability and enables the GC-MS analysis of many compounds. Interaction of diorganyldichlorosilanes $RR'SiCl_2$ with amino acids leads to formation of 2-siloxazolidones-5 which have been successfully applied in asymmetric synthesis [7]. The 3-acetyl-5,7-di-tert-butyl-2,2-diorganyl-2,3-dihydro-1,3,2-benzoxazasiloles was obtained by reaction between *N*-(3,5-di-tert-butyl-2-hydroxyphenyl)acetamide and (dimethyl)dichlorosilane or (diphenyl)dichlorosilane in tetrahydrofuran [8]. Recently, we synthesized a new heterocyclic 4-acetyl-2,2-dimethyl-3,4-dihydro-2H-1,4,2-benzoxazasiline via reaction of *N*-(2-hydroxyphenyl)acetamide with Me_3SiCl and followed by transsilylation of the resulting *N*-(2-(trimethylsilyloxy)phenyl) acetamide with chloromethyl(dimethyl)chlorosilane [9]. We are continuing the investigation of Si-containing 2-acetamidophenols. We have studied the interaction of *N*-(2-hydroxyphenyl)acetamide with methyl(organyl)dichlorosilanes $RMeSiCl_2$ (R = Me, Vinyl and Ph) and here we report the obtained results.

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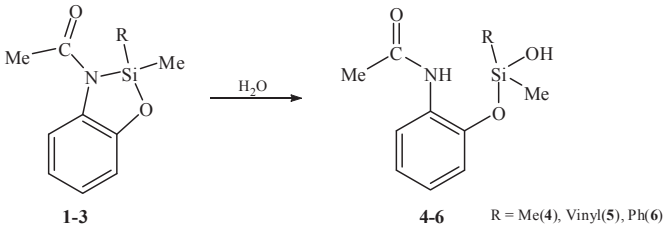
2. Results and discussion

2.1. Synthesis

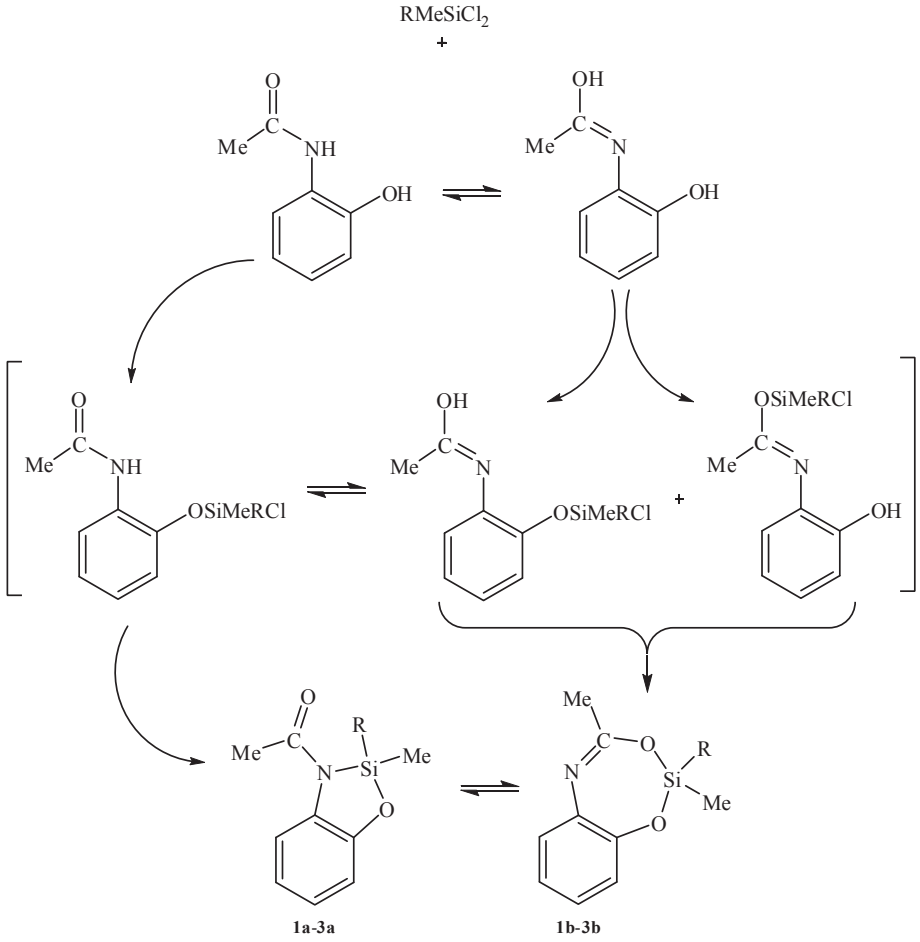
N-(2-Hydroxyphenyl)acetamide reacts with methyl(organyl) dichlorosilanes $RMeSiCl_2$ (R = Me, Vinyl and Ph) in benzene to give compounds **1**–**3** with moderate yields (58–67%, Scheme 1). Due to the poorly solubility of *N*-(2-hydroxyphenyl)acetamide in aprotic solvents the reaction proceeds under heterogeneous condition. Possible this factor leads to a lowering of yields of compounds **1**–**3.** Reaction was carried out in the presence of triethylamine Et_3N as an acceptor of hydrogen chloride. After removal of the solvent compounds **1**–**3** were isolated by vacuum distillation as colorless, viscous, hygroscopic liquids. The ^1H NMR spectra of the freshly distilled compounds **1**–**3** contain the signals of two tautomers: amides **1a**-**3a** and imidates **1b**-**3b**. The reason of their formation may be caused by the existence of tautomerism of initial *N*-(2-hydroxyphenyl)acetamide or of its O-silylated derivative or of compounds **1**–**3** (Scheme 1). These processes may be concurrent. It should be noted that the amide-imidate tautomerism of organic anilides was studied by spectral and quantum-chemical methods [10]. Our previous investigation showed that of *N*-(2-hydroxyphenyl)acetamide easy reacts with Me_3SiCl forming O-TMS-derivative [9]. It is beyond question that the formation of O-silylated intermediate in the first stage takes place.

The monocrystals of the amide **1a** were obtained by the spontaneous crystallization of freshly distilled compound **1**. The spontaneous crystallization was caused by cooling of the glass vessel with substance to liquid nitrogen temperature. Compounds **1**–**3** are sensitive to air moisture. So, for example, treatment of the thin layer of crystals of amide **1a** by stream of warm air leads to Si-N bond cleavage and formation of the corresponding silanol - *N*-[2-(hydroxydimethylsilyloxy)phenyl]acetamide **4** (Scheme 2). Compound **4** is a powdery substance which is soluble in benzene, chloroform, acetonitrile. Unfortunately we have failed to obtain single crystal of this compound for X-ray analysis. Silanol **4** is extremely hygroscopic (absorbing moisture from air) and decomposes readily into *N*-(2-hydroxyphenyl)acetamide and unidentified polysiloxanes.

N-(2-{[Hydroxy(methyl)vinylsilyl]oxy}phenyl)acetamide **5** and



Scheme 2. Hydrolysis of compounds **1**–**3**.



Scheme 1. Reaction of methyl(organyl)dichlorosilanes **1**–**3** with *N*-(2-hydroxyphenyl)acetamide.