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Synthesis of resorcinarene phosphonium salts and the effect of counteranion on their structure

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ABSTRACT

An efficient method for the synthesis of resorcinarene phosphonium salts, obtained from benzyl derivatives of resorcinarene, has been described. An effect of anion on the stability and structure of phosphonium salts of resorcinarenes has been discussed.

1. Introduction

Phosphorus compounds play an extraordinarily important role in living organisms, being the building components of nucleic acids. Due to a vast array of chemical species that may be formed by phosphorus, its compounds are also very frequently employed in organic synthesis.[1] One of such classes of phosphorus compounds comprises phosphonium salts. Phosphonium salts are synthesized in solution by a broad array of methods,[2] which include reactions of phosphines with alcohols or oxiranes, with aromatic organic halides in the presence of metal salts, or with diazo compounds. A conventional method of preparing alkyl-substituted phosphonium salts is the reaction of ternary phosphines with alkyl halides in appropriate organic solvents. These methods are applied for preparation of ionic liquids,[3] chiral catalysts of asymmetric reactions in the phase transfer processes,[4] bifunctional organo-catalysts.[5] Their use in material sciences[6] as well as medical sciences is especially interesting. In particular, these compounds find application as intracellular *anti*-oxidants,[7] *anti*-cholinesterase inhibitors,[8] or chemotherapeutics.[9] However, one of the most important features thereof is the capability for forming phosphonium ylides that are employed in the synthesis of vitamins, terpenoids, steroids, hormones, prostaglandins, amino acids, nucleotides, physiologically active compounds, transition metal complexes, and in polymerization processes.[10] The reported study describes a simple and efficient, one-step method of synthesis of phosphonium salts of resorcinarene. The compounds of this type are not described in the literature. They appear to be interesting as a base for obtaining, e.g., stilbene derivatives of resorcinarene, as well as cyclochiral heterocyclic resorcinarene derivatives.[11]

2. Results and discussion

The starting compounds for the synthesis were benzyl derivatives of resorcinarene, namely the hydroxy derivative **1a**[12] and the methyl ether derivative **1b**.[13] The triphenylphosphonium salts of resorcinarene, **2a**–**f**, were obtained by reacting the derivatives of resorcinarene, **1a** and **1b**, with triphenylphosphine (PPh_3) in the presence of selected mineral and organic acids in acetonitrile, as shown in Scheme 1. The selection of acids was guided by the range of their strengths, corresponding to the pKa values of from −9 to 4.8.

The reactions of stoichiometric proportions of reagents in refluxing acetonitrile gave the corresponding triphenylphosphonium salts of resorcinarene in yields up to 90%. The highest yield of the phosphonium salt of resorcinarene was obtained by using hydrobromic acid (HBr), a strong acid. In general, the yields of these compounds are higher when synthesized from the methyl ether derivative **1b**. Moreover, somewhat higher yields were obtained when strong mineral acids were used. Table 1 presents the yields of the reactions carried out using the resorcinarene derivatives **1a** and **1b**.

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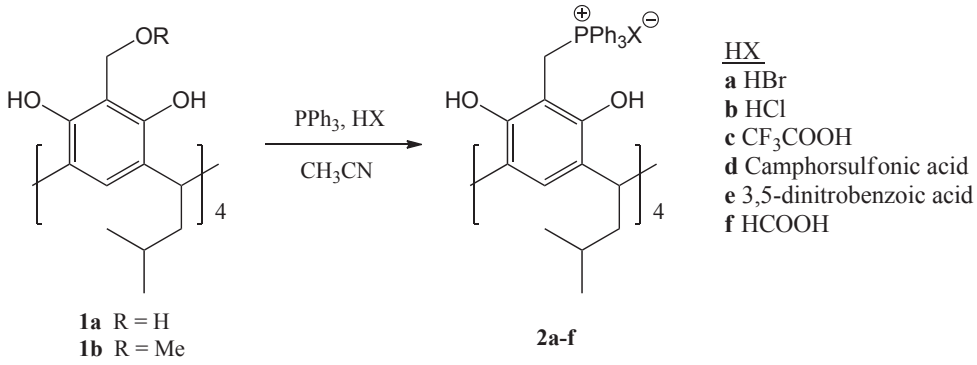

Scheme 1. The synthesis of triphenylphosphonium salts of resorcinarene, **2a**–**f.**

Table 1
The yields of the synthesis of phosphonium salts of resorcinarene, **2a**–**f**, with relation to the starting derivatives of resorcinarene **1a** and **1b**

HX	The yield of the synthesis of **2a**–**f** using the derivative **1a**; %	The yield of the synthesis of **2a**–**f** using the derivative **1b**; %
a HBr	78	90
b HCl	76	85
c CF3COOH	71	83
d Camphorsulfonic acid	71	83
e 3,5-Dinitrobenzoic acid	65	79
f HCOOH	64	74

The analysis of ^{1}H NMR spectra of the obtained salts demonstrates the relationship between the chemical shift of the protons of benzyl CH_2 group and the strength of the acids. In the ^{1}H NMR spectrum, signals of these protons are split into a doublet with a coupling constant of $^{2}J_{H-P}$=13.7 Hz, what is related to the ^{1}H–^{31}P spin–spin coupling. Such coupling constant values are known for other phosphine salts described in the literature.[14] On the other hand, no significant changes in chemical shift of CH_2 carbon are observed in relation to the strength of the acids. Not observed in the ^{31}P NMR spectra ^{1}H–^{31}P spin–spin coupling between the hydrogen atom of the benzyl group and the phosphorus atom. Chemical shifts of the phosphorus atom ^{31}P are typical for the phosphonium salts and contain in the range 22–26 ppm. The corresponding data are summarized in Table 2.

The observed situation was somewhat different in the case of using acetic acid. The reaction with acetic acid in tetrahydrofuran led to formation of red-brown color of the solution of the phosphine derivative of resorcinarene, **3a**. The inner salt was precipitated by adding diethyl ether to its concentrated solution in THF. The yield of product formation from the methoxy derivative of resorcinarene, **1a**, is slightly higher (68%) than that from the hydroxybenzyl derivative of resorcinarene, **1b** (62%). The ^{1}H NMR spectrum is poorly resolved, and the signal from CH_2 group is a broad singlet at δ=4.32 ppm. In this case, formation of the inner betaine-type salt is probably observed (Scheme 2). This is caused by quite strong alkaline character of the acetate ion formed in the reaction, which acetate ion pulls protons off the hydroxy group of resorcinarene, leading to formation of an inner salt. This observation is in agreement with the literature reports on the role of weak acids in formation of phosphonium salts and in the Wittig reaction.[16]

Table 2
Chemical shifts of hydrogen (^{1}H NMR) and carbon (^{13}C NMR) atoms of the benzyl group and phosphorus atom (^{31}P NMR) of the phosphonium salts of resorcinarene, **2a**–**f**

X^-	^{1}H NMR: δ CH_2 [ppm]	^{13}C NMR: δ CH_2 [ppm]	^{31}P NMR: δ P [ppm]	pKa[15]
2a Br^-	d, 4.72	41.7	22.2	–9
2b Cl^-	d, 4.93	41.7	22.3	–7
2c $CF3COO^-$	d, 4.64	41.7	22.2	0.52
2d Camphorsulfonic acid anion	d, 4.64	42.1	22.1	1.20
2e 3,5-Dinitrobenzoic acid anion	d, 4.47	41.3	26.1; 22.0	2.77
2f $HCOO^-$	2d, 4.54; 4.24	42.1; 41.0	26.1	3.75

The suggested mechanism of formation of phosphonium salts of resorcinarene is based on formerly described observations on the tendency of the derivatives **1a** and **1b** to lose a molecule of water (**1a**) or methanol (**1b**), especially under acidic conditions.[12,13] In the presence of strong acids, this leads probably to formation of a benzyl cation of resorcinarene as an intermediate. Its further reaction with a strong nucleophile, which is the: PPh_3 molecule, leads to formation of the triphenylphosphine salt of resorcinarene, which is stabilized by a weakly alkaline anion formed from the corresponding acid—see Scheme 3.

Formation of the betaine derivative of resorcinarene was observed also under acid-free conditions, as a result of prolonged heating of the derivatives **1a** and **1b** with PPh_3 at the boiling point of tetrahydrofuran. In this case, the reaction proceeds probably via a step of formation of the *o*-quinomethine intermediate, which undergoes the Michael reaction with a strong nucleophile, PPh_3, to form an inner salt of the betaine type—see Scheme 4.

The ^{1}H NMR spectrum of the derivative **3b** in DMSO-d_6 is diffuse and resembles the ^{1}H NMR spectrum of the product **3a** obtained using acetic acid. This may be explained by the possibility of forming many resonance structures of the derivative **3b**, being formally drawn and shown in Fig. 1. The number of possible resonance structures doubles if one takes both protons of hydroxy groups present in the resorcinarene unit into account. The chemical shift of protons of the benzyl group CH_2 appears at δ=4.26 ppm as a broad singlet.

An intermediate situation, indicating the presence of both forms, i.e., the triphenylphosphine salt of resorcinarene as well as its betaine form, is observed when formic acid is used. In this case, the ^{1}H NMR spectrum (DMSO-d_6) is also diffuse, although two doublets can be seen, one at δ=4.24 ppm, corresponding to the range of betaine structures, and the another at δ=4.54, indicating formation of the phosphine salt of resorcinarene—see Scheme 5.