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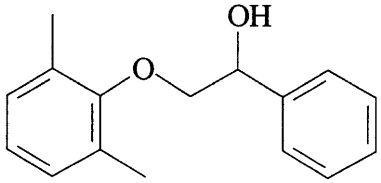
JMS Letters

Dear Sir,

Contribution to the Study of 2-Aryloxy-1-phenyl- and 2-Aryloxy-2-phenylethanols. Differentiation by Mass Spectrometry.

2-Aryloxy-1-phenylalkanols are important models for mechanistic studies of the alkaline cleavage of lignin.[1,2] Racemic 2-aryloxy-1-phenylpropanols are usually synthesized by the reduction of the corresponding ketones.[3,4] The borohydride reduction normally produces a mixture of stereoisomers, with the *erythro* isomer predominating over the *threo* isomer, and the composition of the diastereoisomeric mixture can be determined by ^{1}H NMR spectroscopy.[5]

Looking for a stereoselective synthesis of new analogues of mexiletine, an antiarrhythmic drug, we were interested in 1-phenyl-2-(2,6-xylyloxy)ethanol (**1**).



1

We tried to obtain **1** by nucleophilic ring opening of styrene oxide with 2,6-dimethylphenate, but S_N2 ring opening of unsymmetrical epoxides is an unselective process[6–8] and leads to a mixture of both possible alcohols **1** and 2-phenyl-2-(2,6-xylyoxy)ethanol (**2**), to our knowledge not described in the literature.

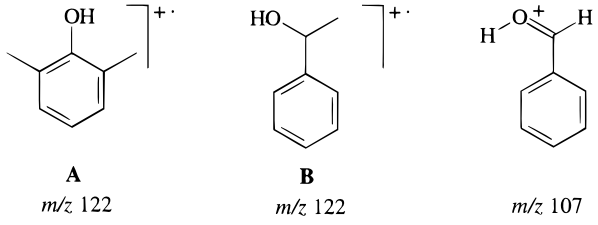
Alcohols **1** and **2**, isolated by silica gel chromatography, show in Lucas assay the typical behaviour of benzylic and primary alcohols, respectively; anyway, at least 50 mg have to be destroyed for this analysis. ^{1}H and ^{13}C NMR (200 MHz) spectra of these two constitutional isomers are similar and do not allow a reliable identification. We therefore investigated the possibility of a real discrimination through mass spectrometry. The mass spectra were recorded with a Hewlett-Packard Model 5995c gas chromatograph/mass spectrometer at low resolution (Table 1).

As expected, **2** does not exhibit the molecular ion, the higher peak being at *m/z* 211 ($[M - 31]^+$). Furthermore, the two isomers differ in the relative abundances of the ions at *m/z* 107.

In Fig. 1, putative structures of higher *m/z* fragments in the mass spectrum of **1** are reported. These attributions were verified by studying the **1**-1-D (**3**) and **1**-OD (**4**) low-resolution mass spectra (Table 2). Partial deuterium substitution in the OH group was performed by diluting a sample of **1** with CD_3OD; **3** was obtained by reduction of the corresponding ketone with $LiAlD_4$. Structures were confirmed by ^{1}H NMR (300 MHz). From the mass pattern of deuterated analogues, we may conclude that only xylenol radical ion **A** does contribute to the *m/z* 122 peak; the isomeric radical ion **B** does not occur. In fact, carbynolic radical ion **B** would carry a deuterium atom when derived from both **3** and **4**, at the hydroxy and methyne groups respectively; this would increase the relative abundance of *m/z* 123 peak. Actually, the *m/z* 123 peak is almost as large as the base peak in **4**. The same peak reflects the ^{13}C isotopic abundance in the mass spectra of both **1** and **3**, being more than 10-fold smaller than the base peak. Incidentally, cleavage of the xylyloxy alkyl bond should occur with transfer of hydrogen (or deuterium) from the hydroxy to the ether oxygen, as shown in Scheme 1.

Table 1. Mass spectra of compounds 1 and 2

Compound	*m/z* [relative intensity (%)]
1	242 (8) ($[M]^{+\cdot}$), 122 (100), 121 (14), 107 (44), 91 (27), 79 (40), 77 (49)
2	211 (4) ($[M-31]^+$), 122 (100), 121 (25), 120 (34), 107 (27), 91 (43), 79 (14), 77 (32)



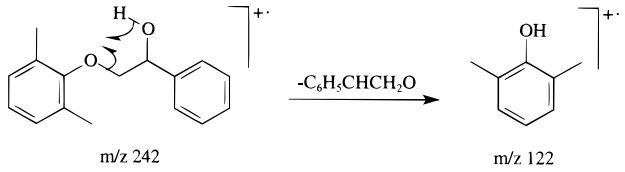
A *m/z* 122 **B** *m/z* 122 *m/z* 107

Figure 1. Putative structures of fragments in the mass spectrum of **1**.

Table 2. Mass spectra of compounds 1, 3 and 4[a] (higher *m/z* values shown only)

m/z	242 **1**	243 **3**	243 **4**
244	—	2	1
243	1	9	7
242	8	—	8
123	9	9	78
122	100	100	100
121	14	12	—
108	3	21	31
107	44	18	38

[a] **1** = 2,6-$(CH_3)_2C_6H_3OCH_2CH(C_6H_5)OH$;
3 = 2,6-$(CH_3)_2C_6H_3OCH_2CD(C_6H_5)OH$;
4 = 2,6-$(CH_3)_2C_6H_3OCH_2CH(C_6H_5)OD$.



m/z 242 m/z 122

Scheme 1.

We can conclude that differences between the fragmentation pathways of 2-aryloxy-1-phenyl- and 2-aryloxy-2-phenylethanols can be utilized in a useful method for their identification.

Yours,

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