

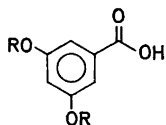
## A Simple Synthesis of Olivetol

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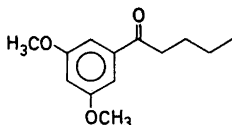
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Olivetol (3,5-dihydroxy-1-pentylbenzene) **5**, was first obtained by degrading the lichen acid, olivetonic acid.<sup>1</sup> Asahina, who isolated the substance, and several others,<sup>2-6</sup> have described syntheses of olivetol, but they usually give poor yields. The renewed attention to the psychotomimetically active components of hashish (marihuana) has made it desirable to develop a simple way of preparing olivetol, since the syntheses of those compounds often involve olivetol.<sup>6-12</sup>

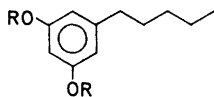
We now report an improved synthesis of olivetol, starting from the commercially available  $\alpha$ -resorcylic acid, **1**, which is methylated to 3,5-dimethoxybenzoic acid, **2**, by means of dimethyl sulphate.<sup>4</sup> The acid **2** is converted to 1-(3,5-dimethoxyphenyl)-1-pentanone, **3**, by reaction with butyllithium. To prevent the consumption of two moles of butyllithium the lithium salt of the acid is formed *in situ* with lithium hydride rather than with lithium hydroxide<sup>13</sup> since the latter involves isolation and drying of the salt.



1. R = H  
2. R = CH<sub>3</sub>



3.



4. R = CH<sub>3</sub>  
5. R = H

Catalytic hydrogenation of the ketone with palladium on carbon<sup>14</sup> gives a quantitative yield of olivetol dimethyl ether, **4**. The final demethylation is performed with hydroiodic acid as described by Asahina.<sup>2</sup>

*Experimental.* Melting points were determined on a Kofler micro hot stage. IR spectra were recorded on a Perkin Elmer No. 257 instrument. The NMR spectra were obtained on a Varian A-60 spectrometer using CDCl<sub>3</sub> solutions, with tetramethylsilane as internal standard.

1-(3,5-Dimethoxyphenyl)-1-pentanone, **3**. To a solution of 3,5-dimethoxybenzoic acid,<sup>4</sup> **2** (18.2 g, 0.1 mole), in dry tetrahydrofuran (250 ml) was added lithium hydride (1 g, 85% LiH). The reaction mixture was stirred for 14 h and then refluxed for 0.5 h. The solution was kept under inert atmosphere during the whole experiment. A solution of butyllithium in ether<sup>15</sup> (ca. 1.3 M) was added under stirring and ice-cooling until the reaction mixture gave a positive Gilman test.<sup>16</sup> Addition of ice-water (500 ml), extraction with ether, drying (MgSO<sub>4</sub>) of the organic phase and removal of the solvent under reduced pressure, gave a light yellow oil, which was dissolved in an equal volume of ethanol (99.5%) and was kept in the refrigerator. Colourless crystals were obtained after one night and were collected. Evaporation of the mother liquor to half the volume gave a second crop. Total yield 18.3 g (83%) 1-(3,5-dimethoxyphenyl)-1-pentanone, m.p. 42–44°C (Reported m.p. 42–43°C,<sup>2</sup> 53°C.<sup>4</sup>) The ketone was further characterized by its IR and NMR spectra. IR:  $\nu_{\max}$ (CHCl<sub>3</sub>) 2970, 1688, 1603(s), 1465, 1435, 1162(s), and 830(w) cm<sup>-1</sup>. NMR: (CDCl<sub>3</sub>)  $\delta$  7.09(d, 2H), 6.64(t, 1H), 3.82(s, 6H), 2.91(t, 2H), and 2.1–0.7(broad m, 7H).

Olivetol dimethyl ether, **4**. The ketone **3** (5.64 g, 0.025 mole), in methanol (200 ml) was hydrogenated at room temperature and atmospheric pressure, with 20% Pd(OH)<sub>2</sub> on carbon<sup>14</sup> (0.66 g) as catalyst. The theoretical amount of hydrogen was consumed in 2–3 h. The solution was filtered and the solvent removed under reduced pressure. The resulting oil, characterized as olivetol dimethyl ether by its IR and NMR spectra,<sup>6</sup> was used in the demethylation step without further purification.

Olivetol, **5**. The dimethyl ether **4** (4.88 g, 0.023 mole) and HI ( $d=1.7$ , 40 ml, decolorized with red phosphorus<sup>2</sup>) was stirred 3 h at 115–

125°C under inert atmosphere. The mixture was poured into ice water (100 ml) and extracted with methylene chloride. The organic phase was washed with water, dried over  $MgSO_4$  and the solvent removed under reduced pressure. Distillation of the resulting oil, gave pure olivetol, 3.5 g (76 %), b.p. 160–170°C/3–4 mm, characterized by its IR and NMR spectra.<sup>6</sup>

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## Mass Spectrometric Studies on Organic Selenium-Oxygen Compounds

### 2. Mass Spectra of Diphenyl Selenoxide and 4,4'-Dimethyl-diphenyl Selenoxide

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The behaviour of sulphoxides on electron impact has been thoroughly investigated and a survey showing the principles of their fragmentation is given by Budzikiewicz, Djerassi and Williams.<sup>1</sup> Up to now, however, nothing seems to be reported in the literature on mass spectrometric studies on selenoxides. In connection with work in progress on the behaviour of different kinds of organic selenium-oxygen compounds on electron impact the mass spectra of diphenyl selenoxide (I) and 4,4'-dimethyldiphenyl selenoxide (II) are given and briefly discussed here.



The discussion is limited to fragments containing the main selenium isotope <sup>78</sup>Se. The final fragmentation of the different non-selenious ions, proceeding along well-known routes,<sup>2</sup> is not considered here. The main fragmentation paths mentioned below are summarized in the scheme for the case of I. Transitions supported by appropriate metastable peaks are indicated by asterisks.

An initial skeletal rearrangement of the molecular ion to a selenenic acid ester ion, involving a migration of a phenyl group from selenium to oxygen, and followed by a cleavage of the Se–O bond to the ions  $(C_6H_5O)^+$  at  $m/e$  93 and  $(C_6H_5Se)^+$  at  $m/e$  157 forms a characteristic feature of the spectrum of I, Fig. 1. Such a 1,2-shift of a phenyl group on electron impact is well-known in the case of certain sulphoxides and some other types of sulphur-oxygen compounds<sup>1</sup> and has recently also been observed in esters of aromatic selenonic acids<sup>3</sup> and diaryl selenones.<sup>4</sup>

A noteworthy fragmentation process, supported by the appropriate metastable peak, is the elimination of the selenium