

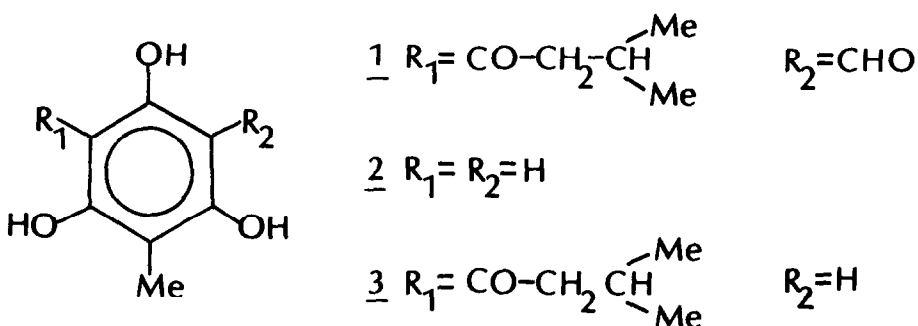
## THE SYNTHESIS OF GRANDINOL

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Recently, the isolation and structure elucidation of a new root inhibitor from the adult leaves of *Eucalyptus grandis* named grandinol 1, were reported.<sup>1</sup> Since its structure was proposed mainly on spectral data, the synthesis which definitively confirms this structure is presented.



Trinitrotoluene was reduced with Sn and HCl, the Sn precipitated with NaOH and the filtrate acidified with HCl and boiled under a stream of nitrogen to afford 2,4,6-tri-hydroxytoluene<sup>2</sup> 2 (32%): m.p. 210-211°;  $\nu_{\text{max}}$  (nujol): 3400 (b, OH) and 1620 cm<sup>-1</sup> (aromatic C = C). <sup>1</sup>H NMR (CDCl<sub>3</sub> + DMSO-d<sub>6</sub>):  $\delta$  1.98 (s, 3H, aromatic methyl), 5.96 (s, 2H, aromatic protons) and 8.03 (b, 3H, hydroxyl protons). Mass spectrum: M<sup>+</sup> 140 (100%), 139 (71%), 123 (14%), 111 (14%), 91 (15%) and 69 (24%).

Friedel-Crafts acylation of 2 (1 eq. of isovaleryl chloride and 10 eq. of  $\text{TiCl}_4$  in 1:1  $\text{CH}_2\text{Cl}_2 - \text{CS}_2$  at  $25^\circ$ ) produced the keto-phenol 3 as crystals (23%), m.p.  $148^\circ$ .  $\nu_{\text{max}}$  (KBr): 3300 (s, OH), 1630 (CO) and  $1605 \text{ cm}^{-1}$  (aromatic C = C).  $^1\text{H NMR}$  ( $\text{CDCl}_3 + \text{DMSO}-d_6$ ):  $\delta$  0.95 (d,  $J=7 \text{ Hz}$ , 6H,  $-\text{CH}-(\text{CH}_3)_2$ ), 1.97 (s, 3H, aromatic methyl), 2.16 (m, 1H,  $-\text{CH}-(\text{CH}_3)_2$ ), 2.93 (d,  $J=7 \text{ Hz}$ , 2H,  $-\text{CH}_2-\text{CH}-$ ), 6.00 (s, 1H, aromatic proton) and 11.36 (b, 3H, hydroxyl protons). Mass spectrum:  $M^+$  224 (17%), 209 (11%), 167 (100%), 140 (7%) and 69 (15%).

The last step in the synthesis, i.e., the formylation of the keto-phenol 3, was achieved using the dichloromethyl methyl ether reagent<sup>3</sup> and  $\text{TiCl}_4$  as catalyst ( $\text{CH}_2\text{Cl}_2$  at  $0^\circ$ , 1h) to give 1, (25%), m.p.  $130-132^\circ$ , (lit.<sup>1</sup> m.p.  $130-132^\circ$ ). The synthetic product showed spectral data identical with those reported for the natural product.<sup>1</sup>

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