



# A synthesis of racemic deliquinone

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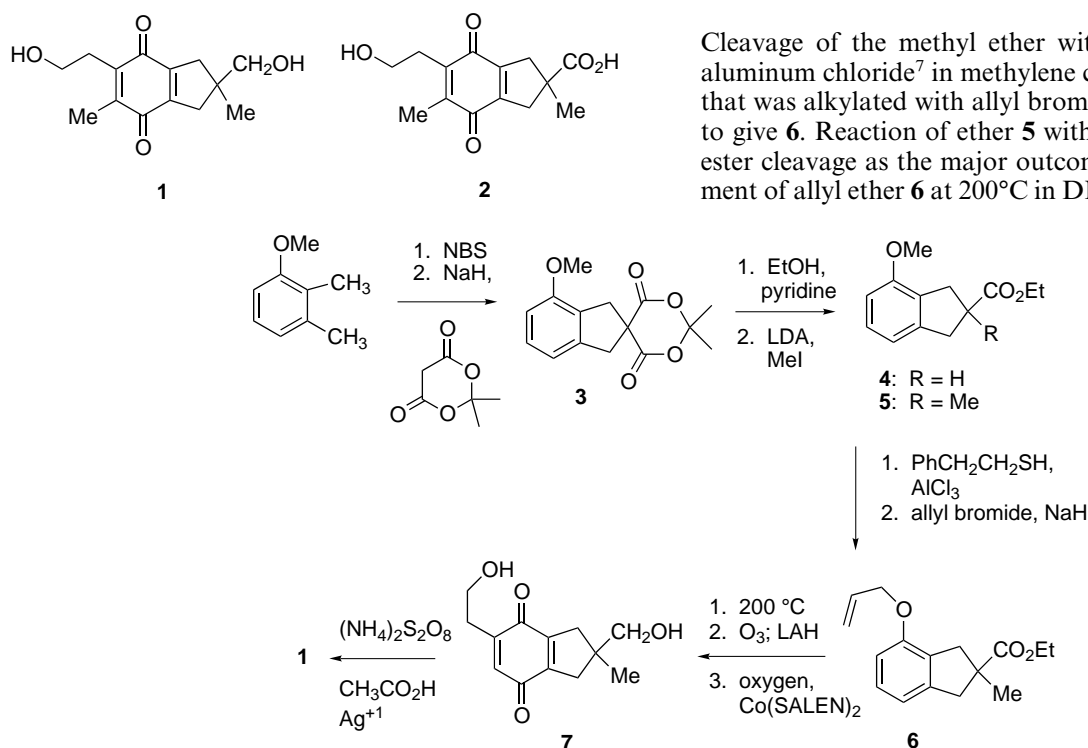
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**Abstract**—A 10-step synthesis of deliquinone is described. A key step in the synthesis is a persulfate-mediated radical addition to a quinone. © 2001 Elsevier Science Ltd. All rights reserved.

Deliquinone (**1**) was isolated from *Russula delica*.<sup>1</sup> Puraquinonic acid (**2**), a related compound, was isolated from *Mycena pura*.<sup>2</sup> It induces differentiation of HL-60 cells.<sup>3</sup> In view of our interest in quinone-containing natural products that inhibit viruses and cancer,<sup>4</sup> we sought to develop a flexible and scalable synthetic route. We report herein the first synthesis of deliquinone. This route should also be applicable to the synthesis of **2**. Clive and co-workers recently reported the synthesis of **2**.<sup>5</sup> This route is strategically distinct from their synthesis and represents a more direct approach.

Bromination of commercially available 2,3-dimethylanisole with NBS in CCl<sub>4</sub> provided a dibromide in 87% yield. Reaction of the dibromide with Meldrum's acid and NaH in DMSO afforded adduct **3**<sup>6</sup> (Scheme 1). The reaction with pyridine and ethanol resulted in esterification and decarboxylation to produce ester **4** in 87% yield. Deprotonation of **4** with LDA in THF at –78°C followed by the addition of methyl iodide produced ester **5** in 96% yield. This efficient four-step procedure constitutes a new way to generate an indane structure common to many terpenes.<sup>2</sup>

Cleavage of the methyl ether with phenethylthiol and aluminum chloride<sup>7</sup> in methylene chloride gave a phenol that was alkylated with allyl bromide and NaH in DMF to give **6**. Reaction of ether **5** with TMSI or BCl<sub>3</sub> led to ester cleavage as the major outcome. Claisen rearrangement of allyl ether **6** at 200°C in DMF provided a phenol



**Scheme 1.** Synthesis of deliquinone.

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in 77% yield from **5**. Cleavage of the alkene with ozone ( $\text{CH}_2\text{Cl}_2$ ,  $-78^\circ\text{C}$ ) followed by reduction with LAH in THF provided the alcohol in 63% yield. To achieve this yield, a solution of the ozonide in THF must be added to LAH in THF at  $0^\circ\text{C}$ . Oxidation of the phenol with salcomine ( $\text{Co}(\text{SALEN})_2$ ) and oxygen<sup>8</sup> generated quinone **7** in quantitative yield.

Reaction of quinone **7** with dimethyl zinc in THF from  $-78$  to  $-20^\circ\text{C}$  led to recovered starting material at low temperatures and led to decomposition of **7** at higher temperatures.<sup>9</sup> However, the reaction of **7** with acetic acid, ammonium persulfate and 1% silver nitrate in aqueous acetonitrile afforded **1**<sup>10</sup> in 68% isolated yield. This represents the first use of persulfate-mediated radical additions in natural products synthesis.<sup>11</sup> The  $^1\text{H}$  and  $^{13}\text{C}$  NMR of our synthetic material were identical to the spectra reported in the literature.<sup>1</sup>

This synthetic route will enable researchers to synthesize quantities of deliquinone and its analogs. As seen in the transformation of **7** into **1**, the use of persulfate and a catalytic amount of a silver salt constitutes an effective way to produce alkyl radicals. Approaches to other members of the indane family of natural products will be reported in due course.

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10. Preparation of **1**: A mixture of quinone **7** (0.03 g, 0.108 mmol), acetic acid (1.5 equiv.), silver nitrate (0.2 equiv.) and ammonium persulfate (1.2 equiv.) in 0.5 mL of 1:1 acetonitrile:water was heated at  $65^\circ\text{C}$  for 3 h. The solution was diluted with methylene chloride. The organic layer was washed with water, dried over sodium sulfate and concentrated in vacuo. The crude residue was purified by preparative thin layer chromatography using 3:1 ethyl acetate:hexane to furnish compound **1** as a viscous yellow liquid in 68% yield.  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  187.0, 186.5, 147.2, 146.8, 142.8, 141.5, 70.2, 61.7, 43.0, 40.8, 40.7, 30.1, 25.1, 12.4. HRMS calcd for  $\text{C}_{14}\text{H}_{18}\text{O}_4$ : 250.1205; found: 250.1208.
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