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ANODIC OXIDATION OF 4-ALLYL-2-METHOXYPHENOL SYNTHESES OF DEMETHOXYASATONE AND DEMETHOXYISOASATONE

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Anodic oxidation of 4-allyl-2-methoxyphenol was carried out under various conditions, using an undivided cell, to afford two dienones (3 and 4) and two dimeric compounds (5 and 6). The dienone (4) was readily converted into demethoxyasatone (6), which was further subjected to photochemical reaction giving demethoxyisoasatone (7) in a good yield.

In connection with our synthetic study on asatone and related compounds,<sup>1,2</sup> we further examined anodic oxidation of 4-allyl-2-methoxyphenol (1) and obtained some interesting results remarkably different from those of 2,6-dimethoxy-4-allylphenol (2).<sup>3</sup>

An undivided cell with platinum electrodes was used. A solution of 4-allyl-2-methoxyphenol (1.65 mmoles) in MeOH (75 ml) containing  $\text{LiClO}_4$  (17.5 mmoles) as a supporting salt, was electrolyzed at room temperature for 1.5 h at a controlled potential of +1400 mV <u>vs</u> SCE.<sup>4</sup> The reaction solution was concentrated under reduced pressure below 40°C, and then separated by column chromatography [Polymer HP-255 / MeOH - H<sub>2</sub>O (95 : 5)] followed by preparative TLC [Kieselgel PF<sub>254</sub> / hexane - EtOAc (3 : 2 or 4 : 1)] to give four oxidation products ( $\frac{3}{2}$ ,  $\frac{4}{2}$ ,  $\frac{5}{2}$ , and  $\frac{6}{2}$ ) in 3, 8.5, 10, and 21% yields, respectively. Clearly, the dimer ( $\frac{6}{2}$ ) will be produced from the dienone ( $\frac{4}{2}$ ). In fact, dienone ( $\frac{4}{2}$ ), an oily substance, changed spontaneously at room temperature into the dimer ( $\frac{6}{2}$ ).

The structures of the two dienones (3 and 4) were determined on the basis of their spectral data [3: mp 56 - 56.5°C (from hexane);  $C_{11}H_{14}O_3$  (m/e 194(M<sup>+</sup>));  $V_{max}$  (film) 1680, 1650, and 1620 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 2.49(2H, br.d, J = 7Hz), 3.19(3H, s), 3.67(3H, s), 5.04(1H, br.d, J = 18Hz), 5.07(1H, br.d, J = 10Hz), 5.53(1H, d, J = 3Hz), 5.70(1H, m), 6.30(1H, d, J = 10Hz), and 6.68(1H, dd, J = 10,3Hz). 4 as a



colorless viscous liquid:  $C_{11}H_{14}O_3$  (m/e 194(M<sup>+</sup>));  $\mathcal{V}_{max}$ (film) 1690, 1660, and 1640sh cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 2.98(2H, br.d, J = 8Hz), 3.35 (6H, s), 5.11 (1H, br.d, J = 17Hz), 5.16(1H, br.d, J = 10Hz), 5.79(1H, m), 5.96(1H, d, J = 10Hz), 6.09(1H, br.s), and 6.72(1H, dd, J = 10,2Hz)]. One of the two dimeric compounds [5: mp 104 - 105°C (from hexane),  $C_{20}H_{22}O_4$ ] is regarded as dehydrodieugenol from its spectral data.<sup>5</sup> As described earlier, the remaining one (6) must be the Diels-Alder product of the dienone (4), having the following physical data: mp 77 - 78°C (from hexane);  $C_{22}H_{28}O_6$  [m/e 388(M<sup>+</sup>)];  $\mathcal{V}_{max}$ (KBr) 1735, 1710, and 1640 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 2.32(1H, dd, J = 15,7Hz), 2.58(1H, dd, J = 15,8Hz), 2.70 - 2.95(4H, complex), 3.05(4H, s),<sup>6</sup> 3.30(3H, s), 3.38(3H, s), 3.40(3H, s), 4.87 - 5.20(4H, complex), 5.42(1H, br.d, J = 6Hz), 5.50 - 6.12(2H, complex), 5.93(1H, d, J = 10Hz), and 6.27(1H, d, J = 10Hz). Of two possible structures (6 and 6'), the structure of this dimer should be represented by 6, as follows.

When irradiated in hexane using a pyrex filter (room temp., overnight), the dimer (6) was readily converted into demethoxyisoasatone (7) in a 60% yield [mp 133 - 134°C (from hexane);  $C_{22}H_{28}O_6$  (m/e 388(M<sup>+</sup>));  $\gamma_{max}$ (KBr) 1730 and 1645 cm<sup>-1</sup>;  $\delta$ (CDCl<sub>3</sub>) 2.35(2H, dd, J = 14, 6Hz), 2.74(2H, dd, J = 14,8Hz), 2.81(2H, s), 2.86(4H, s), 7 3.27(6H, s), 3.34(6H, s), 5.06(2H, br.d, J = 17Hz), 5.11(2H, C)

br.d, J = 10Hz), and 5.69(2H, m)]. In particular, the NMR spectrum of  $\frac{7}{2}$  strongly indicates that the carbon skeleton of  $\frac{7}{2}$  is quite similar to that of isoasatone which has a symmetric character.<sup>1</sup>

The anodic oxidation of 4-allyl-2-methoxyphenol (1) in MeOH was further carried out at a controlled current density of 1.5 mA·cm<sup>-2</sup>,<sup>8</sup> and monitored by HPLC<sup>9</sup> [3 (1.3%), 4 (37%), and 5 (11.5%) at 2 Faraday/mole; 3 (1.6%), 4 (68%), 5 (7.4%),<sup>10</sup> and 6 (4.6%) at 3 Faraday/mole].

Finally, we examined the anodic oxidation of 1 in the basic media containing excess 1M NaOH at a controlled current density of  $1.5 \text{ mA} \cdot \text{cm}^{-2}$ .<sup>11</sup> At 1 Faraday/mole dehydrodieugenol (5) was produced in an almost quantitative yield. In this case, it should be noted that any reaction product with a MeO group at the benzylic position has not been detected in contrast with the case of 2,6-dimethoxy-4-allyl-phenol (2).<sup>3</sup>

The present study indicates that such an asatone-type compound as 6 can be synthesized in a good yield through the corresponding dienone (4) which has been produced from 1 on anodic oxidation.

## References and Footnotes

- S. Yamamura, Y. Terada, Y. Chen, M. Hong, H. Hsu, K. Sasaki, and Y. Hirata, Bull. Chem. Soc. Jpn, 49, 1940 (1976), and references cited therein.
- 2. Asatone has been shown to have an antileukemic activity in mice [private communication from Dr. J. D. Douros (NIH)].
- 3. M. Iguchi, A. Nishiyama, Y. Terada, and S. Yamamura, Tetrahedron Letters, <u>1977</u>, 4511.
- 4. Electrolysis current was initiated at 115 mA, and then gradually decreased.
- 5. H. Erdtman, Biochem. Z., <u>258</u>, 172 (1933); C. H. Ludwig, B. J. Nist, and
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- 6. One of the three methine protons is included.
- 7. This signal becomes two doublets [ $\delta$  2.40(2H, d, J = 5Hz) and 2.73(2H, d, J = 5Hz)] on measurement of the NMR spectrum using  $C_6D_6$  as a solvent.
- 8. The working electrode potential (+750 mV  $\underline{vs}$  SCE) was almost constant.

- 9. The high performance liquid chromatography (HPLC) was carried out at 20 ± 0.1°C, using polymer HP-255 ( $\phi$  3 mm x 50 cm) [solvent system: MeOH H<sub>2</sub>O (95 : 5) containing 0.1M NaOH; flow rate: 0.75 ml/min].
- 10. Dehydrodieugenol (5) seems to be further oxidized.
- 11. The working electrode potential was gradually increased from +200 mV to +240 mV  $\underline{\rm vs}$  SCE.

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