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SYNTHETIC STUDIES ON ASATONE-TYPE NEOLIGNANS
OXIDATION OF 4-ALLYLPHENOLS WITH THALLIUM (III) NITRATE

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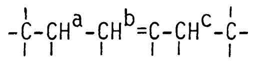
Oxidation of 4-allylphenols in MeOH has been carried out using thallium (III) nitrate to give two different types of reaction product. In the cases of 4-allylphenols with an electron-donating group (MeO), methoxylation takes place on the aromatic ring resulting in the formation of asatone-type compound as well as of 2,5-cyclohexadien-1-one. In the case of 4-allyl-2-methoxy-6-nitrophenol, however, the allyl group was attacked by the reagent to give three phenols.

Previously, many studies have been made on oxidation of phenols with thallium (III) salt by many workers, particularly by McKillop, Nogradi and their co-workers using thallium (III) nitrate trihydrate (TTN) in MeOH.[1]

In connection with the electrochemical oxidation of several phenols giving asatone (1)[2] and its related compounds,[3] we carried out oxidation of 4-allylphenols with TTN in MeOH and obtained some interesting results.

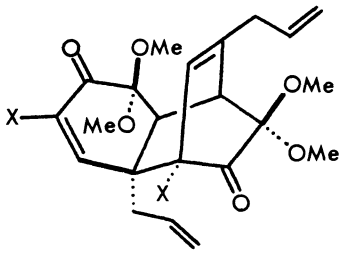
When treated with TTN (1.1 equiv) in MeOH at -40 °C for 1 h, eugenol (2) was readily converted into three oxidation products (3, 4 and 5) in 6, 33 and 17% yields, respectively. Among them, both 3 and 4 have been obtained on anodic oxidation of 2. Particularly, the latter is regarded as demethoxyasatone, which can be derived from the corresponding 2,4-cyclohexadien-1-one (6).[3] The structure of the remaining one (5) [$C_{20}H_{22}O_5$; m/e 240 (M^+- 102); ν_{max}(film) 3400br., 1730, 1640, 1600 and 1500 cm^{-1}; δ($CDCl_3$) 3.05(2H, d, J= 6.5Hz), 3.27(3H, s), 3.2-3.3(2H, superimposed on MeO signal), 3.38(3H, s), 4.30(1H, d, J= 6Hz), 4.50(1H, d, J= 2Hz), 4.7-5.1(4H, complex), 5.6-6.1(2H, complex), 6.05(1H, br.d, J= 6Hz) and 6.40(1H, s)][4] was determined on the basis of its spectral data coupled with the acetylation experiment [Ac_2O - pyridine (1 : 1), room temp., overnight] leading to the formation of the corresponding diacetate (7) [mp 140-143 °C (from hexane); $C_{24}H_{26}O_7$; ν_{max}(Nujol) 1770, 1730, 1630 and 1485 cm^{-1}; δ($CDCl_3$) 2.24(3H, s), 2.30(3H, s), 3.00(2H, d, J= 6.5Hz), 3.17 (3H, s), 3.38(3H, s), 3.35-3.45(2H, superimposed on MeO signal), 4.15(1H, d, J= 2Hz), 4.20(1H, d, J= 6Hz), 4.8-5.1(4H, complex), 5.5-6.05(2H, complex), 6.08(1H, br.d, J= 6Hz) and 6.87(1H, s)].[5]

As judged from the NMR spectrum of 5 (δ4.30, 4.50 and 6.05), a partial structure [A] must be present, in which the two doublets at δ4.30 and 4.50 are assignable to H^a and H^c, respectively. Furthermore, the double resonance experiments indicate that the broad doublet at δ6.05 is coupled with both H^a and H^c. From these data together with the remaining signals, two possible structures (5 and 8) are considered. However, the former (5) is adopted on the basis of the following result: on acetylation of 5, the signal at δ4.30 (H^a in 5) was observed at the almost same position (δ4.20 in 7) whereas the signal at δ4.50 (H^c in 5) was found in higher magnetic field (δ4.15 in 7), indicating that one of the two phenolic OH groups is close to H^c. Probably, the newly formed compound (5) is formed through a plausible intermediate (9).



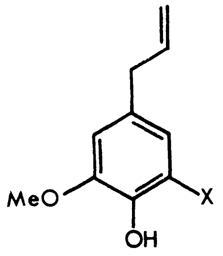
$-\overset{|}{\underset{|}{C}}-\underset{|}{C}H^a-\underset{|}{C}H^b=\underset{|}{C}-\underset{|}{C}H^c-\overset{|}{\underset{|}{C}}-$

[A]



1 X = OMe

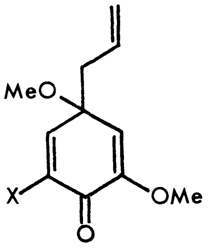
4 X = H



2 X = H

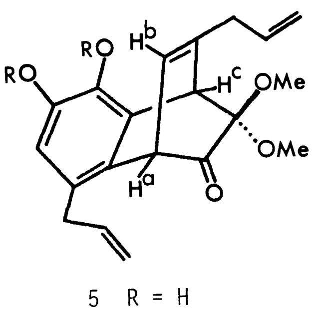
10 X = OMe

13 X = NO_2



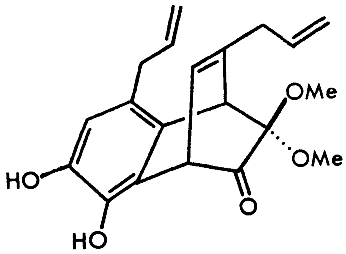
3 X = H

11 X = OMe



5 R = H

7 R = Ac



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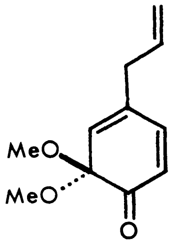

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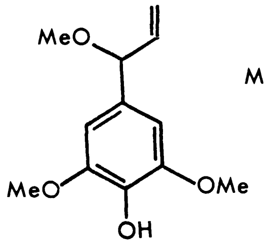

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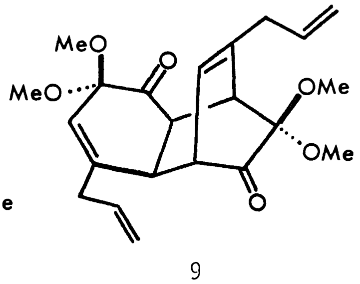

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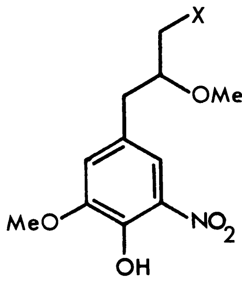
On oxidation with TTN (1.1 equiv) in MeOH (-50 - -40 °C, 1 h), 4-allyl-2,6-dimethoxyphenol (10) was readily converted into the corresponding 2,5-cyclohexadien-1-one (11) in 47 - 54% yield. In addition, the compound (12) was obtained as a minor product (5 - 7% yield). Both of them have been also produced on anodic oxidation of 10.[3,6]

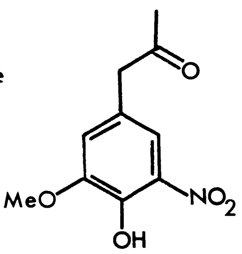
We further examined the oxidation of 4-allyl-2-methoxy-6-nitrophenol (13) having a strong electron-attracting group (NO_2). On treatment of 13 with TTN (1.1 equiv) in MeOH (0 °C, 3 h), the allyl group was attacked by TTN to give three phenols (14, 15 and 16) in 18 - 21, 35 - 42 and

0 - 4% yields, respectively, whose structures were based on their spectral data.[7] In this case, the double bond of the side chain is readily attacked by TTN rather than the phenolic OH group. Under essentially the same conditions as described above, safrol (17) was also oxidized with TTN (1.1 equiv) to afford three phenols (18, 19 and 20) in 25 - 30, 9 - 10 and 35 - 38% yields, respectively, whose structures were also established on the basis of their spectral data.[8]

In conclusion, in the cases of 4-allylphenols with an electron-donating group, methoxylation takes place on the aromatic ring. However, it seems to be difficult to make asatone-type compounds from the 4-allylphenol with such a strong electron-attracting group as NO_2.



14 X = NO_3
16 X = OH



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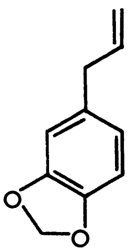
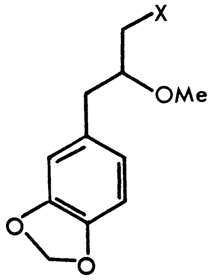
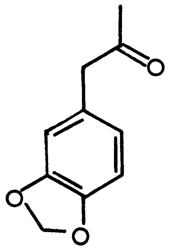


17



18 X = NO_3
20 X = OMe



19

References and Notes

1. A. McKillop, D.H. Perry, M. Edwards, S. Antus, L. Farkas, M. Nogradi, and E.C. Taylor, J. Org. Chem., 41, 282 (1976) and references cited therein; S. Antus, M. Nogradi, E. Baitz-Gacs, L. Radics, H.D. Becker, B. Karlsson, and A.M. Pilotti, Tetrahedron, 34, 2573 (1978); B. Karlsson, A.M. Pilotti, S. Antus, and M. Nogradi, Acta Chem. Scand. Ser. B, 32, 569 (1978).
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3. M. Iguchi, A. Nishiyama, Y. Terada, and S. Yamamura, Tetrahedron Lett., 1977, 4511; Chemistry Lett., 1978, 451; Analytical Lett., 1979, 1079.
4. The molecular formulae of each compound cited herein were based on their exact mass spectra except for the compounds (5) and (7). The molecular formula of 5 was estimated on the basis of that of 7, whose elemental analysis was carried out by Miss T. Sakai (Analytical Center, Meijo University).
5. The structure of 7 is also supported by its CMR spectrum: δ($CDCl_3$) 20.27(q), 20.57(q), 36.21(t), 38.96(t), 46.29(d), 49.45(q), 50.92(q), 53.20(d), 91.64(s), 116.54(t), 117.24(t), 122.17(d),* 132.24(s), 133.12(s), 134.00(d), 134.24(s), 135.35(d), 136.52(s), 140.86(s), 147.07(s), 167.28 (s), 167.63(s) and 195.23(s).

* This signal corresponds to two methine carbon atoms.

6. In this case, asatone (**1**) has not been found in the reaction mixture.

7. **14**: $C_{11}H_{14}N_2O_8$; m/e 302(M^+), 225, 208, 195 and 182; ν_{max}(film) 3250, 1730, 1630 and 1540 cm^{-1}; δ($CDCl_3$) 2.81(2H, d, J= 6Hz), 3.37(3H, s), 3.63(1H, qd, J= 6, 4.5Hz), 3.91(3H, s), 4.36(1H, dd, J= 12, 6Hz), 4.51(1H, dd, J= 12, 4.5Hz), 6.99(1H, d, J= 1.5Hz) and 7.49(1H, d, J= 1.5Hz).

   15: mp 101.5 - 103 °C (from EtOAc-hexane); $C_{10}H_{11}NO_5$; m/e 225(M^+); ν_{max}(Nujol) 3300, 1720sh., 1710, 1620 and 1550 cm^{-1}; δ($CDCl_3$) 2.22(3H, s), 3.70(2H, s), 3.92(3H, s), 6.97(1H, d, J= 2Hz) and 7.52(1H, d, J= 2Hz).

   16: $C_{11}H_{15}NO_6$; m/e 257(M^+), 227, 225, 165 and 152; ν_{max}($CHCl_3$) 3450br., 1625 and 1545 cm^{-1}; δ($CDCl_3$) 2.80(2H, d, J= 6Hz), 3.38(3H, s), 3.3-3.8(3H, complex), 3.92(3H, s), 7.03(1H, d, J= 2Hz) and 7.53(1H, d, J= 2Hz). On acetylation of **16** with Ac_2O-pyridine giving a diacetate, the complex signals at δ3.3-3.8 corresponding to the hydroxymethyl group in **16** were shifted to lower magnetic field [δ4.03(1H, dd, J= 11, 5Hz) and 4.17(1H, dd, J= 11, 5Hz)].

8. **18**: $C_{11}H_{13}NO_6$; m/e 255(M^+), 210, 178, 164, 149, 147 and 135; ν_{max}(film) 1630br., 1500, 1285 and 1250 cm^{-1}; δ($CDCl_3$) 2.75(1H, d, J= 7Hz), 2.79(1H, d, J= 6.5Hz), 3.35(3H, s), 3.60(1H, m), 4.32 (1H, dd, J= 12, 6Hz), 4.71(1H, dd, J= 12, 4Hz), 5.88(2H, s) and 6.6-6.8(3H, complex),

   19: $C_{10}H_{10}O_3$; m/e 178(M^+) and 135; ν_{max}(film) 1710, 1610 and 1495 cm^{-1}; δ($CDCl_3$) 2.12(3H, s), 3.55(2H, s), 5.90(2H, s) and 6.56-6.78(3H, complex).

   20: $C_{12}H_{16}O_4$; m/e 224(M^+), 207, 192, 179, 149 and 135; ν_{max}(film) 1610 and 1495 cm^{-1}; δ($CDCl_3$) 2.74(2H, d, J= 6.5Hz), 3.35(3H, s), 3.38(3H, s), 3.3-3.6(3H, superimposed on MeO signals), 5.90 (2H, s) and 6.6-6.8(3H, complex).

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