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EFFICIENT SYNTHESIS OF SEVERAL ANIBA AND MAGNOLIA NEOLIGNANS

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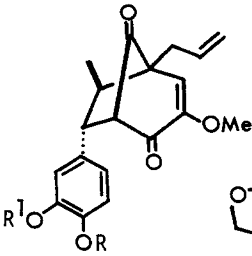
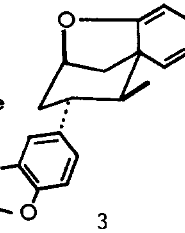
Summary: The novel neolignans isolated from the plants *Aniba burchellii*, *A. simulans* and *Magnolia denudata* have been efficiently synthesized by means of electrochemical method.

From view points of biological and physiological activities, the novel neolignans from *Aniba*[1] and *Magnolia*[2,3] species are quite attractive to us. In this field, a pioneering work was carried out by Buchi and Mak,[4] in which both guianin and futoenone were synthesized from 2-allyl-4,5-methylenedioxyphenol in short steps. On the basis of biogenetic consideration, we wish to describe efficient synthesis of the *Aniba* and *Magnolia* neolignans (1 ~ 5) and related compounds by means of electrochemical method.

A 30 ml glassy carbon (GC -20) beaker and a tip of platinum wire were used as an anode and a cathode, respectively, without separation, unless otherwise stated. When electrolyzed at a constant current [0.19 mA/cm^2 (*ca*. +600 mV *vs*. SCE)][5] in MeOH (25 ml) containing E-isosafrole (10 mM) as well as $LiClO_4$ (2 mM) as a supporting electrolyte, 2-allyl-4,5-dimethoxyphenol (6) (0.5 mM) was readily converted into a dienone (7)[6] in 87% yield. In the



1 : R·R^1= CH_2
2 : R = H, R^1= Me
14 : R = $CH_2C_6H_4OMe$-p, R^1= Me



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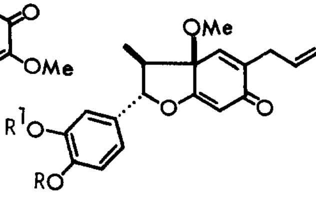
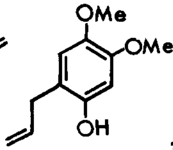


4 : R·R^1= CH_2
5 : R = R^1= Me



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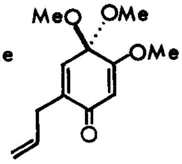

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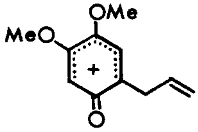

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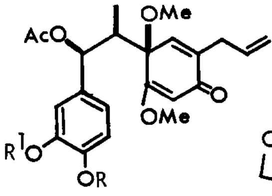
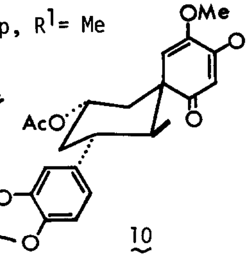


9 : R·R^1= CH_2
12 : R = R^1= Me



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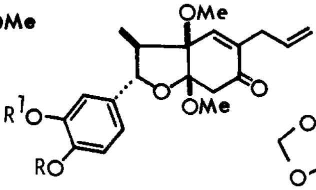
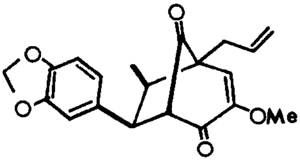


11 : R·R^1= CH_2
13 : R = R^1= Me



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case of aqueous CH_3CN, 2-allyl-5-methoxy-1,4-benzoquinone was obtained in 83% yield. However, on electrolysis of 6 in acidic media [MeOH - AcOH (2 : 1)][7] at a constant current [0.19 mA/cm^2 (+760 - 1040 mV vs. SCE)][5], the generated cation (8) reacted selectively with E-isosafrole in a manner of endo addition to afford one of the Aniba neolignans (1),[1,4] in 81% yield. We further carried out anodic oxidation of 6 in AcOH - CF_3COOH (4 : 1) containing n-Bu_4NBF_4, using platinum electrodes in an undivided cell [CCE at 40 mA (+1100 - 1400 mV vs. SCE)][5], to afford a desirable dimer (9)[8] in 4% yield, in addition to two main products (1 and 10[9]) in 29 and 26% yields, respectively. The dimer (9) was further treated with alc.KOH at room temperature to afford only a ketal (11)[10], which was then heated with Ac_2O - camphorsulfonic acid at 70 - 80 °C to give denudatin A (4)[2] in quantitative yield. Similarly, denudatin B (5)[2] was also synthesized, via 13,[11] from the corresponding dimer (12)[12] which was obtained in low yield on anodic oxidation of 2-allyl-4,5-dimethoxyphenol (6) in the presence of E-isoeugenol methyl ether.

When electrolyzed at a constant current [40 mA (+930 - 1090 mV vs. SCE)][5] in Ac_2O containing E-isoeugenol p-methoxybenzyl ether and n-Bu_4NBF_4 as a supporting electrolyte, 2-allyl-4,5-dimethoxyphenol (6) was readily converted into the corresponding dimer (14)[13] with a bicyclo[3.2.1]octane skeleton, in 55% yield, which was further heated in aq.AcOH at 55 °C to give one of the Aniba neolignans (2)[1], in almost quantitative yield.

Finally, anodic oxidation of 6 (1 mM) was carried out in AcOH - CF_3COOH (4 : 1) containing Z-isosafrole (6 mM) as well as excess n-Bu_4NBF_4 as a supporting electrolyte using platinum electordes in an undivided cell [40 mA (+750 - 1100 mV vs. SCE)][5] to afford futoenone (3)[4] and an epimer (15)[14] of 1, in 15 and 25% yields, respectively. The latter is produced on Diels-Alder reaction of the generated cation (8) with Z-isosafrole in a manner of exo addition, while futoenone (3) must be derived from the corresponding endo adduct.

We wish to thank Drs. K. Ito and T. Iida (Meijo University) for providing us with the IR and ^1H NMR spectra of denudatins A and B, futoenone and related neolignans.

References and Notes

1. J. B. Fernandes, O. R. Gottlieb, and J. G. S. Maia, Phytochemistry, 15, 1033 (1976); M. A. de Alvarenga, U. Brockson, O. Castro, O. R. Gottlieb, and M. T. Magalhase, ibid., 16, 1797 (1977).
2. T. Iida, K. Ichino, and K. Ito, Phytochemistry, 21, 2939 (1982); ibid., 22, 763 (1983).
3. Recently, denudatins A and B were reported to have a strong antifeeding activity [T. Kusumi, H. Ohishi, H. Kakisawa, N. Ohno, and I. Nakayama, 44th Annual Meeting of the Chemical Society of Japan (Kyoto, April, 1983), Abstract II, p. 1185].
4. G. Buchi and C-P. Mak, J. Am. Chem. Soc., 99, 8074 (1977).
5. Each anodic oxidation was quenched at 2.2 - 2.5 F/mol.
6. 7: $C_{12}H_{16}O_4$ (m/e 224.1048(M^+)); IR (film) 1675 cm^{-1}; $\delta(CDCl_3)$ 3.32(6H, s), 3.81(3H, s).
7. A number of acidic solvent systems [MeOH - AcOH (3 : 2), Ac_2O - AcOH (1 : 4), AcOH - HCOOH (4 : 1) and HCOOH] have been examined. These results will be published elsewhere.
8. 9: $C_{23}H_{26}O_7$ (m/e 414.1674(M^+)); IR (film) 1740, 1655 cm^{-1}; $\delta(CDCl_3)$ 0.70(3H, d, J= 7Hz), 2.13(3H, s), 2.40(1H, br.q, J= 7Hz), 6.20(1H, br.s).
9. 10: $C_{23}H_{26}O_7$ (m/e 414.1649(M^+)); IR (film) 1735, 1630 cm^{-1}; $\delta(CDCl_3)$ 0.40(3H, d, J= 6Hz), 1.98(3H, s), 5.10(1H, br.tt, J= 5, 10Hz).
10. 11: $C_{21}H_{24}O_6$ (m/e 372.1586(M^+)); IR (film) 1685 cm^{-1}; $\delta(CDCl_3)$ 0.88(3H, d, J= 7Hz), 2.42 (1H, dq, J= 6, 7Hz), 3.43(3H, s), 3.56(3H, s), 4.87(1H, d, J= 6Hz).
11. 13: $C_{22}H_{28}O_6$ (m/e 388.1886(M^+)); IR (film) 1685 cm^{-1}; $\delta(CDCl_3)$ 0.86(3H, d, J= 7Hz), 2.46 (1H, dq, J= 6, 7Hz), 3.43(3H, s), 3.56(3H, s), 4.91(1H, d, J= 6Hz).
12. This dimer (12) has not yet been obtained in pure state.
13. 14: $C_{28}H_{30}O_6$ (m/e 462.2044(M^+)); IR (film) 1760, 1695 cm^{-1}; $\delta(CDCl_3)$ 1.13(3H, d, J= 7Hz), 2.3 - 2.8(3H, complex), 3.10(1H, dd, J= 6, 7Hz), 3.7 - 3.9(1H, superimposed on MeO signals).
14. 15: $C_{20}H_{20}O_5$ (m/e 340.1321(M^+)); IR (film) 1760, 1695 cm^{-1}; $\delta(CDCl_3)$ 1.03(3H, d, J= 6.5Hz), 2.10(1H, quintet, J= 6.5Hz), 2.53(1H, br.d, J= 6.5Hz), 3.52(1H, br.s).

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