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THREE NOVEL NEOLIGNANS FROM HETEROTROPA TAKAOI M.

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In connection with asatone and related neolignans,[1,2] our continuous efforts have been made on searching for asatone-type neolignans in the plant Aristolochiaceae, leading to the isolation of three new neolignans (1, 2, and 3) from Heterotropa takaoi Maekawa. In the present paper, we wish to describe the isolation and structures of these neolignans. The last one (3) was photochemically synthesized from E-asarone.

Fresh leaves and roots of the above plant[3] were disintegrated into large amounts of MeOH and left at room temperature for a month, and then filtered. The filtrate was concentrated under reduced pressure, and then extracted with AcOEt. The extract was roughly separated by column chromatography [Silica gel (Mallinckrodt, 100 mesh)] using hexane-AcOEt (2 : 1) to give three fractions. The first fraction was further separated by repeated column chromatography [1) Florisil (Nakarai Chemicals, 60-100 mesh), hexane-AcOEt (3 : 1); 2) Silica gel (Mallinckrodt, 100 mesh), hexane-AcOEt (4 : 1)] followed by preparative TLC [Kieselgel PF$_{254}$; hexane-AcOEt (3 : 1), and then CHCl$_3$-AcOEt (10 : 1)] to afford heterotropanone (1) in 0.00023% yield, in addition to asatone (4)[1] as a main product. The second fraction was also chromatographed on silica gel (Mallinckrodt, 100 mesh) using CHCl$_3$ to give a greenish viscous liquid, which was further subjected to preparative TLC [Kieselgel PF$_{254}$; CHCl$_3$-AcOEt (20 : 1)][4] to afford isoheterotropanone (2) in 0.00074% yield. The remaining one was also separated by repeated column chromatography [1) Silica gel (Mallinckrodt, 100 mesh), hexane-AcOEt (4 : 1); 2) Florisil (Nakarai Chemicals, 60-100 mesh), CHCl$_3$; 3) Alumina (Nakarai Chemicals, 300 mesh), hexane-AcOEt (2 : 1)][5] followed by preparative TLC [10% AgNO$_3$-SiO$_2$ (Kieselgel PF$_{254}$), hexane-AcOEt (1 : 1)] to give heterotropan (3) in 0.00048% yield. The physical data of these three neolignans thus obtained are shown below.

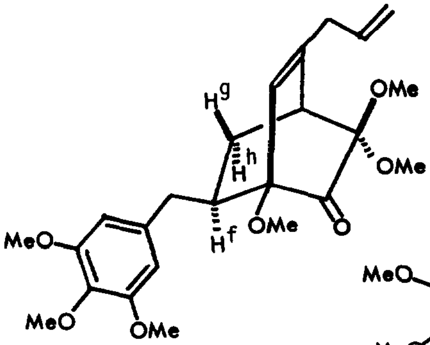
1 as a colorless viscous liquid: $C_{24}H_{32}O_7$ [m/e 432(M$^+$), 404, 389, 372, 223, and 181; $[\alpha]_D^{23}$ ±0°; ν_{max}(film) 1745, 1635, 1590, 1510sh., and 1500 cm^{-1}; PMR (CDCl$_3$): δ1.13(1H, ddd, J= 3, 5, 14Hz), 1.92(1H, ddd, J= 3, 9, 14Hz), 2.09(1H, d, J= 11Hz), 2.47(1H, m), 2.81(1H, dt, J= 2, 3Hz), 2.99(2H, br.d, J= 7Hz), 3.10(1H, dd, J= 3, 11Hz), 3.28(3H, s), 3.34(3H, s), 3.60(3H, s), 3.82(3H, s), 3.84(6H, s), 5.13(1H, tdd, J= 1, 2, 9Hz), 5.15(1H, tdd, J= 1, 2, 17Hz), 5.84(1H, br.s), 5.87(1H, tdd, J= 7, 9, 17Hz), and 6.35(2H, s); CMR (CDCl$_3$): δ27.1(t), 37.4(t), 39.5(t), 39.7(d), 41.2(d), 49.2(q), 50.7(q), 53.7(q), 56.0(q)*, 60.6(q), 86.1(s), 94.2(s), 106.1(d)*, 117.2(t), 118.8(d), 133.9(d), 135.0(s)*, 144.8(s), 152.8(s)*, and 201.7(s).

2 as a colorless viscous liquid: $C_{24}H_{32}O_7$ [m/e 432(M$^+$), 404, 389, 357, 223, and 181]; $[\alpha]_D^{23}$ ±0°; ν_{max}(film) 1750, 1640, 1590, 1510sh., and 1505 cm^{-1}; PMR (CDCl$_3$): δ1.52(1H, ddd, J= 3, 10,

14Hz), 1.69(1H, ddd, J= 3, 5, 14Hz), 2.07(1H, d, J= 12Hz), 2.29(1H, m), 2.82(1H, dt, J= 2, 3Hz), 2.95(2H, br.d, J= 7Hz), 3.12(1H, dd, J= 2, 12Hz), 3.42(6H, s), 3.57(3H, s), 3.84(3H, s), 3.87(6H, s), 5.10(1H, tdd, J= 1, 2, 9Hz), 5.12(1H, tdd, J= 1, 2, 17Hz), 5.79(1H, tdd, J= 7, 9, 17Hz), 5.87(1H, br.s), and 6.35(2H, s); CMR ($CDCl_3$): δ26.2(t), 36.2(t), 39.6(t), 41.4(d), 41.7(d), 49.0(q), 50.7(q), 52.9(q), 56.0(q)*, 60.6(q), 86.5(s), 94.7(s), 105.8(d)*, 117.3(t), 120.2(d), 133.7(d), 136.1(s)*, 146.2(s), 152.8(s)*, and 201.0(s).

3 as a colorless viscous liquid: $C_{24}H_{32}O_6$ [m/e 416(M^+) and 208]; $[\alpha]_D^{23}$ ±0°; ν_{max}(film) 1610, 1590, and 1510 cm^{-1}; PMR (C_6D_6): δ1.19(6H, d, J= 6Hz),[6] 2.78(2H, m), 3.30(6H, s), 3.42(6H, s), 3.54(6H, s), 4.15(2H, d, J= 5.5Hz),[6] 6.11(2H, s), and 6.66(2H, s); CMR ($CDCl_3$): δ15.1 (q), 34.0(d), 42.5(d), 56.1(q), 56.3(q), 56.7(q), 97.7(d), 112.4(d), 122.1(s), 142.3(s), 147.2(s), and 151.6(s).

* This signal is assignable to two carbon atoms.



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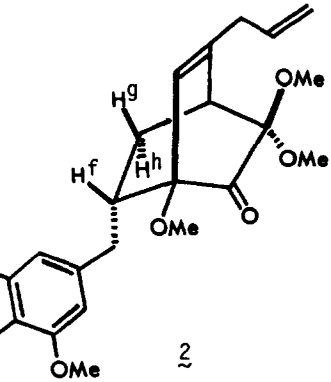

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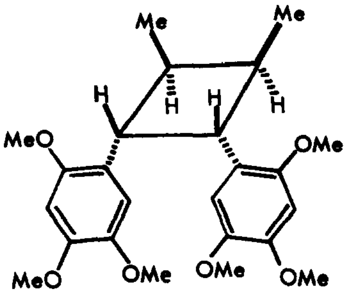

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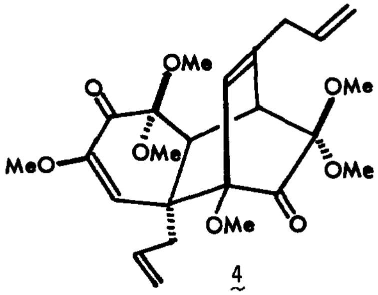

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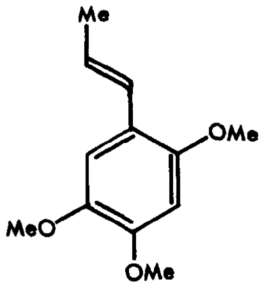

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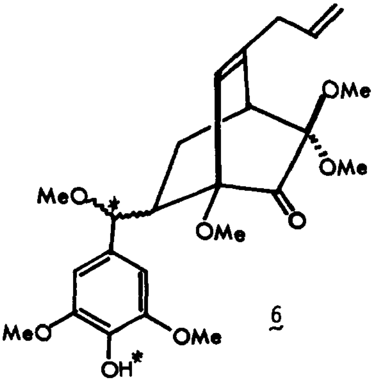

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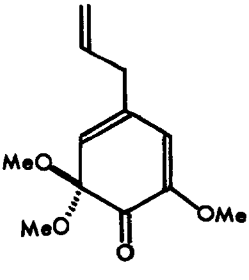

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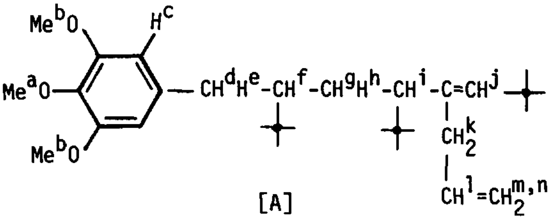


[A]

The structures of heterotropanone (1) and isoheterotropanone (2) were unambiguously established on the basis of their spectral data, as discussed below.

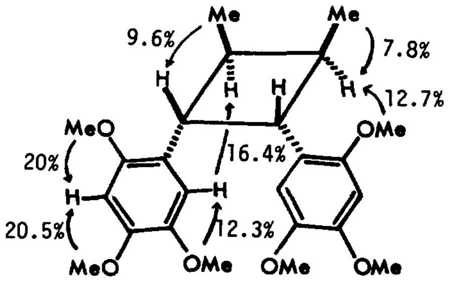
Heterotropanone (1) has six MeO groups (δ3.28, 3.34, 3.60, 3.82, and 3.84) and one CO group (ν_{max} 1745 cm^{-1}). The presence of a partial structure [A] can be confirmed by analysis of the PMR spectrum of 1 with aid of double resonance experiments [δ3.82(H^{a}), 3.84(H^{b}), 6.35(H^{c}), 2.09 (H^{d}),[7] 3.10(H^{e}), 2.47(H^{f}), 1.13(H^{g}), 1.92(H^{h}), 2.81(H^{i}), 5.84(H^{j}), 2.99(H^{k}), 5.87(H^{l}), 5.13(H^{m}), and 5.15(H^{n})]. On irradiation at δ5.84, particularly, the signals assignable to H^{i} and H^{k} became triplet and slightly broad singlet, respectively. Furthermore, the signal at δ5.84 was changed to slightly broad singlet on irradiation at δ2.81 as well as at δ2.99[8]. These spectral data are quite similar to those of the oxidation product (6), which has been synthesized from 2,6-dimethoxy-4-allylphenol,[9] except for some asterisk-positions in 6. Furthermore, the CMR spectrum indicates that heterotropanone (1) with a bicyclic carbon skeleton has the two quaternary carbon atoms (δ86.1 and 94.2), to which three MeO groups must be attached, and one CO group (δ201) in addition to the carbon atoms included in [A].[10] The closs similarity between 1 and 6 was further confirmed by their mass spectra, as discussed below.

The mass spectrum of heterotropanone (1) has two characteristic peaks at m/e 223 and 181, and the corresponding peaks are observed at m/e 223 and 197 in 6. The common fragment ion at m/e 223 must be formed by retro-Diels-Alder reaction of 1 as well as of 6 on electron impact.

Isoheterotropanone (2), whose spectral data are quite similar to those of 1, must be the stereoisomer of 1, as described below.

Of the two protons (H^{g} and H^{h}) in 1, the signal at higher magnetic field (δ1.13) can be assigned to H^{g}, whose coupling constant with H^{f} is 5Hz indicating that the relationship between H^{g} and H^{f} must be in a trans configuration. In the case of 2, the corresponding one is 10Hz, indicating that the dihedral angle between H^{g} and H^{f} is ~0°. From the above results, the stereostructures of heterotropanone and isoheterotropanone can be represented by 1 and 2, respectively. Presumably, these two neolignans are produced *in vivo* from elemicin and an unstable dienone (7).

As seen in the spectral data of heterotropan (3), there is a symmetric character in its structure. Furthermore, two possible stereostructures (3 and 8) can be deduced from its PMR spectrum with aid of NOE measurements, as described below.



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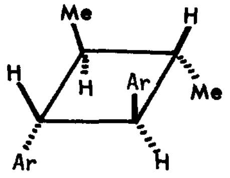

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Finally, the stereostructure of heterotropan was proved to be depicted as 3 by the following chemical evidence: E-asarone (5) was irradiated in hexane using a pyrex filter (room temp., 10 days) to afford heterotropan as the sole photodimer,[11] in 15% yield.[12]

The present study demonstrates the first example of such a new type of neolignan as heterotropanone in this field. Furthermore, pharmacological studies on these neolignans are now in our hand.

References and Notes

1. S. Yamamura, Y. Terada, Y. Chen, M. Hong, H. Hsu, K. Sasaki, and Y. Hirata, Bull. Chem. Soc. Japan, 49, 1940 (1976); S. Yamamura, Y. Chen, H. Hsu, and Y. Hirata, Phytochemistry, 15, 426 (1976); N. Hayashi, Y. Yamamura, S. Ohama, and K. Komae, ibid., 15, 1567 (1976).
2. Y. Terada and S. Yamamura, Chemistry Letters, 1978, 553.
3. Collected at Sanage in Aichi-ken early in April.
4. Small amount of asatone (4) was also isolated.
5. Isoasatone A[2] was obtained in ca. 0.004% yield.
6. A virtual coupling is observed.
7. Dihedral angle between H^d and H^f seems to be almost 90°.
8. The signal at δ5.87 became sharp doublet of doublet.
9. M. Iguchi, A. Nishiyama, Y. Terada, and S. Yamamura, Tetrahedron Letters, 1977, 4511.
10. Particularly, each δ-value assignable to H^i is in good agreement with one another (δ2.81 in 1; δ2.82 in 2; δ2.82 in 6).
11. A mixture of E- and Z-asarone was recovered.
12. H. Nozaki, I. Otani, R. Noyori, and M. Kawanishi, Tetrahedron, 24, 2183 (1968); K. Tokumaru, "Yukikagaku Hannoron", p. 200, Tokyo Kagakudozin Ltd., Tokyo, 1973.

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