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THE ISOLATION AND STRUCTURES OF TWO NOVEL NEOSESQUILIGNANS, HETEROTROPATRIONE AND ISOHETEROTROPATRIONE

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In connection with asatone-type neolignans, extensive studies on chemical constituents of the plant Aristolochiaceae have been made.[1~4] We further examined chemical components of the plant Heterotropa takaoi Maekawa, and could isolate two novel neosesquilignans designated as heterotropatrione and isoheterotropatrione. We here describe the isolation and structures of these new neosesquilignans.

According to essentially the same procedure as described in the previous papers,[2,3] the MeOH extract of the fresh leaves and roots of the above plant[5] was roughly separated by column chromatography [silica gel (Mallinckrodt, 100 mesh)] using hexane-AcOEt (2 : 1) and then hexane-AcOEt (1 : 1) to afford two fractions. The first fraction was rechromatographed on silica gel [Mallinckrodt, 100 mesh; $CHCl_3$-AcOEt (1 : 1)] followed by preparative TLC [10% $AgNO_3$-SiO_2 (Kieselgel PF_{254}); $CHCl_3$-AcOEt (1 : 1)] to afford heterotropatrione (**1**) in 0.00042% yield. The remaining fraction was also subjected to repeated column chromatography [1) silica gel (Mallinckrodt, 100 mesh; hexane-AcOEt (1 : 1); 2) silica gel (Mallinckrodt, 100 mesh; $CHCl_3$-AcOEt (10 : 1)] to give an almost colorless oil, which was further purified by preparative TLC (Kieselgel PF_{254}; $CHCl_3$-AcOEt (10 : 1)] to afford isoheterotropatrione (**2**) in 0.0019% yield. The physical data of these two neosesquilignans thus obtained are shown below.

Heterotropatrione (**1**), a colorless viscous liquid: $C_{36}H_{48}O_{12}$ [m/e 672(M^+), 644, 640, 565, 448, and 317]; $[\alpha]_D^{23}$ ±0°; ν_{max}(film) 1750br., 1730sh., and 1645 cm^{-1}; PMR ($CDCl_3$): δ0.94(1H, ddd, J= 3,4,13Hz), 1.94-2.99(11H, complex), 3.04(3H, s), 3.25(3H, s), 3.27(3H, s), 3.30 (3H, s), 3.34(3H, s), 3.39(3H, s), 3.47(3H, s), 3.51(3H, s), 3.57(3H, s), 4.84-5.22(4H, complex), 5.32(1H, s), 5.45(1H, br.s), 5.59(1H, br.s), and 5.60-6.10(2H, complex).

Isoheterotropatrione (**2**), a colorless viscous liquid: $C_{36}H_{48}O_{12}$ [m/e 672(M^+), 644, 640, 565, 448, 418, and 343]; $[\alpha]_D^{23}$ ±0°; ν_{max}(film) 1760, 1725, and 1645 cm^{-1}; PMR ($CDCl_3$): δ1.41-1.92(2H, complex), 2.00-3.01(10H, complex), 3.05(3H, s), 3.28(3H, s), 3.32(3H, s), 3.33 (3H, s), 3.37(3H, s), 3.38(3H, s), 3.40(3H, s), 3.47(3H, s), 3.57(3H, s), 4.88-5.23(4H, complex), 5.04(1H, br.s), 5.38(1H, s), 5.39-6.07(2H, complex), and 5.84(1H, br.s).

The above spectral data and CMR spectra (see Table 1) indicate that these two neosesquilignans with the same molecular formula ($C_{36}H_{48}O_{12}$) are stereoisomers to each other.

As shown in Table 1, their CMR spectra include the signals corresponding to those of asatone (**3**).[1] In addition, the remaining signals show the one to one correspondence to each carbon atom of heterotropanone (**4**) [or isoheterotropanone (**5**)][3] except for the aromatic ring of **4** (or **5**).

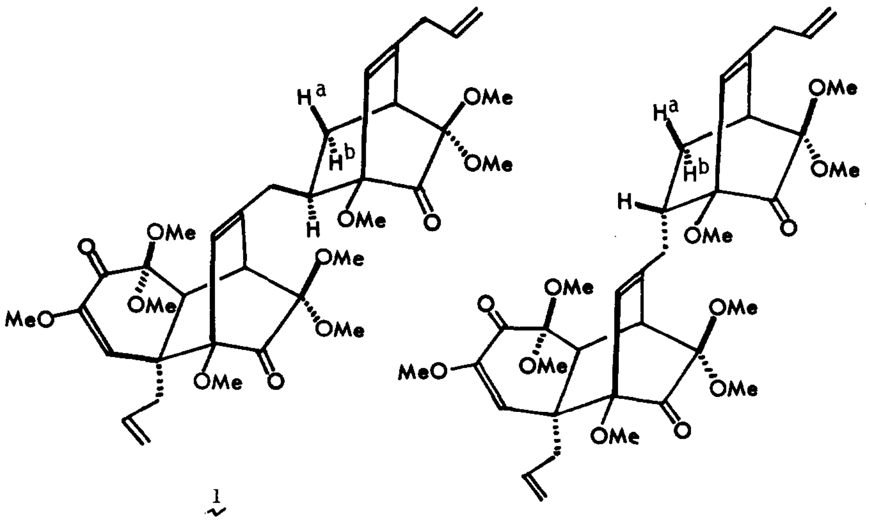
Of the two allyl groups in asatone (3), the angular one must be present in both 1 and 2, as judged by their CMR spectra which have the signals corresponding to those of the angular allyl group in isoasatone A (6) (δ 41.5, 117.3, and 135.0).[2] Further information of their stereostructures can be given by the PMR spectra, as follows.

Table 1. CMR spectra of neosesquilignans and related neolignans

	1	2	3	4*	5*	6**	
$>C=O$	201.3	200.4					(s)
	201.3	201.6	201.4	201.7	201.0	201.2	(s)
$H\underline{C}=\underline{C}(OMe)-\underline{C}=O$	121.1	120.6	121.7			122.7	(d)
	150.2	150.5	150.2			150.2	(s)
	187.9	187.5	188.7			187.7	(s)
$-CH_2-CH=CH_2$	39.4	39.6	39.0	39.5	39.6		(t)
	41.1	41.4	41.3			41.5	(t)
	116.7	117.0	116.9				(t)
	117.1	117.4	118.2	117.2	117.3	117.3	(t)
	133.8	134.2	133.4	133.9	133.7		(d)
	134.8	135.2	135.2			135.0	(d)
$-CH=C<$	115.8	117.0	116.6			116.0	(d)
	120.7	120.6		120.2	120.2		(d)
	144.0	145.8	144.9			141.2	(s)
	144.0	146.6		146.2	146.2		(s)
$-\underline{C}(OMe)-$	85.1	85.7		86.1	86.5		(s)
	91.8	91.6	92.1			91.8	(s)
$-\underline{C}(OMe)_2$	93.2	93.4	93.2			93.3	(s)
	94.3	94.7		94.2	94.7		(s)
	98.3	98.2	98.7			98.5	(s)
MeO-	48.9	49.4		49.2	49.0		(q)
	49.5	49.4	50.1			50.2	(q)
	49.9	49.8	50.1			50.5	(q)
	49.9	50.3	50.2			50.5	(q)
	50.3	50.7	50.2			50.8	(q)
	50.6	50.7		50.7	50.7		(q)
	52.9	52.3		53.7	52.9		(q)
	54.6	54.7	54.8			54.8	(q)
	55.4	55.4	55.5			55.4	(q)
$-C-$	49.5	49.8	49.8			50.2	(s)
$-CH-$	33.0	36.9		39.7	41.4		(d)
	41.1	41.7		41.2	41.7		(d)
	43.9	44.1	43.9			39.6	(d)
	44.6	44.1	44.5			43.2	(d)
$-CH_2-$	28.0	27.1		27.1	26.2		(t)
	36.7	35.6		37.4	36.2		(t)

* In the cases of 4 and 5, the signals corresponding to the aromatic ring are not cited.

** In the case of 6, the signals due to a propenyl group are observed at δ 18.4(q), 128.2(d), and 128.7(d).



1

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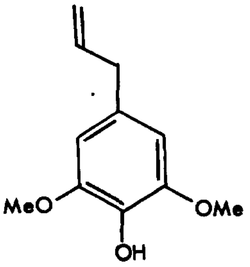

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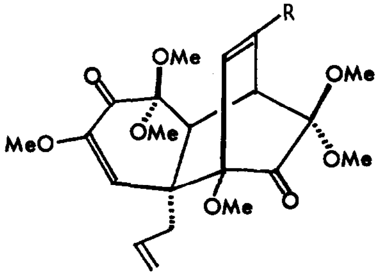
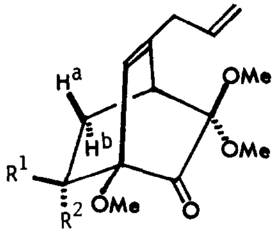


3 R = $CH_2CH{=}CH_2$

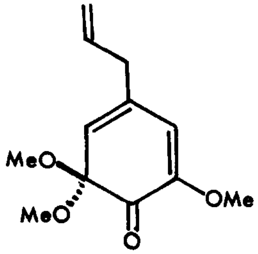
6 R = $CH\overset{E}{=}CHMe$



4 R^1= $CH_2\cdot C_6H_2(OMe)_3$, R^2= H

5 R^1= H, R^2= $CH_2\cdot C_6H_2(OMe)_3$

8 R^1= H, R^2= $CH_2\cdot C_6H_2(OMe)_2(OH)$



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Heterotropanone (4) has the PMR signal assignable to H^a at δ1.13(1H, ddd, J= 3,5,14Hz).[3,6] In the case of heterotropatrione (1), the corresponding signal was also observed at δ0.94(1H, ddd, J= 3,4,13Hz). Therefore, the tentative stereostructure of heterotropatrione is represented by 1, although the diastereoisomeric structure corresponding to 1 can not be ruled out. The tentative stereostructure of isoheterotropatrione is also depicted as 2,[7] as judged by the PMR signals due to H^a and H^b (δ1.41~1.92).[6] In fact, this is confirmed by the following chemical evidence.

On reduction with active zinc powder in AcOH (60°, 1 hr),[1] isoheterotropatrione (2) was readily converted into a mixture of 2,6-dimethoxy-4-allylphenol (7) and a keto phenol (8)[8] which was further treated with CH_2N_2 in ether containing MeOH to give isoheterotropanone (5) in high yield.

Presumably, these neosesquilignans, both of which are optically inactive, are produced from asatone (3) and the dienone (9),[9] both of which have been synthesized in our laboratory.[10]

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5. Collected at Sanage in Aichi-ken early in April.
6. In the case of isoheterotropanone (**5**), the corresponding signal (H^a) is observed at δ 1.52 in addition to the signal (H^b) at δ 1.69.
7. The diastereoisomeric structure corresponding to **2** can not be ruled out.
8. Physical data of **8**: $C_{23}H_{30}O_7$ [m/e 418(M^+), 343, and 167]; ν_{max}(film) 3500br., 1755, 1615, and 1520 cm^{-1}.
9. As suggested by the zinc reduction of **2**, another possibility is also considered, in which **1** (or **2**) is derived from demethylheterotropanone (or demethylisoheterotropanone (**8**)).
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