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ISOASATONE A AND ISOASATONE B, TWO NOVEL NEOLIGNANS, FROM *HETEROTROPA TAKAOI* M.

Yukimasa TERADA and Shosuke YAMAMURA*
Faculty of Pharmacy, Meijo University, Tenpaku-ku, Nagoya 468

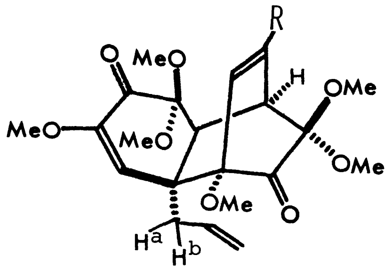
Two new neolignans, isoasatone A (3) and isoasatone B (4) have been isolated from the plant *Heterotropa takaoi* M., and their structures also been elucidated by comparing their spectral data with those of asatone (1).

Two novel neolignans, asatone (1) and isoasatone (2), were first isolated from the plant *Asarum teitonense* Hayata growing in Taiwan.[1] Of these two neolignans, the former has also been detected in the plants *Aristolochiaceae* growing in Japan.[2] Furthermore, recent pharmacological studies on asatone (1) prompted us to examine such a physiologically active substance as 1 in the plants *Aristolochiaceae*.[3] Thus, we could isolate two new neolignans, named isoasatone A (3) and isoasatone B (4), from the plant *Heterotropa takaoi* Maekawa. In this paper we wish to describe the isolation and structures of these two neolignans.

Fresh leaves and roots of the above plant[4] were disintegrated into large amount of MeOH and left at room temperature for 10 days, and then filtered. The filtrate was concentrated under reduced pressure to give a dark greenish viscous liquid, which was chromatographed on silica gel (Mallinckrodt, 100 mesh). Elution with hexane - EtOAc (2 : 1) afforded a dark green oil, which was further separated by preparative TLC [Kieselgel PF_{254}, hexane - ether (1 : 2)] to give a crystalline solid of isoasatone A [3, mp 122 - 124°C (from hexane - ether)] in 0.0075% yield. Further elution with EtOAc followed by preparative TLC [Kieselgel PF_{254}, benzene - acetone (1 : 1)] afforded white crystals of isoasatone B [4, mp 129 - 131°C (from hexane - ether)] in 0.0021% yield.

Isoasatone A (3) with a molecular formula ($C_{24}H_{32}O_8$) has the same carbon skeleton as that of asatone (1)[1] on the basis of the following chemical evidence: catalytic hydrogenation of 3 in EtOAc over 10% Pd-C was carried out at room temperature overnight to afford tetrahydroasatone[1] in 61% yield. In addition, the IR and mass spectra of 3 [ν_{max}(film) 1745, 1720, and 1640cm^{-1}; m/e 448 (M^+), 416, 384, and 224] are also similar to those of 1. As seen in Table 1, however, only one different point is that isoasatone A has one propenyl group (δ 1.73, 5.97, and 6.27) instead of one of the two allyl groups in 1. Particularly, the partial structure [A] including the propenyl group in 3 can be confirmed by the following double resonance experiment. On irradiation at δ1.73, the olefinic proton signal at δ6.27 was collapsed to a doublet (J = 16Hz) forming an AB system with the signal at δ5.97, and the broad doublet at δ5.66 was changed to a sharp doublet (J = 2Hz). On the other hand, the presence of the remaining allyl group is also confirmed by comparison of the NMR signals assignable to the methylene protons (H^a and H^b) (δ 2.15 and 2.60-2.95 in 1; 2.34 and 2.76 in 3) between 1 and 3. Thus, the structure of isoasatone A can be depicted as 3.

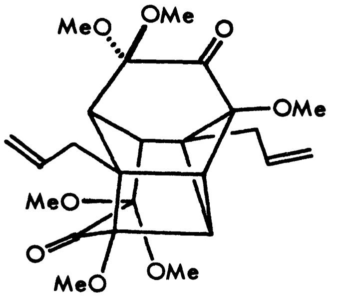
Isoasatone B (4) has a molecular formula ($C_{24}H_{32}O_9$) with the following spectral data: m/e 464 (M^+), 446, 432, 400, 368, 327, 240, and 224; ν_{max}(KBr) 3470, 1750, 1720, and 1640cm^{-1}. Clearly, the retro-Diels-Alder reaction must take place on electron impact, leading to the formation of two fragment ions, to which the remarkable peaks at m/e 240 and 224 are assignable, as seen in the case of asatone (1).[1] Finally, the structure of isoasatone B can be unambiguously established as 4 on



1 R = $-CH_2CH=CH_2$

3 R = $-CH\overset{E}{=}CH-CH_3$

4 R = $-CH\overset{E}{=}CH-CH_2OH$



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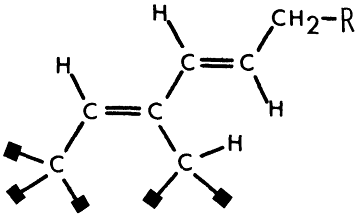

[A] R = H

[B] R = OH

the basis of the NMR spectrum (see Table 1). This neolignan has a HO-CH_2-CH=CH- grouping (δ 2.30, 4.30, 6.09, and 6.28) in the partial structure [B],[5] while there is one propenyl group in isoasatone A (3), as described earlier. The other remaining signals in their NMR spectra are quite similar to each other [particularly see the methylene proton signals (H^a and H^b)].

Probably, these two neolignans (3 and 4), both of which are optically inactive, are produced in vivo directly from 1, whose biomimetic synthesis has been carried out in our laboratory.[6]

Table 1. NMR spectra of asatone (1), isoasatone A (3), and isoasatone B (4)

Asatone [δ ($CDCl_3$)]	Isoasatone A [δ (C_6D_6)]	Isoasatone B [δ ($CDCl_3$)]
		2.30(1H, br.s, OH)
	1.73(3H, d, J= 6Hz)	
2.15($1H^a$, dd, J= 14.5, 7.5Hz)	2.72($1H^a$, dd, J= 14, 7Hz)*	2.31($1H^a$, dd, J= 14, 7Hz)
2.60-2.95(2H + $1H^b$, complex)	2.95-3.52(2H + $1H^{b*}$)**	2.80($1H^b$, dd, J= 14, 8Hz)
2.88(2H, br.s)		3.35(1H, d, J= 2Hz)
		3.45-3.68(1H)**
3.05(3H, s), 3.31(3H, s)	3.00(3H, s), 3.18(3H, s)	3.10(3H, s), 3.31(3H, s)
3.38(3H, s), 3.42(3H, s)	3.20(3H, s), 3.30(3H, s)	3.45(3H, s), 3.53(3H, s)
3.47(3H, s), 3.60(3H, s)	3.45(3H, s), 3.46(3H, s)	3.55(3H, s), 3.62(3H, s)
		4.30(2H, d, J= 4Hz)
4.90-5.28(4H, complex)	5.23(1H, br.d, J= 10Hz)	5.09(1H, br.d, J= 12Hz)
	5.26(1H, br.d, J= 17Hz)	5.10(1H, br.d, J= 16Hz)
5.39(1H, s)	5.49(1H, s)	5.43(1H, s)
5.55(1H, q, J= 2Hz)	5.66(1H, br.d, J= 2Hz)	5.86(1H, br.d, J= 2Hz)
	5.97(1H, d, J= 16Hz)	6.09(1H, dt, J= 16, 4Hz)
	6.27(1H, dq, J= 16, 6Hz)	6.28(1H, d, J= 16Hz)
5.50-6.20(2H, complex)	6.40(1H, m)	5.92(1H, m)

* δ ($CDCl_3$) 2.34($1H^a$, dd, J= 14, 7Hz) and 2.76($1H^b$, dd, J= 14, 8Hz). ** Superimposed on MeO signals.

References and Footnotes

1. 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. 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).
3. Private communication from Dr. J. D. Douros (NIH): asatone has been shown to have an antileukemic activity in mice.
4. Collected at Sanage in Aichi-ken in December.
5. The partial structure [B] was also confirmed by double resonance experiment.
6. M. Iguchi, A. Nishiyama, Y. Terada, and S. Yamamura, Tetrahedron Letters, 1977, 4511.

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