

ABSOLUTE CONFIGURATION OF FARFUGIN A.

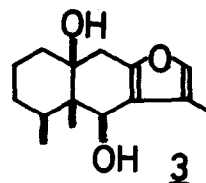
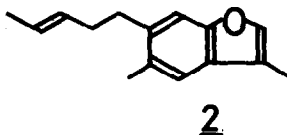
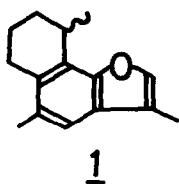
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Previously we reported the structure of farfugin A (1) and farfugin B (2), benzofuran derivatives isolated from *Farfugium japonicum*.<sup>1,2)</sup> In the subsequent paper<sup>3)</sup>, we will describe the skeletal rearrangement of furanoeremophilane-6 $\beta$ ,10 $\beta$ -diol(3)<sup>4)</sup> into 1 and 2. Farfugin A (1) formed from 3 was optically active. This fact directed our attention to the mechanism of this rearrangement. Here we will report the determination of absolute configuration of farfugin A (1) which is indispensable for elucidation of the mechanism.<sup>5)</sup>

Condensation of p-cresol with ethyl acetoacetate in polyphosphoric acid (PPA) at 80° for 1 hr gave 4,6-dimethylcoumarin (4)<sup>6)</sup> (yield 45 %), m.p. 150.5-151.5°. The dihydro derivative (5)<sup>7)</sup>, m.p. 35.0-35.5°, obtained by hydrogenation of 4 over Pd-C, was converted to 3-(2-methoxy-5-methylphenyl)-butanoic acid (6) (yield 35 %), m.p. 60.5-61.5°, by hydrolysis and methylation with NaOH-H<sub>2</sub>O-Me<sub>2</sub>SO<sub>4</sub> in a single step. The resolution of the acid (6) was accomplished by recrystallization of its strychnine salt from CHCl<sub>3</sub>-EtOH-H<sub>2</sub>O. Levorotatory acid (6a), m.p. 60°, [ $\alpha$ ]<sub>D</sub> -20°(in CHCl<sub>3</sub>)<sup>8)</sup>, was obtained from the crystalline salt, while the mother liquor gave its enantiomer (6b), m.p. 60-60.5° [ $\alpha$ ]<sub>D</sub> +14°(in CHCl<sub>3</sub>)<sup>8)</sup>.



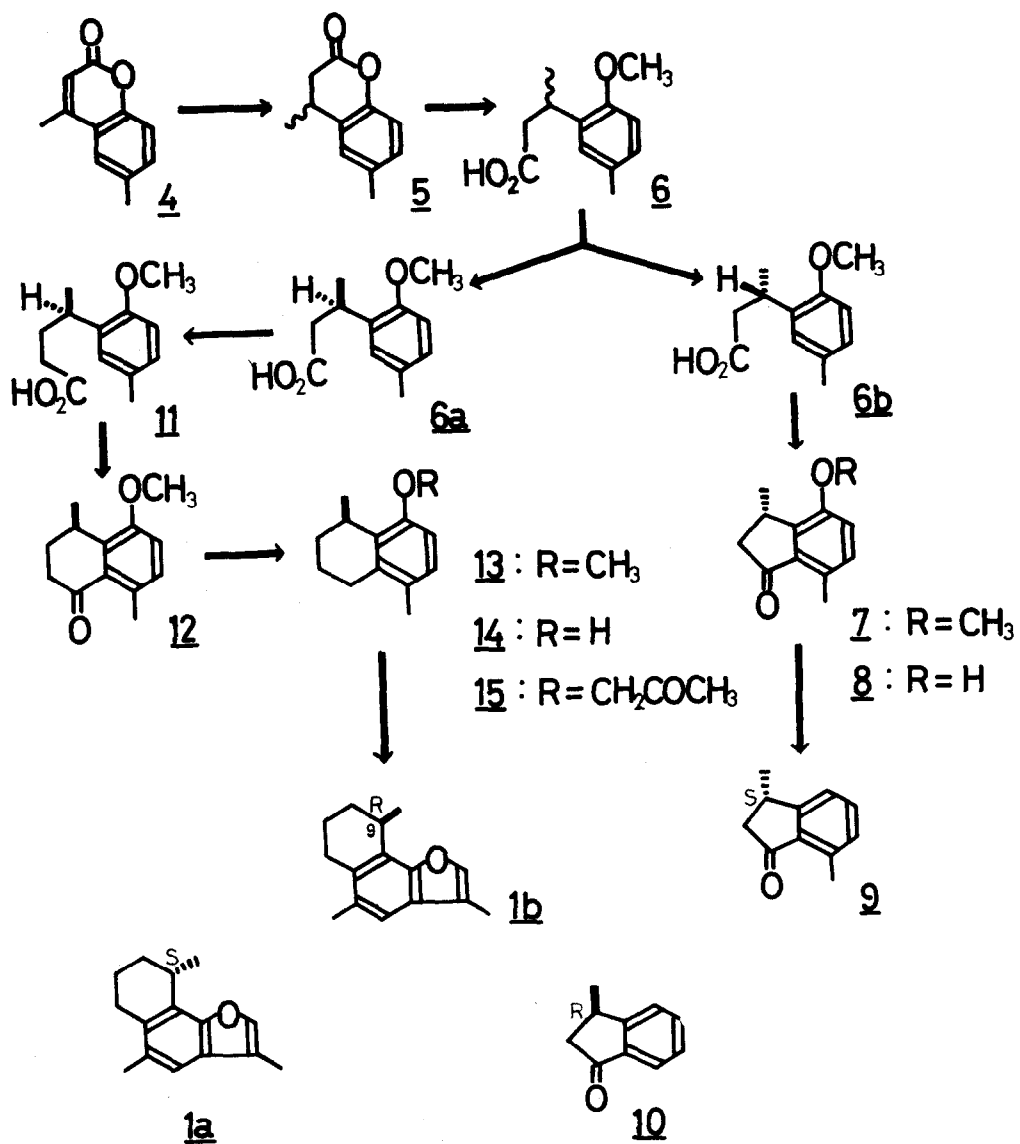


TABLE Spectral Data

Compounds	Molecular Formulae	M <sup>+</sup>	IR (cm <sup>-1</sup> )	UV (nm) <sup>a)</sup> λ <sub>max</sub> (ε)	PMR (δ in ppm) <sup>b)</sup>
<u>6</u>	C <sub>12</sub> H <sub>16</sub> O <sub>3</sub>	208	~3000 1710 1502		1.30(3H, d, J=7), 2.27(3H, s), 3.80(3H, s), 6.60-6.95(3H, m)
<u>7</u>	C <sub>12</sub> H <sub>14</sub> O <sub>2</sub>	190	1715 1590 1500	238(8000) 246(8300) 253(8600) 308(3500) 317(3300)	1.34(3H, d, J=7), 2.53(3H, s), 2.20(1H, dd, J=19; J=3), 2.85(1H, dd, J=19; J=7), -3.4(1H, m), 3.82(3H, s), 6.88(1H, d, J=8), 7.00(1H, d, J=8)
<u>9</u>	C <sub>11</sub> H <sub>12</sub> O	160	1715 1600 1480	243(12000) 288(2500) 298(2600) 260(sh) 294(sh)	1.38(3H, d, J=7), 2.65(3H, s), 2.26(1H, dd, J=19; J=4), 2.90(1H, dd, J=19; J=7), -3.4(1H, m), 7.0-7.6(3H, m)
<u>1b</u>	C <sub>15</sub> H <sub>18</sub> O	214	1600 1550 1535 1100	*252(10500) 281(2300) 291(2500)	1.38(3H, d, J=7.5), 2.18(3H, d, J=1.5), 2.28(3H, s) 7.10(1H, s), 7.26(1H, m)

a) Determined in cyclohexane (\* in EtOH).

b) Determined in CDCl<sub>3</sub>. Coupling constants are expressed in Hz.

The absolute configuration of these acids was deduced from comparison of the optical property of indanones 7 and 9 prepared from (+)-acid 6b with that of well established (-)-(3R)-3-methyl-1-indanone (10)<sup>9)</sup>. Cyclization of 6b with PPA gave 7 (quantitative yield), an oil, which was demethylated with HBr to afford a phenol (8)<sup>10)</sup>, m.p. 203° (yield 65 %). Phosphorylation of 8 according to Kenner<sup>11)</sup>, followed by reduction with Li in liquid NH<sub>3</sub> and oxidation with Jones' reagent, furnished 3,7-dimethylindanone (9) (yield 50 %), an oil. The ORD curves (in cyclohexane) of 7<sup>12)</sup> [([α]<sub>D</sub><sup>20</sup>]<sub>589</sub> +40, [([α]<sub>D</sub><sup>20</sup>)]<sub>365</sub> +1100, [([α]<sub>D</sub><sup>20</sup>)]<sub>358</sub> +720, [([α]<sub>D</sub><sup>20</sup>)]<sub>350</sub> +1000, [([α]<sub>D</sub><sup>20</sup>)]<sub>340</sub> +220, [([α]<sub>D</sub><sup>20</sup>)]<sub>335</sub> +330, [([α]<sub>D</sub><sup>20</sup>)]<sub>325</sub> -1200(shoulder), [([α]<sub>D</sub><sup>20</sup>)]<sub>313</sub> -2200, [([α]<sub>D</sub><sup>20</sup>)]<sub>297</sub> ±0] and 9<sup>12)</sup> [([α]<sub>D</sub><sup>20</sup>]<sub>589</sub> +8, [([α]<sub>D</sub><sup>20</sup>)]<sub>368</sub> +600, [([α]<sub>D</sub><sup>20</sup>)]<sub>359</sub> +410, [([α]<sub>D</sub><sup>20</sup>)]<sub>352</sub> +640, [([α]<sub>D</sub><sup>20</sup>)]<sub>339</sub> +60(shoulder), [([α]<sub>D</sub><sup>20</sup>)]<sub>324</sub> -1200(shoulder), [([α]<sub>D</sub><sup>20</sup>)]<sub>311</sub> -2000(shoulder), [([α]<sub>D</sub><sup>20</sup>)]<sub>300</sub> -2700, [([α]<sub>D</sub><sup>20</sup>)]<sub>290</sub> -2300] are almost mirror images to that of 10. Thus, as to asymmetric center the (-)-acid (6a) possesses the same configuration (R) as that of 10.

Homologation of the (-)-acid (6a) by Arndt-Eistert reaction gave an acid (11)<sup>13)</sup> (yield 76 %), m.p. 87.5°, which was converted to a tetrahydronaphthol (14) (yield 70%) according to the procedures (11→12→13→14) described in the

literatures<sup>13)</sup>. An optical active benzofuran (1b)<sup>5b)</sup> (yield from 14; 33 %), m.p. 77°,  $[\alpha]_D -27^\circ$ , an enantiomer of farfugin A (1),  $[\alpha]_D +39^\circ$ , was obtained by the reaction sequence (14→15→1b) already reported<sup>1)</sup>.

These observations lead to the absolute configuration of 1a for farfugin A whose configuration at C-9 must be (S).

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5. a) To achieve the resolution of intermediates (6a and 6b) and determine absolute configurations of the compounds (1, 6a and 6b) in question, we followed the reaction pathway described here. b) Spectral data (IR, UV, PMR and MS) of new compounds are listed in the table.
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