Chemistry of Natural Compounds, Vol. 37, No. 5, 2001

MOLECULAR STRUCTURE OF A NOVEL POLYMORPHIC MODIFICATION OF PINOSTROBIN

V. I. Yamovoi, E. A. Kul′magambetova, A. T. Kulyyasov, K. M. Turdybekov, and S. M. Adekenov

UDC 547.737:547.972

*5-Hydroxy-7-methoxyflavanone (pinostrobin) was isolated from buds of balsamic poplar (*Populus balsamifiera *L.). An x-ray structure analysis of its novel polymorphic modification is performed.*

Key words: flavonoids, x-ray structure analysis, *Populus balsamifiera*.

Flavonoids are widely distributed in nature and possess a wide spectrum of therapeutic, enzyme inhibitory [1], antioxidant [2-7], anti-inflammatory [8, 9], antiviral [10, 11], antimicrobial [12], and other [13, 14] types of biological activities.

Plants of the *Populus* (poplar) genus in the Salicaceae (willow) family are especially interesting with respect to chemical modification of their compounds as a source of polyphenols, flavonoids [15].

We investigated the chemical composition of balsamic poplar (*Populus balsamifiera*) and isolated 5-hydroxy-7-methoxyflavanone, known as pinostrobin (**1**).

The crystal structure of pinostrobin **1a** was studied by Shoja [16]. The compound that we isolated had spectra identical to those of pinostrobin. The lattice constants were similar to those of 5-hydroxy-7-methoxy-2-phenyl-4H-1-benzopyran-4-one (**2**) [17]. Therefore, we performed an x-ray structure analysis (XSA). The results showed that the molecular structures of the previously studied **1a** and **1b** studied by us are polymorphic modifications of pinostrobin.

Figure 1 shows a general view of the molecule. Table 1 lists the atomic coordinates. The bond lengths (Table 2) and angles (Table 3) are close to the usual values [18].

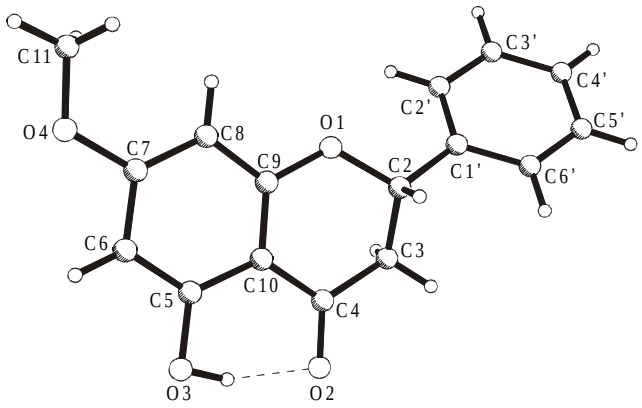

Fig. 1. Molecular structure of the novel polymorphic modification of pinostrobin.

Institute of Phytochemistry, Ministry of Education and Science, Republic of Kazakhstan, Karaganda, ul. M. Gazalieva, 4, fax: (3212) 43 37 73, e-mail: arglabin@mail.krg.kz. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 361-363, September-October, 2001. Original article submitted January 29, 2001.

 0009-3130/01/3705-0424$25.00

TABLE1. Fractional Atomic Coordinates (Å×10^4; for H, ×10^3)

Atom	x	y	z	Atom	x	y	z
O1	3225(4)	6307(2)	1706(5)	C9	3804(5)	6093(3)	215(8)
O2	1869(4)	4301(3)	–849(7)	C10	3344(5)	5429(3)	–725(8)
O3	3608(5)	4621(3)	–3201(7)	C11	7019(7)	7490(4)	–544(9)
O4	6474(4)	6846(3)	–2507(6)	C1'	1462(6)	6270(4)	3710(8)
C2	1907(6)	6028(4)	2005(10)	C2'	2319(6)	6536(4)	4909(8)
C3	1725(7)	5148(4)	1594(9)	C3'	1842(7)	6778(4)	6438(9)
C4	2286(6)	4911(4)	–75(9)	C4'	515(7)	6724(4)	6850(10)
C5	4009(6)	5258(4)	–2226(9)	C5'	–337(7)	6452(4)	5666(9)
C6	5036(6)	5747(4)	–2824(8)	C6'	135(6)	6216(4)	4137(10)
C7	5444(5)	6396(3)	–1806(8)	H03	299(6)	439(4)	–250(8)
C8	4846(5)	6591(3)	–315(8)				

TABLE 2. Bond Lengths (d, Å)

Bond	d	Bond	d
O1-C2	1.441(7)	O1-C9	1.400(8)
O2-C4	1.232(8)	O3-C5	1.348(8)
O4-C7	1.407(7)	O4-C11	1.400(8)
O4-C3	1.463(9)	C2-C1'	1.51(1)
C3-C4	1.53(1)	C4-C10	1.469(8)
C5-C6	1.405(9)	C5-C10	1.433(9)
C6-C7	1.384(8)	C7-C8	1.401(9)
C8-C9	1.405(8)	C9-C10	1.384(8)
C1'-C2'	1.353(9)	C1'-C6'	1.406(9)
C2'-C3'	1.40(1)	C3'-C4'	1.40(1)
C4'-C5'	1.34(1)	C5'-C6'	1.39(1)

The exception is angle C1′C2C3, which is 114.6(6)° and significantly distorted from the tetrahedral value, whereas in **1a** the value is 108.7°. A comparison of the endocyclic torsion angles of **1a** with the corresponding ones in **1b** showed that the difference for C5...C7...C10 is less than 4.8°; O1...C3...C9, equal to 5.4°; and O1C2C3C4, greater than 10°.

Atoms of the six-membered ring of **1b** are coplanar within ±0.01 Å. The deviations of O4 and C11 from the average plane of the six-membered ring are -0.02 and 0.07 Å, respectively. Atom O3 is practically in the plane of the ring.

The heterocycle of **1a** is more distorted relative to an ideal 2α-chair than that of **1b** (ΔC_s^2 = 3.33 and 2.57°, respectively). The deviation of C2 to the β-side is 0.54 and 0.66 Å in **1b** and **1a**, respectively. The phenyl ring adopts the equatorial *β*-orientation relative to the heterocycle.

Both modifications contain an intramolecular H-bond O3—H...O2 (distance O...O2 = 2.69 and 2.57 Å; H...O1, 1.79 and 1.60 Å; angle O3H3O2 = 160.3(4.0)° and 174.2° in **1b** and **1a**, respectively).

It should be noted that **1b** and **1a** have slightly different conformations. The methoxy and phenyl are oriented differently relative to the backbone (torsion angles C11O4C7C6 are 176.9° and 6.6(8)°; H2C2C1′C6′, 19.2° and 50.9(6)°, respectively).

In our opinion, the differences in the conformations are due to the different packing in the crystal lattice (space group *Pbca* for **1a** and $P2_1/c$ for **1b**).

TABLE 3. Bond Angles (ω, deg)

Angle	ω	Angle	ω
C2'-O1-C9	119.0(5)	C7-O4-C11	116.4(5)
O1-C2-C3	112.0(5)	O1-C2-C1'	112.2(5)
C3-C2-C1'	114.6(6)	C2-C3-C4	113.2(6)
O2-C4-C3	121.0(6)	O2-C4-C10	120.9(6)
C3-C4-C10	118.1(5)	O3-C5-C6	116.1(6)
O3-C5-C10	119.8(5)	C6-C5-C10	124.0(6)
C5-C6-C7	115.5(6)	O4-C7-C6	111.2(5)
O4-C7-C8	125.4(5)	C6-C7-C8	123.3(5)
C7-C8-C9	119.1(5)	O1-C9-C8	117.6(5)
O1-C9-C10	121.2(5)	C8-C9-C10	121.2(6)
C4-C10-C5	124.3(5)	C4-C10-C9	118.7(6)
C5-C10-C9	116.8(5)	C2-C1'-C2'	121.9(5)
C2-C1'-C6'	121.5(6)	C2'-C1'-C6'	116.5(6)
C1'-C2'-C3'	119.2(6)	C2'-C3'-C4'	123.7(6)
C3'-C4'-C5'	117.1(7)	C4'-C5'-C6'	119.2(6)
C1'-C6'-C5'	124.1(6)		

EXPERIMENTAL

IR spectra were obtained on a Vector 22 instrument; UV spectra (ethanol solutions), on a Specord UV-VIS. NMR spectra were recorded on a Bruker DRX-500 (500.13 MHz working frequency for ^{1}H; 125.76 MHz, for ^{13}C) spectrometer using standard Bruker programs. High-resolution mass spectra (EI, 70 eV) were obtained in a Finnigan MAT 8200 instrument.

Air-dried balsamic poplar buds were extracted with ethanol. The extract was evaporated in vacuo to a thick residue and chromatographed over L40/100 and L100/160 silica-gel columns using eluents of petroleum ether—benzene, benzene—ethylacetate, and ethylacetate—ethanol in various ratios to afford four flavonoids, one of which was **1**.

Pinostrobin (5-hydroxy-7-methoxyflavanone), white crystals, $C_{16}H_{14}O_4$, mp 96-99°C (EtOAc).

IR spectrum (ν, cm^{-1}, KBr): 3062, 3032 (CH, arom.), 2972, 2935, 1646 (C=O), 1618, 1579 (C=C), 1445, 1381, 1339, 1302, 1259, 1209, 1158, 1092, 998, 960, 916, 887, 840, 800, 766, 742, 717.

IR spectrum (ν, cm^{-1}, CCl_4): 3078, 3040 (CH, arom.), 1640 (C=O), 1574 (C=C), 1503, 1465, 1487, 1371, 1338, 1267, 1212, 1185, 1152, 1091, 1064, 1031, 834, 696.

UV spectrum (λ, nm, log ε, EtOH): 212 (4.31), 289 (4.29), 334 (3.53).

Mass spectrum, *m*/*z* (I_{rel}, %): 270 (100.0) $[M]^+$, 252 (6.1), 193 (35.8), 138 (29.6), 114 (6.9), 110 (11.9), 95 (19.1), 77 (9.6), 51 (5.9), 39 (4.5).

Calc. for $C_{16}H_{14}O_4$, 270.08920; found, 270.08932.

^{13}C NMR (acetone-d_6, 125.76 MHz, δ, ppm): 42.61 (t, C-3), 55.22 (q, –OCH_3), 79.00 (d, C-2), 93.64 (d, C-6), 94.57 (d, C-8), 126.25 (d, C-4′), 128.40 (d, C-2′, C-6′), 128.45 (d, C-3′, C-5′), 138.92 (s, C-1′), 162.94 (s), 164.00 (s), 167.89 (s), 196.14 (s, C-3).

^{1}H NMR (acetone-d_6, 500 MHz, δ, ppm): 5.58 (1H, dd, 13.0, 3.0, H-2), 3.175 (1H, dd, 17.0, 13.0, H-3a), 2.83 (1H, dd, 17.0, 13.0, H-3b), 6.04 (1H, d, 2.0, H-6), 6.08 (1H, d, 2.0, H-8), 7.56 (2H, m, H-2′+H-6′), 7.44 (2H, m, H-3′+H-5′), 7.40 (1H, m, H-4′), 3.85 (3H, s, OMe).

X-ray structure Analysis. Lattice constants and intensities of 2300 independent reflections were measured on a Nicolet P4 (Cu Kα-radiation, graphite monochromator, $2\Theta \leq 71.59^\circ$) diffractometer. Crystals are monoclinic: a = 10.172(2), b = 16.079(2), c = 8.079(3) Å, β = 91.74(1)°, V = 1320.8(7) Å^3, d_{calc} = 1.359 g/cm^3, Z = 4 ($C_{16}H_{14}O_4$), space group $P2_1/c$. The structure was solved by direct methods using the SHELXTL PLUS (PC version) programs and refined by anisotropic full-matrix least-squares methods for nonhydrogen atoms. Hydrogen atoms except for the hydroxyl H were assigned geometrically. H3 was found in a difference electron-density synthesis. A total of 1658 reflections with $I > 2\sigma(I)$ were used in the calculations. The final discrepancy factors were R = 0.0996 and R_w = 0.0905.

REFERENCES

1. A. D. Gordienko, *Khim.-Farm. Zh.*, No. 3, 75 (1990).
2. V. A. Kostyuk, A. I. Potapovich, S. M. Tereshchenko, et al., *Biokhimiya*, **53**, No. 8, 1365 (1988).
3. A. I. Dorozhko, A. V. Brodskii, and I. B. Afanasʹev, *Biokhimiya*, No. 10, 1660 (1988).
4. B. Meyer, W. Schneider, and E. F. Elstner, *Arzneim. Forsch.*, **45**, No. 2, 174 (1995).
5. A. Zh. Seitembetova, V. V. Polyakov, S. M. Adekenov, and D. D. Mukhambetov, *Akmolinskii Med. Zh., Astana*, No. 3, 84 (1998).
6. V. V. Polyakov, A. Zh. Seitembetova, and S. M. Adekenov, *Akmolinskii Med. Zh., Astana*, No. 1, 83 (1999).
7. A. Zh. Seitembetova, V. V. Polyakov, and S. M. Adekenov, in: *International Conference "Medicinal Raw Material and Phytopreparations for Medicine and Agriculture,"* Karaganda (1999), p. 158.
8. M. El-Ghazaly, M. T. Khayyal, S. M. Okpanyi, and M. Arens-Corell, *Arzneim. Forsch.*, **45**, No. 3, 333 (1992).
9. S. von Kruedener, W. Schneider and E. F. Elstner, *Arzneim. Forsch.*, **45**, No. 2, 169 (1995).
10. S. M. Adekenov, E. A. Kulʹmagambetova, and L. N. Pribytkova, Kazakhstan Pat. Appl. No. 990047.1, Dec. 20, 1999, "5,7,4′-trihydroxy-3′,5′-dimethoxyflavone with antivirus activity."
11. V. E. Berezin, A. P. Bogoyavlinskaya, V. P. Tolmacheva, A. T. Kulyyasov, E. A. Kulʹmagambetova, L. N. Pribytkova, and S. M. Adekenov, in: *Search and Development of Methods for Preparing Phytopreparations* [in Russian], p. 340.
12. V. B. Braslavskii, V. A. Kurkin, G. G. Zapesochnaya, and N. A. Bezrukova, *Rastit. Resur.*, **27**, No. 3, 130 (1991).
13. V. V. Polyakov, R. S. Nadirov, S. M. Adekenov, A. Zh. Seitembetova, and E. E. Nikonov, *Akmolinskii Med. Zh., Astana*, No. 3, 126 (1999).
14. R. E. Niyazova, E. A. Kulʹmagambetova, A. T. Kulyyasov, S. M. Adekenov, and A. T. Ivashchenko, *Poisk.*, No. 4-5, 56 (2000).
15. V. V. Polyakov and S. M. Adekenov, *Biologically Active Compounds of Populus L. Plants and Preparations Based on Them* [in Russian], Gylym, Almaty (1999).
16. M. Shoja, *Z. Kristallogr.*, **189**, 89 (1989).
17. M. Shoja, *Acta Crystallogr. Sect. C, Cryst. Struct. Commun.*, **45**, 828 (1989).
18. F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, and R. Taylor, *J. Chem. Soc. Perkin Trans. II*, S1 (1987)