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1-[2(*Z*)-Bromo-3-phenyl-2-propenyl]-pyridin-2(1*H*)-one

MARTIN G. BANWELL, VANESSA S. BRIDGES AND DAVID C. R. HOCKLESS

Research School of Chemistry, Institute of Advanced Studies, Australian National University, Canberra, ACT 0200, Australia

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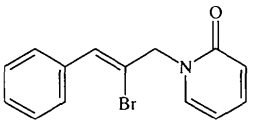
Abstract

The X-ray analysis of the title compound, $C_{14}H_{12}BrNO$, established the *Z* geometry about the propenyl double bond and also confirmed that the propenyl side chain is attached to the heterocyclic ring at the N atom rather than through the O atom.

Comment

As part of a program directed towards the synthesis of analogues of the promising anticancer agent camptothecin (Comins, Hong & Jianhua, 1994; Comins, Hong, Saha & Jianhua, 1994; Curran & Ko, 1994; Fang, Xie & Lowery, 1994; Fortunak, Mastrocola, Mellinger & Wood, 1994; Kolb, VanNieuwenhze & Sharpless, 1994; Peel & Sternbach, 1994; Rama Rao, Yadav & Valluri, 1994; Snyder, Shen, Bornmann & Danishefsky, 1994) quantities of 1-[2(Z)-bromo-3-phenyl-2-propenyl]pyridin-2(1*H*)-one, (I), were required. For the purpose of further synthetic manipulations a *cis* relationship between the bromo and phenyl substituents was necessary.



(I)

The ^{1}H NMR spectrum of the title compound does not show allylic coupling between atom H3′ and the methylene protons on atom C1′, thus eliminating one possible means of establishing the geometry about the C2′=C3′ double bond (Jackman & Sternhell, 1969). Furthermore, compound (I) was prepared by alkylation of the sodium salt of 2-hydroxypyridine and in addition to the desired *N*-alkylated product, the *O*-alkylated isomer was also obtained. These products were not readily distinguishable by spectroscopic methods, so unequivocal determination of the mode of attachment of the side chain to the heterocyclic ring in compound (I) was also required.

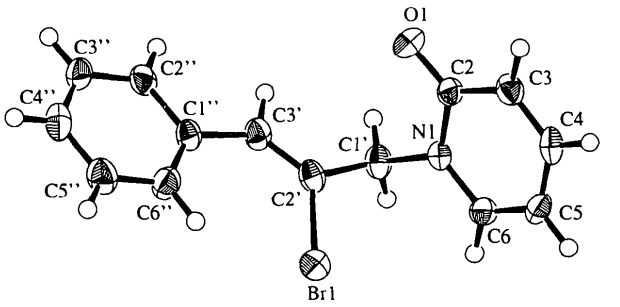


Fig. 1. View of 1-[2(*Z*)-bromo-3-phenyl-2-propenyl]pyridin-2(1*H*)-one showing the labelling of the non-H atoms. Displacement ellipsoids are shown at 50% probability levels and H atoms are drawn as circles of arbitrary radii.

Experimental

The title compound was prepared by treating the sodium salt of 2-hydroxypyridine with (Z)-2,3-dibromo-1-phenyl-1-propene (Mori, Chiba, Okita, Kayo & Ban, 1985) in DMF according to the method of Hopkins, Jonak, Minnemeyer & Tieckelmann (1967). The solvent was removed and subjection of the residue to chromatography (silica gel, 5% ethyl acetate/95% hexane to methanol gradient elution) afforded, upon concentration of the methanol fractions, a light yellow solid. This material was partitioned between water and dichloromethane, and concentration of the organic phase afforded the title compound, which was recrystallized from an ethyl acetate/hexane solution (m.p. 372–374 K).

Crystal data

$C_{14}H_{12}BrNO$
M_r = 290.16
Monoclinic
$P2_1/c$
a = 9.374 (2) Å
b = 11.217 (1) Å
c = 12.015 (2) Å
β = 104.03 (2)°
V = 1225.7 (3) Å^3
Z = 4
D_x = 1.572 Mg m^{-3}
Cu $K\alpha$ radiation
λ = 1.5418 Å
Cell parameters from 25 reflections
θ = 49–50°
μ = 4.423 mm^{-1}
T = 213 K
Irregular prism
0.280 × 0.160 × 0.120 mm
Colourless

Data collection

Rigaku AFC-6*R* diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scans (North, Phillips & Mathews, 1968)
T_{min} = 0.899, T_{max} = 1.000
2043 measured reflections
1943 independent reflections
1632 observed reflections [$I > 3\sigma(I)$]
R_{int} = 0.058
θ_{max} = 60.06°
$h = -10 \rightarrow 10$
$k = 0 \rightarrow 12$
$l = 0 \rightarrow 13$
3 standard reflections monitored every 150 reflections
intensity decay: 2.18%

Refinement

Refinement on F
R = 0.0350
wR = 0.0380
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.53 e Å^{-3}
$\Delta\rho_{min}$ = −0.56 e Å^{-3}

$S = 2.410$
1632 reflections
154 parameters
H-atom parameters not refined
Unit weights applied

Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$

	x	y	z	U_{eq}
Br(1)	0.13557 (5)	0.07867 (4)	0.28446 (4)	0.0447 (1)
O(1)	0.4124 (3)	0.2746 (3)	0.0691 (2)	0.0429 (9)
N(1)	0.3574 (3)	0.2900 (3)	0.2433 (3)	0.0269 (9)
C(2)	0.3599 (4)	0.3356 (4)	0.1356 (3)	0.029 (1)
C(3)	0.2998 (5)	0.4527 (4)	0.1125 (3)	0.035 (1)
C(4)	0.2433 (5)	0.5129 (4)	0.1886 (4)	0.036 (1)
C(5)	0.2436 (4)	0.4626 (4)	0.2961 (4)	0.034 (1)
C(6)	0.3012 (4)	0.3529 (4)	0.3207 (3)	0.031 (1)
C(1′)	0.4153 (4)	0.1689 (4)	0.2724 (4)	0.035 (1)
C(2′)	0.3049 (4)	0.0735 (4)	0.2215 (3)	0.033 (1)
C(3′)	0.3227 (4)	−0.0056 (4)	0.1453 (4)	0.034 (1)
C(1″)	0.2354 (4)	−0.1045 (3)	0.0824 (3)	0.030 (1)
C(2″)	0.3038 (4)	−0.1748 (3)	0.0142 (4)	0.033 (1)
C(3″)	0.2279 (5)	−0.2650 (4)	−0.0536 (4)	0.038 (1)
C(4″)	0.0833 (5)	−0.2880 (4)	−0.0545 (4)	0.040 (1)
C(5″)	0.0151 (5)	−0.2206 (4)	0.0130 (4)	0.043 (1)
C(6″)	0.0894 (5)	−0.1303 (4)	0.0810 (4)	0.040 (1)

Table 2. *Selected geometric parameters* (Å, °)

Br(1)—C(2′)	1.918 (4)	C(1′)—C(2′)	1.511 (6)
O(1)—C(2)	1.241 (5)	C(1″)—C(3′)	1.473 (6)
N(1)—C(1′)	1.473 (5)	C(2′)—C(3′)	1.315 (6)
C(1′)—N(1)—C(2)	118.0 (3)	Br(1)—C(2′)—C(1′)	111.7 (3)
C(1′)—N(1)—C(6)	119.6 (3)	Br(1)—C(2′)—C(3′)	123.5 (3)
N(1)—C(1′)—C(2′)	112.3 (3)	C(1′)—C(2′)—C(3′)	124.7 (4)
C(2″)—C(1″)—C(3′)	116.6 (4)	C(1″)—C(3′)—C(2′)	135.8 (4)
C(3′)—C(1″)—C(6″)	125.7 (4)		

The θ scan width used was $(1.10 + 0.3\tan\theta)°$ at a speed of 16.0° min^{-1} (in ω). The weak reflections were rescanned a maximum of four times and the counts accumulated to ensure good counting statistics. Stationary background counts were made on each side of the reflection with a 2:1 ratio of peak to background counting time. H atoms were located from a difference map and fixed at ideal positions with $U_{iso} = 1.2U_{eq}$(C). The structure was solved by Patterson methods and expanded using Fourier techniques (Beurskens *et al.*, 1992). All calculations were performed using *TEXSAN* (Molecular Structure Corporation, 1993).

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1993). Program(s) used to refine structure: *TEXSAN*. Software used to prepare material for publication: *TEXSAN*.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: AS1181). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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(+)-(*S*)-1-{4-[(2-Benzothiazolyl)(methyl)-amino]piperidyl}-3-(3,4-difluorophenoxy)-2-propanol (Lubeluzole)†

OSWALD M. PEETERS, NORBERT M. BLATON AND CAMIEL J. DE RANTER*

Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Faculteit Farmaceutische Wetenschappen, Katholieke Universiteit Leuven, Van Evenstraat 4, B-3000 Leuven, Belgium

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Abstract

The crystal structure and absolute configuration of the (+) enantiomer of the title compound, $C_{22}H_{25}F_2N_3O_2S$, have been determined. The absolute configuration is *S*.

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