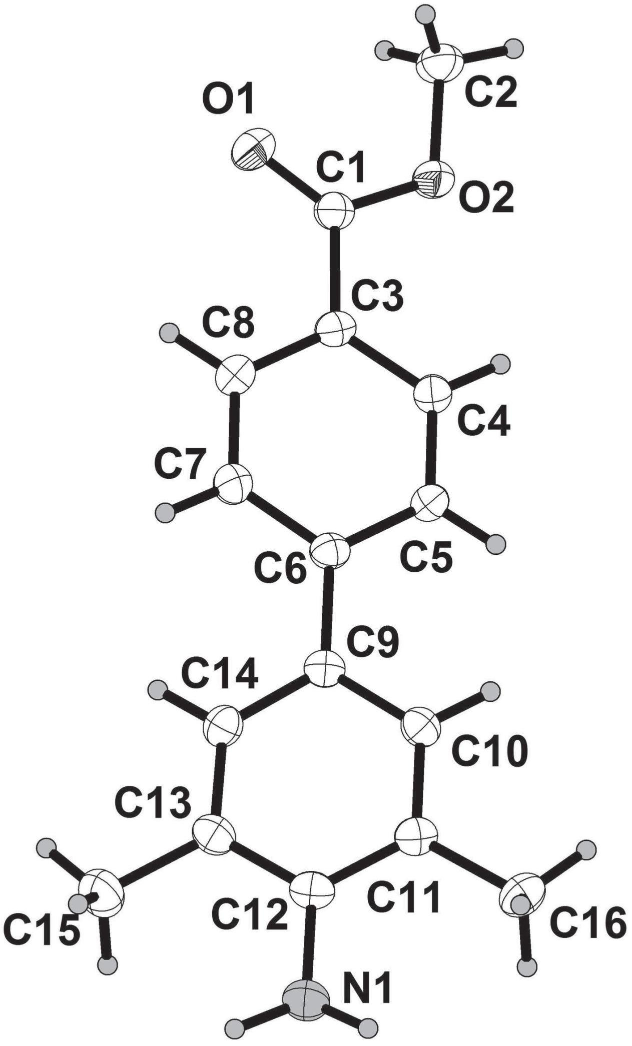
Mao-Yuan Zhang and Da-Bin Shi*

Crystal structure of methyl 4′-amino-3′,5′-dimethyl-[1,1′-biphenyl]-4-carboxylate, $C_{16}H_{17}NO_2$



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Abstract

$C_{16}H_{17}NO_2$, orthorhombic, $P2_12_12_1$ (no. 19), $a = 6.3761(2)$ Å, $b = 12.0521(4)$ Å, $c = 17.3288(5)$ Å, $V = 1331.64(7)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0462$, $wR_{ref}(F^2) = 0.1243$, $T = 153(2)$ K.

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The asymmetric unit of the title crystal structure is shown in the figure. Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Block, white
Size:	0.20 × 0.20 × 0.20 mm
Wavelength:	Cu $K\alpha$ radiation (1.54178 Å)
μ:	0.67 mm^{-1}
Diffractometer, scan mode:	Agilent CCD, φ and ω-scans
θ_{max}, completeness:	73.6°, >97%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	2972, 2125, 0.026
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2010
$N(param)_{refined}$:	184
Programs:	CrysAlis^{PRO} [1], SHELX [2, 3]

Source of material

Synthesis of 4-iodo-2,6-dimethylaniline [4, 5]. In a round bottom flask 2,6-dimethylaniline (18.12 g, 150 mmol, 1.0 equiv) and $NaHCO_3$ (37.8 g, 450 mmol, 3.0 equiv) were introduced in MeOH (400 mL). Iodine (40 g, 157.5 mmol, 1.05 equiv) in CH_2Cl_2 (200 mL) was added and the reaction mixture was stirred at room temperature for 12 hours. Then, the solids were filtered off the mixture and rinsed with CH_2Cl_2. The filtrate was concentrated under vacuum leading to a dark orange oil. A saturated solution of sodium thiosulfate was added and the reaction mixture was stirred for 2 hours. After extraction with CH_2Cl_2, the combined organic layers were dried over $MgSO_4$ and concentrated under vacuum. The product was obtained as brown oil (25.6 g, 69% yield). Synthesis of the title compound [6]. A mixture of (4-(methoxycarbonyl)phenyl)boronic acid (9.37 g, 52.09 mmol, 1.1 equiv), 4-iodo-2,6-dimethylaniline (11.7 g, 47.35 mmol, 1.0 equiv), palladium tetrakis(triphenylphosphine) (1.64 g, 1.42 mmol, 3 mol%), and K_2CO_3 (21.6 g, 156 mmol, 3.3 equiv) in 330 mL of dioxane/H_2O (3/1) was stirred under nitrogen for 72 h at 90 °C. After the mixture was cooled to room temperature, it was extracted with CH_2Cl_2 and washed with H_2O several times. The organic layer was dried with $MgSO_4$, and

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***Corresponding author: Da-Bin Shi,** School of Pharmaceutical Sciences, Zunyi Medical College, Zunyi 563000, People's Republic of China, e-mail: sdb007.student@sina.com
Mao-Yuan Zhang: School of Pharmaceutical Sciences, Zunyi Medical College, Zunyi 563000, People's Republic of China

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
O1	−0.3748(2)	−0.01044(15)	−0.03251(9)	0.0348(4)
O2	−0.0797(2)	−0.01015(13)	−0.10231(7)	0.0266(4)
N1	0.6156(3)	0.37525(17)	0.38730(10)	0.0318(4)
H1A	0.545(5)	0.389(3)	0.4359(16)	0.052(8)*
H1B	0.717(5)	0.426(2)	0.3745(13)	0.039(7)*
C1	−0.1904(3)	0.01148(17)	−0.03871(11)	0.0232(4)
C2	−0.1975(4)	−0.05720(19)	−0.16556(11)	0.0306(5)
H2A	−0.3055	−0.0063	−0.1810	0.046*
H2B	−0.2601	−0.1258	−0.1494	0.046*
H2C	−0.1053	−0.0707	−0.2083	0.046*
C3	−0.0620(3)	0.06490(17)	0.02223(10)	0.0221(4)
C4	0.1455(3)	0.09717(18)	0.01065(10)	0.0244(4)
H4	0.2096	0.0838	−0.0367	0.029*
C5	0.2570(3)	0.14897(18)	0.06889(10)	0.0240(4)
H5	0.3950	0.1704	0.0598	0.029*
C6	0.1671(3)	0.16990(16)	0.14115(10)	0.0215(4)
C7	−0.0423(3)	0.13758(18)	0.15166(11)	0.0263(4)
H7	−0.1073	0.1513	0.1987	0.032*
C8	−0.1544(3)	0.08566(18)	0.09357(11)	0.0270(4)
H8	−0.2926	0.0645	0.1023	0.032*
C9	0.2866(3)	0.22263(15)	0.20517(10)	0.0210(4)
C10	0.4705(3)	0.28263(16)	0.19202(10)	0.0228(4)
H10	0.5217	0.2879	0.1419	0.027*
C11	0.5800(3)	0.33479(15)	0.25138(11)	0.0226(4)
C12	0.5052(3)	0.32717(16)	0.32712(10)	0.0231(4)
C13	0.3237(3)	0.26408(17)	0.34238(11)	0.0256(4)
C14	0.2205(3)	0.21392(16)	0.28138(11)	0.0241(4)
H14	0.1010	0.1723	0.2919	0.029*
C15	0.2467(4)	0.2485(2)	0.42396(12)	0.0374(6)
H15A	0.1360	0.1945	0.4245	0.056*
H15B	0.1949	0.3178	0.4435	0.056*
H15C	0.3602	0.2231	0.4558	0.056*
C16	0.7758(3)	0.40006(18)	0.23400(12)	0.0299(5)
H16A	0.8878	0.3748	0.2666	0.045*
H16B	0.7504	0.4774	0.2434	0.045*
H16C	0.8140	0.3896	0.1809	0.045*

the solvent was removed with a rotary evaporator. The crude product was purified by column chromatography using silica gel and petroleum ether/ethyl acetate (20/1) as the eluent. The product was obtained after removal of the solvents (7.2 g, 60% yield). The crystal suitable for X-ray analysis was obtained by slow evaporation of methanol at room temperature over a period of seven days, yield: 0.62 g (88.5%). Melting point: 113–114 °C. Elemental analysis–found: C, 75.22%; H, 6.73%; N, 5.52%; calculated for $C_{16}H_{17}NO_2$: C, 75.27%; H, 6.71%; N, 5.49%.

Experimental details

All hydrogen atoms were identified in difference Fourier syntheses. The structure was solved by direct methods [2] and refined on F^2 by full-matrix least-squares technique using the SHELX program [3]. Except the solvent molecules, hydrogen atoms attached to carbon were placed in geometrically idealized positions and refined using a riding model.

Discussion

In recent years, biphenyl moieties have emerged as versatile and useful building units in a variety of synthetic transformations, which can build all kinds of biologically active molecules [7–9]. For example, biphenyl mannoside FimH inhibitors were designed. Diverse modifications to the biphenyl ring to improve drug like physical and pharmacokinetic properties of mannosides were assessed for FimH binding affinity based on their effects on hemagglutination and biofilm formation along with direct FimH binding assays [10].

The title compound is composed of two substituted phenyl moieties. The dihedral angle between the planes of two aromatic rings is 18.5°. The bond lengths of C12—N1 and C1—O1 are 1.385(3) Å and 1.210(2) Å, respectively. And the bond lengths of C1—O2 and C2—O2 are 1.334(2) Å and 1.445(2) Å, respectively. As a result of the conjugation of these aromatic rings, the bond length of C6—C9 is 1.488(3) Å, which is shorter than that of typical C—C (1.53 Å). The bond angle (C1—O2—C2) and (O1—C1—O2) are 115.37(16)° and 122.99(19)°, respectively. There is an intermolecular hydrogen bond (d D$\cdots$A 3.254 Å; H$\cdots$A 2.335 Å) between H1A and O1 atom (symmetry code: $-x$, $y+1/2$, $-z+1/2$), which produce one dimensional chains to stabilize the crystal structure. In the crystal packing, dipole-dipole and van der Waals interactions are effective besides an intermolecular hydrogen bond in the molecular packing. Bond lengths and angles of the title molecule are in the typical ranges [11, 12].

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