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5-Butyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-(2,4,6-trimethylphenyl)isoxazole

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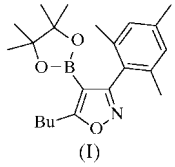
A novel [3+2]-cycloaddition reaction of alkynylboronates and nitrile oxides gave the title compound, $C_{22}H_{32}BNO_3$, as a single regioisomer. The X-ray crystal structure analysis of this compound shows two independent molecules in the asymmetric unit, each with approximately coplanar isoxazole and boronate rings.

Comment

Aromatic and heteroaromatic boronic acids and esters represent one of the most valuable and heavily used classes of synthetic intermediates in organic chemistry. We have recently been investigating new routes for the preparation of arylboronic esters through the cycloaddition reactions of alkynylboronates (Davies *et al.*, 1999; Davies, Johnson & Harrity, 2001). In extending this novel synthetic strategy to heteroarylboronic esters, we have recently reported a highly regioselective [3+2]-cycloaddition reaction of nitrile oxides and alkynylboronates (Davies, Wybrow *et al.*, 2001). This route permits the synthesis of a range of densely substituted isoxazole boronic esters in a single step from readily available starting materials and represents an efficient alternative to traditional metallation techniques (Iddon, 1994).



(I)

The title compound, (I), was prepared in 73% yield by heating a solution of 2,4,6-trimethylbenzonitrile *N*-oxide and two equivalents of 2-hex-1-ynyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in ether at reflux for 64 h. The product, (I), was isolated as a single regioisomer and its regiochemical assignment was tentatively made on the basis of the ^{13}C NMR spectrum (C-5: δ 181.6 p.p.m.). In an effort to confirm the assigned regiochemistry and to provide a more routine method for regiochemical identification through correlation with ^{13}C NMR shift, we undertook the X-ray analysis of (I). Accordingly, slow cooling of a solution of (I) in hexanes (341–298 K) provided suitable crystals for X-ray analysis and confirmed the regiochemical assignment as that shown.

The asymmetric unit of (I) was found to contain two independent molecules, denoted 1 and 2 (Fig. 1), each containing near coplanar isoxazole and dioxaborolane rings, with torsion

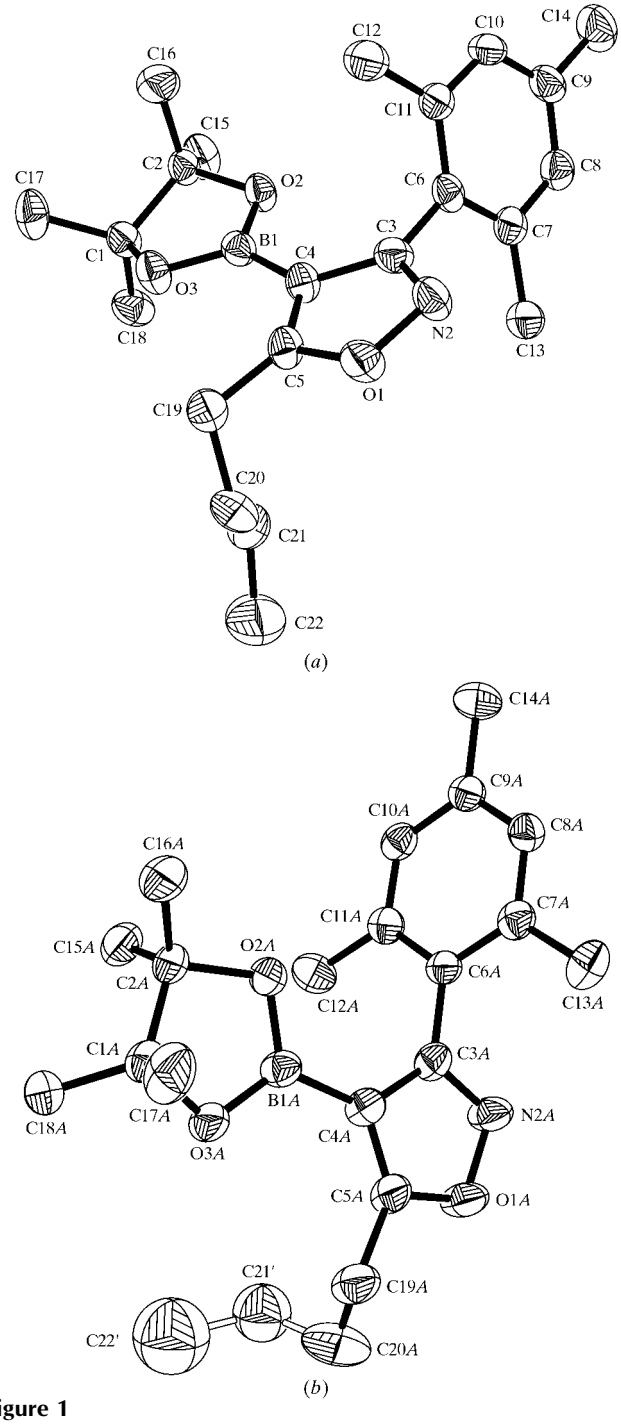


Figure 1
View of (*a*) molecule 1 and (*b*) molecule 2 of the title compound showing the labelling of the non-H atoms and the major disorder components of the butyl chains. Displacement ellipsoids are shown at the 50% probability level.

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angles between the rings of 6.2 (6) and 11.3 (7)°, respectively, in the two molecules. Additionally, the butyl chain shows a 52/48% occupancy disorder (designated C21*A*/*B* and C22*A*/*B*) for molecule 1 and a 56/44% occupancy disorder (designated C21/21′ and C22/22′) for molecule 2; isotropic displacement parameters were refined for the disordered atoms C21, C21′, C22 and C22′. The near coplanarity of these rings suggested conjugation of the oxazole O atom with the boronate moiety, which would, in turn, be reflected in the length of the carbon–boron bond. Surprisingly, however, the C4—B1 bond length of 1.544 (6) Å is only slightly short in comparison with other arylboronic esters in which the boronate group is almost orthogonal to the aromatic ring and therefore cannot participate in conjugation [for example, hydroquinone boronic esters with a torsion angle of 85° show a C—B bond length of 1.572 (3) Å; Davies *et al.*, 1999]. The orientation of the boronic ester moiety results in the 2,4,6-trimethylphenyl group being twisted out of the plane of the other two rings. The torsion angles in molecules 1 and 2 are 74.6 (5) and 69.1 (6)°, respectively, which are in good agreement with that of related ethyl 3-(9-anthryl)-5-methyl-4-isoxazolecarboxylate [80.2 (5)°; Mosher *et al.*, 1996]. Bond lengths, angles and torsion angles not reported in Table 1 are within expected ranges.

Experimental

The title compound was prepared as described in the *Comment* and the crude product was purified by flash column chromatography (eluant: hexane/ethyl acetate, 5:1) to yield colourless crystals (m.p. 330.5–332.8 K). ^{1}H NMR (δ, 250 MHz, $CDCl_3$): 0.94 (3H, *t*, *J* = 7.3 Hz, CH_3–CH_2), 1.11 (12H, *s*, CH_3), 1.36 (2H, *sext*, *J* = 7.3 Hz, CH_3–CH_2–CH_2), 1.75 (2H, *pent*, *J* = 7.3 Hz, CH_3–CH_2–CH_2), 2.04 (6H, *s*, Ar–CH_3), 2.28 (3H, *s*, Ar–CH_3), 3.00 (2H, *t*, *J* = 7.3 Hz, CH_3–CH_2–CH_2–CH_2), 6.84 (2H, *br s*, Ar–H). ^{13}C NMR (δ, 62.9 MHz, $CDCl_3$): 13.7, 19.9, 21.2, 22.1, 24.5, 26.8, 30.3, 83.0, 127.2, 127.6, 136.8, 137.6, 165.8, 181.6. Analysis calculated for $C_{22}H_{32}BNO_3$: C 71.55, H 8.73, N 3.79%; found: C 71.30, H 8.84, N 3.71%.

Crystal data

$C_{22}H_{32}BNO_3$	D_x = 1.120 Mg m^{-3}
M_r = 369.30	Mo $K\alpha$ radiation
Monoclinic, *C*2/*c*	Cell parameters from 52 reflections
a = 33.132 (6) Å	θ = 1.5–24.0°
b = 9.9664 (18) Å	μ = 0.07 mm^{-1}
c = 27.505 (5) Å	*T* = 150 (2) K
β = 105.331 (4)°	Square prism, colourless
V = 8759 (3) Å^3	0.23 × 0.12 × 0.08 mm
Z = 16	

Table 1
Selected geometric parameters (Å, °).

B1—C4	1.544 (6)	N2*A*—C3*A*	1.310 (5)
O1—C5	1.364 (4)	N2*A*—O1*A*	1.427 (4)
O1—N2	1.418 (4)	O1*A*—C5*A*	1.354 (4)
C3—C4	1.446 (5)	C3*A*—C4*A*	1.441 (5)
C3—C6	1.481 (5)	C3*A*—C6*A*	1.479 (5)
C4—C5	1.364 (5)	C4*A*—C5*A*	1.355 (5)
C5—C19	1.480 (5)	C5*A*—C19*A*	1.497 (5)
B1*A*—C4*A*	1.541 (6)		
C5—O1—N2	108.9 (3)	C3*A*—N2*A*—O1*A*	104.4 (3)
C3—N2—O1	105.3 (3)	C5*A*—O1*A*—N2*A*	108.6 (3)
N2—C3—C4	112.5 (4)	N2*A*—C3*A*—C4*A*	113.2 (4)
C5—C4—C3	103.3 (3)	C5*A*—C4*A*—C3*A*	102.8 (4)
O1—C5—C19	114.4 (3)	O1*A*—C5*A*—C19*A*	113.8 (4)

Data collection

Bruker SMART1000 CCD area-detector diffractometer	7714 independent reflections
ω scans	2827 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (*SADABS*; Bruker, 1999)	R_{int} = 0.123
T_{min} = 0.577, T_{max} = 1.000	θ_{max} = 25.0°
20 283 measured reflections	*h* = −22 → 39
	k = −11 → 11
	l = −32 → 29

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.063	$w = 1/[\sigma^2(F_o^2) + (0.0574P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.172	$(\Delta/\sigma)_{max} < 0.001$
S = 0.85	$\Delta\rho_{max}$ = 0.67 e Å^{-3}
7714 reflections	$\Delta\rho_{min}$ = −0.27 e Å^{-3}
505 parameters	

Only 28% of the diffraction data have $I > 2\sigma(I)$. This is due to a general weakness in the data and there is no pattern which would suggest missed lattice centring or a spurious cell doubling or tripling. Methyl H atoms were located from difference Fourier syntheses and were refined as part of rigid groups (C—H fixed at 0.98 Å) which were allowed to rotate but not tip or distort, and with U_{iso}(H) = 1.5U_{eq}(C). Other H atoms were placed geometrically (aryl C—H = 0.95 Å and methylene C—H = 0.99 Å) and refined using a riding model with U_{iso}(H) = 1.2U_{eq}(C,N).

Data collection: *SMART* (Bruker, 1997–2001); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 1999); *SHELXTL* (Bruker, 1997); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1469). Services for accessing these data are described at the back of the journal.

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