Synthesis and antifungal properties of benzylamines containing boronate esters

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Abstract: Addition of 3-$H_2NC_6H_4$Bpin (pin = 1,2-$O_2C_2Me_4$) to a series of aldehydes and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acetophenone afforded the corresponding benzylideneamines in moderate to high yields. Hydroboration of these imines with catecholborane (HBcat, cat = 1,2-$O_2C_6H_4$) at room temperature gives, upon aqueous workup, the corresponding borylamines. An X-ray diffraction study was carried out on imine **1h** derived from 9-anthraldehyde and 3-$H_2NC_6H_4$Bpin. Crystals of **1h** were triclinic, a = 9.6793(4) Å, b = 10.7397(4) Å, c = 11.5353(4) Å, α = 105.1890(10)°, β = 97.3030(10)°, γ = 102.1480(10)°, Z = 2 with space group $P\bar{1}$ and crystals of *N*-[3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-4-methoxybenzylamine **2c** were orthorhombic, a = 8.6612(4) Å, b = 10.3794(4) Å, c = 20.6033(9) Å, Z = 4 with space group $P2_12_12_1$. Amines have been tested for their antifungal properties against *Aspergillus niger* and *Aspergillus flavus*.

Key words: benzylamines, boronate esters, aminoboron, hydroboration, antifungal.

Résumé : L'addition de 3-$H_2NC_6H_4$Bpin (pin = 1,2-$O_2C_2Me_4$) à une série d'aldéhyde et à la 4-(4,4,5,5-tétraméthyl-1,3,2-dioxaborolan-2-yl)acétophénone conduit aux benzylidèneamines correspondantes avec des rendements qui vont de bons à excellents. L'hydroboration de ces imines avec du catécholborane (HBcat, cat = 1,2-$O_2C_6H_4$), à la température ambiante, fournit les borylamines correspondances après extraction. Une étude par diffraction des rayons X a été réalisée sur l'imine **1h** provenant du 9-anthraldéhyde et du 3-$H_2NC_6H_4$Bpin. Les cristaux de **1h** sont tricliniques, groupe d'espace $P\bar{1}$, avec a = 9,6793(4) Å, b = 10,7397(4) Å et c = 11,5353(4) Å, α = 105,1890(10)°, β = 97,3030(10)° et γ = 102,1480(10)° et Z = 2; les cristaux de *N*-[3-(4,4,5,5-tétraméthyl-1,3,2-dioxaboralan-2-yl)phényl]-4-méthoxybenzylamine, **2c**, sont orthorhombiques, groupe d'espace $P2_12_12_1$, avec a = 8,661(4) Å, b = 10,3794(4) Å et c = 20,6033(9) Å et Z = 4. Les amines ont été évaluées pour leur activité antifongique contre *Aspergillus niger* et *Aspergillus flavus*.

Mots clés : benzylamines, esters de l'acide boronique, aminobore, hydroboration, antifongique.

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Introduction

The bioinorganic chemistry of boron is an area of growing interest (1–10). For example, boron-containing amino acids are among the most potent inhibitors of the serine proteases chymotrypsin and subtilisin (10). Serine proteases are a diverse group of proteolytic enzymes whose numerous physiological functions include digestion, growth, differentiation, cell signalling and migration, immunological defence, and apoptosis. Proteases are also vital in the generation of most disease processes. Much effort has therefore focused on the synthesis of boron-containing amino acid and peptide derivatives for possible applications as enzyme inhibitors. Although aminoboronic acid derivatives have significant biological activity and are useful synthetic intermediates in organic chemistry (11,12), synthetic routes to these compounds are scarce and involve complicated procedures. As a result, relatively few examples of aminoboron compounds have been studied (13–19). As part of our program to develop synthetically attractive routes to aminoboron compounds, we have prepared a series of boronated benzylamines derived from the reaction of 3-$H_2NC_6H_4$Bpin (pin = 1,2-$O_2C_2Me_4$) with various aldehydes and the boron-containing ketone 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acetophenone and tested these compounds for their antifungal properties. Results are reported herein.

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Experimental

Reagents and solvents used were obtained from Aldrich Chemicals. NMR spectra were recorded on a JEOL JNM-

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GSX270 FT NMR spectrometer. ^{1}H NMR chemical shifts are reported in ppm and referenced to residual protons in deuterated solvent at 270.05 MHz. ^{11}B NMR chemical shifts are referenced to external $F_3B{\cdot}OEt_2$ at 86.55 MHz. ^{13}C NMR chemical shifts are referenced to solvent carbon resonances as internal standards at 67.80 MHz. Multiplicities are reported as (s) singlet, (d) doublet, (t) triplet, (q) quartet, (quint) quintet, (m) multiplet, (br) broad, and (ov) overlapping. Infrared spectra were obtained using a Mattson Genesis II FT-IR spectrometer and reported in cm^{-1}. Melting points were measured uncorrected with a Mel-Temp apparatus. Microanalyses for C, H, and N were carried out at Desert Analytics (Tucson, Arizona).

Transesterification

Protection of the starting boronic acids (10.0 mmol) with 1 equiv of pinacol was carried out in methylene chloride in the presence of 10 g of activated molecular sieves (type 4A). The reactions were allowed to proceed for 5 days at which point the sieves were removed by suction filtration and the product isolated upon removal of the solvent under vacuum.

2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (2-FPBpin)

Yield: 68% of a yellow oil; bp 97°C. IR (Nujol): 2920, 2856, 1699, 1595, 1462, 1379, 1257, 1146, 860, 764, 666. ^{1}H NMR (in $CDCl_3$) δ 10.54 (s, 1H), 7.95 (d, J = 8 Hz, 1H), 7.87 (d, J = 8 Hz, 1H), 7.58 (m, 2H), 1.35 (s, 12H). ^{13}C NMR δ 194.4, 141.1, 135.3, 132.8, 130.6, 130 (br, C-B), 127.7, 84.2, 24.6. ^{11}B NMR δ 31.7 (br).

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (3-FPBpin)

Yield: 77% of a white solid; mp 49°C. IR (Nujol): 2970, 2880, 1710, 1605, 1460, 1361, 1194, 1144, 965, 702. ^{1}H NMR (in $CDCl_3$) δ 10.05 (s, 1H), 8.31 (s, 1H), 8.08 (d, J = 8 Hz, 1H), 8.00 (d, J = 8 Hz, 1H), 7.54 (t, J = 8 Hz, 1H), 1.37 (s, 12H). ^{13}C NMR δ 192.6, 140.7, 137.3, 135.8, 131.3, 130 (br, C-B), 128.4, 84.3, 24.9. ^{11}B NMR δ 31.2 (br). Anal. calcd. for $C_{13}H_{17}O_3B$: C 67.28, H 7.38; found: C 67.38, H 7.28.

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (4-FPBpin)

Yield: 71% of a pale yellow solid; mp 50°C. IR (Nujol): 2972, 2880, 1711, 1460, 1361, 1144, 858, 651. ^{1}H NMR (in $CDCl_3$) δ 10.05 (s, 1H), 7.98 (d, J = 8 Hz, 2H), 7.88 (d, J = 8 Hz, 2H), 1.37 (s, 12H). ^{13}C NMR δ 192.9, 138.8, 135.5, 135 (br, C-B), 128.8, 84.5, 25.1. ^{11}B NMR δ 31.1 (br). Anal. calcd. for $C_{13}H_{17}O_3B$: C 67.28, H 7.38; found: C 67.56, H 7.25.

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)acetophenone

Yield: 97% of a pale yellow solid; mp 60–62°C. IR (Nujol): 2941, 2858, 1691, 1556, 1508, 1460, 1360, 1265, 1215, 1144, 1093, 1016. ^{1}H NMR (in $CDCl_3$) δ 7.91 (m, 4H), 2.60 (s, 3H), 1.35 (s, 12H). ^{13}C NMR δ 197.9, 138.7, 134.7, 130 (br, C-B), 127.0, 83.9, 26.5, 24.6. ^{11}B NMR δ 31.2 (br). Anal. calcd. for $C_{14}H_{19}O_3B$: C 68.32, H 7.78; found: C 68.28, H 7.86.

Preparation of imines

Imines were prepared by combining the starting aldehyde (or ketone) with 1 equiv of 3-$H_2NC_6H_4$Bpin in methylene chloride and 10 g of activated molecular sieves (type 4A). After 3–5 days the sieves were removed by suction filtration and the imine was obtained following removal of the solvent under vacuum. Imine **1j** was isolated following crystallization from hot hexane.

1a

Yield: 81% of an off-white solid; mp 70°C. IR (Nujol): 2925, 1629, 1573, 1452, 1377, 1353, 1140, 1069, 963, 906, 801, 755. ^{1}H NMR (in $CDCl_3$) δ 8.52 (s, 1H), 7.91 (m, 2H), 7.68 (m, 2H), 7.49 (m, 3H), 7.40 (m, 2H), 1.37 (s, 12H). ^{13}C NMR δ 160.6, 151.7, 136.5, 132.6, 131.5, 129.0, 129 (br, C-B), 128.9, 128.8, 126.2, 125.0, 84.1, 25.1. ^{11}B NMR δ 31.5 (br).

1b

Yield: 79% of a bright yellow solid; mp 111°C. IR (Nujol): 2925, 2856, 1708, 1628, 1602, 1525, 1461, 1360, 1319, 1147, 1075, 967, 908, 852, 705. ^{1}H NMR (in $CDCl_3$) δ 8.61 (s, 1H), 8.35 (d, J = 8 Hz, 2H), 8.09 (d, J = 8 Hz, 2H), 7.76 (d, J = 8 Hz, 1H), 7.67 (s, 1H), 7.48–7.38 (ov m, 2H), 1.37 (s, 12H). ^{13}C NMR δ 157.6, 150.5, 149.5, 141.9, 133.7, 130 (br, C-B), 129.6, 129.0, 126.1, 125.2, 124.2, 84.3, 25.1. ^{11}B NMR δ 31.2 (br).

1c

Yield: 92% of a white solid; mp 92°C. IR (Nujol): 2968, 2893, 1705, 1620, 1605, 1572, 1510, 1456, 1352, 1248, 1140, 1026, 831, 706. ^{1}H NMR (in $CDCl_3$) δ 8.43 (s, 1H), 7.85 (d, J = 8 Hz, 2H), 7.64 (ov m, 2H), 7.39 (ov m, 2H), 6.99 (d, J = 8 Hz, 2H), 3.87 (s, 3H), 1.36 (s, 12H). ^{13}C NMR δ 162.2, 159.7, 151.8, 132.1, 130.6, 130 (br, C-B), 129.4, 128.6, 126.2, 124.9, 114.2, 83.9, 55.4, 25.0. ^{11}B NMR δ 31.6 (br).

1d

Yield: 85% of a pale yellow solid; mp 98°C. IR (Nujol): 2959, 1609, 1561, 1456, 1370, 1314, 1150, 1070, 964, 853, 791, 705. ^{1}H NMR (in $CDCl_3$) δ 8.79 (s, 1H), 7.70 (d, J = 8Hz, 1H), 7.59 (s, 1H), 7.41 (t, J = 8 Hz, 1H), 7.29 (d, J = 8 Hz, 1H), 6.92 (s, 2H), 2.53 (s, 6H), 2.32 (s, 3H), 1.37 (s, 12H). ^{13}C NMR δ 161.1, 152.8, 139.9, 138.8, 132.1, 130.8, 130 (br, C-B), 129.9, 128.7, 126.5, 124.3, 84.1, 25.0, 21.4, 21.3. ^{11}B NMR δ 32.1 (br).

1e

Yield: 82% of an off-white solid; mp 145°C. IR (Nujol): 2935, 2858, 1626, 1591, 1562, 1462, 1414, 1375, 1352, 1267, 1140, 1111, 1070, 962, 916, 856, 818, 706. ^{1}H NMR (in $CDCl_3$) δ 9.21 (s, 1H), 8.16 (d, J = 8 Hz, 1H), 7.85 (d, J = 8 Hz, 1H), 7.76 (s, 1H), 7.69 (m, 1H), 7.55–7.40 (ov m, 4H), 1.38 (s, 12H), 1.33 (s, 12H). ^{13}C NMR δ 162.6, 162.4, 151.5, 135.3, 132.1, 130.8, 130.1, 130 (br, C-B), 128.7, 127.0, 126.4, 125.4, 84.0, 83.8, 24.9, 24.8. ^{11}B NMR δ 31.3 (br).

1f

Yield: 86% of an off-white solid; mp 219°C. IR (Nujol): 2935, 2858, 1630, 1599, 1572, 1462, 1377, 1348, 1140, 964,

852, 706. ^{1}H NMR (in $CDCl_3$) δ 8.53 (s, 1H), 8.28 (s, 1H), 8.07 (d, *J* = 8 Hz, 1H), 7.93 (d, *J* = 8 Hz, 1H), 7.69 (d, *J* = 8 Hz, 1H), 7.64 (s, 1H), 7.48 (t, *J* = 8 Hz, 1H), 7.45–7.33 (ov m, 2H), 1.36 (s, 24H). ^{13}C NMR δ 160.4, 151.5, 137.6, 135.9, 135.6, 132.2, 130.9, 129.7 (br, C-B), 128.6, 128.2, 126.1, 124.8, 84.0, 24.9. ^{11}B NMR δ 31.5 (br).

1g

Yield: 92% of an off-white solid; mp 208°C. IR (Nujol): 2971, 2910, 1710, 1623, 1608, 1511, 1465, 1355, 1271, 1142, 1087, 964, 855, 702. ^{1}H NMR (in $CDCl_3$) δ 8.52 (s, 1H), 7.90 (s, 4H), 7.70 (d, *J* = 8 Hz, 1H), 7.64 (s, 1H), 7.42–7.36 (ov m, 2H), 1.36 (s, 24H). ^{13}C NMR δ 160.6, 151.5, 138.7, 135.3, 132.7, 132 (br, C-B), 129 (br, C-B), 128.8, 128.2, 126.2, 125.1, 84.1, 25.1. ^{11}B NMR δ 31.5 (br).

1h

Yield: 81% of an off-white solid; mp 209°C. IR (Nujol): 2969, 2889, 1606, 1572, 1462, 1413, 1354, 1268, 1141, 1066, 965, 852, 739, 705. ^{1}H NMR (in $CDCl_3$) δ 9.70 (s, 1H), 8.76 (d, *J* = 8 Hz, 2H), 8.55 (s, 1H), 8.06 (d, *J* = 8 Hz, 2H), 7.85 (s, 1H), 7.80 (d, *J* = 8 Hz, 1H), 7.59–7.48 (ov m, 6H), 1.39 (s, 12H). ^{13}C NMR δ 159.8, 152.0, 132.6, 131.1, 130.5, 130.4, 130 (br, C-B), 128.9, 128.7, 127.2, 127.1, 126.1, 125.3, 124.9, 124.7, 83.9, 24.8. ^{11}B NMR δ 31.4 (br).

1i

Yield: 89% of an off-white solid; mp 176°C. IR (Nujol): 2974, 2881, 1628, 1575, 1484, 1424, 1358, 1321, 1145, 1073, 965, 909, 856, 807, 708. ^{1}H NMR (in $CDCl_3$) δ 8.56 (s, 2H), 8.39 (s, 1H), 8.04 (d, *J* = 8 Hz, 2H), 7.73–7.69 (ov m, 4H), 7.55 (t, *J* = 8 Hz, 1H), 7.45–7.36 (ov m, 4H), 1.37 (s, 24H). ^{13}C NMR δ 159.6, 151.3, 137.0, 132.7, 131.2, 130 (br, C-B), 129.5, 129.3, 128.8, 126.3, 124.9, 84.0, 25.0. ^{11}B NMR δ 31.0 (br).

1j

Yield: 37% of a pale yellow solid; mp 149–152°C. IR (Nujol): 2916, 2856, 1630, 1460, 1375, 1321, 1273, 1207, 1142, 1095, 1016. ^{1}H NMR (in $CDCl_3$) δ 7.96–7.86 (ov m, 4H), 7.55 (d, *J* = 8 Hz, 1H), 7.36 (t, *J* = 8 Hz, 1H), 7.25 (s, 1H), 6.92 (d, *J* = 8 Hz, 1H), 2.22 (s, 3H), 1.37 (s, 12H), 1.34 (s, 12H). ^{13}C NMR δ 165.6, 151.0, 141.9, 134.7, 131 (br, C-B), 129.7, 128.4, 126.3, 125.3, 122.3, 83.8, 24.9, 17.6. ^{11}B NMR δ 30.9 (br).

Synthesis of amines

Catecholborane (1.2 mmol) in 5 mL of toluene was added dropwise to a stirred solution of the imine (1.0 mmol) in 10 mL of toluene under an atmosphere of dinitrogen. The reaction was allowed to proceed for 24 h at which point water (5 mL) was added. The organic phase was extracted and the corresponding amine was isolated by flash chromatography through alumina followed by removal of solvent. Conversely, formation of the amine could also be achieved by reduction of the imine with 3 equiv of $NaBH_4$ in 10 mL of methanol, followed by an organic extraction with Et_2O and filtration.

2a

Yield: 78% of a white solid; mp 86°C. IR (Nujol): 3416, 2969, 2885, 1602, 1582, 1515, 1447, 1353, 1320, 1274, 1143, 1073, 965, 863, 706. ^{1}H NMR (in $CDCl_3$) δ 7.36–7.31 (ov m, 5H), 7.18–7.15 (ov m, 3H), 6.73 (m, 1H), 4.35 (s, 2H), 1.33 (s, 12H). ^{13}C NMR δ 147.5, 139.3, 130 (br, C-B), 128.6, 128.5, 127.4, 127.1, 123.9, 119.1, 115.3, 83.5, 48.1, 24.7. ^{11}B NMR δ 31.8 (br). Anal. calcd. for $C_{19}H_{24}NO_2B$: C 73.79, H 7.84, N 4.53; found: C 73.80, H 7.59, N 4.73.

2b

Yield: 58% of a yellow solid; mp 125°C. IR (Nujol): 3418, 2971, 2883, 1599, 1579, 1518, 1459, 1342, 1140, 846, 709. ^{1}H NMR (in $CDCl_3$) δ 8.19 (d, *J* = 8 Hz, 2H), 7.53 (d, *J* = 8 Hz, 2H), 7.19–7.12 (ov m, 3H), 6.64 (m, 1H), 4.48 (s, 2H), 1.33 (s, 12H). ^{13}C NMR δ 147.5, 147.1, 146.7, 130 (br, C-B), 128.9, 127.8, 124.6, 123.8, 119.4, 115.3, 83.8, 47.5, 24.8. ^{11}B NMR δ 32.3 (br). Anal. calcd. for $C_{19}H_{23}N_2O_4B$: C 64.41, H 6.56, N 7.91; found: C 64.75, H 6.40, N 8.16.

2c

Yield: 80% of an off-white solid; mp 105°C. IR (Nujol): 3398, 2974, 2875, 1604, 1579, 1512, 1462, 1363, 1236, 1138, 1086, 1026, 847, 706. ^{1}H NMR (in $CDCl_3$) δ 7.31 (d, *J* = 8 Hz, 2H), 7.22 (ov m, 2H), 7.17 (s, 1H), 6.91 (d, *J* = 8 Hz, 2H), 6.76–6.71 (m, 1H), 4.29 (s, 2H), 3.82 (s, 3H), 1.35 (s, 12H). ^{13}C NMR δ 158.8, 147.6, 131.4, 130 (br, C-B), 128.9, 128.7, 124.0, 119.2, 115.5, 114.0, 83.7, 55.3, 47.8, 24.8. ^{11}B NMR δ 32.6 (br). Anal. calcd. for $C_{20}H_{26}NO_3B$: C 70.81, H 7.74, N 4.13; found: C 71.17, H 7.88, N 4.42.

2d

Yield: 70% of a white solid; mp 126°C. IR (Nujol): 3397, 2967, 2883, 1603, 1581, 1511, 1464, 1376, 1273, 1142, 1086, 857, 707. ^{1}H NMR (in $CDCl_3$) δ 7.26–7.17 (ov m, 2H), 7.11 (m, 1H), 6.89 (s, 2H), 6.77 (m, 1H), 4.21 (s, 2H), 2.33 (s, 6H), 2.29 (s, 3H), 1.35 (s, 12H). ^{13}C NMR δ 148.0, 137.5, 137.2, 132.4, 130 (br, C-B), 129.0, 128.7, 123.7, 118.2, 115.6, 83.7, 42.4, 24.8, 20.9, 19.4. ^{11}B NMR δ 33.0 (br). Anal. calcd. for $C_{22}H_{30}NO_2B$: C 75.20, H 8.62, N 3.99; found: C 74.89, H 8.59, N 4.08.

2e

Yield: 78% of a white solid; mp 138°C. IR (Nujol): 3429, 2943, 2868, 1603, 1581, 1518, 1452, 1377, 1350, 1142, 964, 852, 706. ^{1}H NMR (in $CDCl_3$) δ 7.85 (d, *J* = 8 Hz, 1H), 7.38–7.33 (ov m, 2H), 7.25 (t, *J* = 8 Hz, 1H), 7.18–7.16 (ov m, 3H), 6.75 (m, 1H), 4.55 (s, 2H), 1.33 (s, 12H), 1.32 (s, 12H). ^{13}C NMR δ 147.8, 145.7, 136.1, 130.9, 129 (br, C-B), 128.5, 128.3, 128 (br, C-B), 126.4, 123.6, 119.6, 115.8, 83.6, 83.4, 48.2, 24.8. ^{11}B NMR δ 31.9 (br). Anal. calcd. for $C_{25}H_{35}NO_4B_2$: C 68.99, H 8.12, N 3.22; found: C 69.27, H 8.06, N 3.39.

2f

Yield: 74% of a white solid; mp 166°C. IR (Nujol): 3361, 2970, 2868, 1606, 1583, 1522, 1460, 1363, 1144, 1090, 964, 852, 708. ^{1}H NMR (in $CDCl_3$) δ 7.78 (s, 1H), 7.70 (d, *J* = 8 Hz, 1H), 7.44 (d, *J* = 8 Hz, 1H), 7.30 (t, *J* = 5 Hz, 1H), 7.15–7.10 (ov m, 3H), 6.67 (m, 1H), 4.29 (s, 2H), 1.31 (s, 12H), 1.29 (s, 12H). ^{13}C NMR δ 147.5, 138.7, 134.0, 133.6, 130.6, 129 (br, C-B), 128.7, 128.0, 123.9, 119.3, 115.4, 83.8, 83.6, 48.3, 24.8. ^{11}B NMR δ 31.4 (br). Anal. calcd. for

$C_{25}H_{35}NO_4B_2$: C 68.99, H 8.12, N 3.22; found: C 69.27, H 8.10, N 3.37.

2g

Yield: 68% of a white solid; mp 131°C. IR (Nujol): 3402, 2972, 2870, 1608, 1579, 1518, 1446, 1360, 1275, 1144, 1092, 962, 856, 706. ^{1}H NMR (in $CDCl_3$) δ 7.79 (d, *J* = 8 Hz, 2H), 7.35 (d, *J* = 8 Hz, 2H), 7.16–7.14 (ov m, 3H), 6.65 (m, 1H), 4.31 (s, 2H), 1.31 (s, 24H). ^{13}C NMR δ 147.5, 142.8, 135.1, 129 (br, C-B), 128.7, 127 (br, C-B), 126.8, 124.0, 119.3, 115.4, 83.7, 48.3, 24.9. ^{11}B NMR δ 31.7 (br). Anal. calcd. for $C_{25}H_{35}NO_4B_2$: C 68.99, H 8.12, N 3.22; found: C 69.18, H 7.98, N 3.69.

2h

Yield: 69% of a white solid; mp 205°C. IR (Nujol): 3392, 2968, 2864, 1599, 1581, 1512, 1429, 1350, 1323, 1277, 1140, 966, 852, 731, 708. ^{1}H NMR (in $CDCl_3$) δ 8.57 (s, 1H), 8.38 (d, *J* = 8 Hz, 2H), 8.15 (d, *J* = 8 Hz, 2H), 7.65–7.55 (ov m, 4H), 7.45–7.35 (ov m, 3H), 7.00 (m, 1H), 5.27 (s, 2H), 1.48 (s, 12H). ^{13}C NMR δ 147.8, 131.5, 130.4, 129.5, 129.1, 129 (br, C-B), 128.8, 127.8, 126.4, 125.1, 124.2, 124.1, 118.3, 115.8, 83.7, 40.9, 24.8. ^{11}B NMR δ 33.2 (br). Anal. calcd. for $C_{27}H_{28}NO_2B$: C 79.21, H 6.91, N 3.42; found: C 79.27, H 7.05, N 3.46.

2i

Yield: 70% of a white solid; mp 60°C. IR (Nujol): 3392, 2973, 2883, 2841, 1604, 1581, 1510, 1462, 1377, 1144, 1076, 964, 852, 785, 704. ^{1}H NMR (in $CDCl_3$) δ 7.33 (s, 1H), 7.30–7.24 (ov m, 3H), 7.18–7.14 (ov m, 6H), 6.69 (m, 2H), 4.31 (s, 4H), 1.33 (s, 24H). ^{13}C NMR δ 147.7, 140.0, 130 (br, C-B), 129.0, 128.9, 126.9, 126.6, 124.2, 119.4, 115.6, 83.8, 48.4, 25.0. ^{11}B NMR δ 31.7 (br). Anal. calcd. for $C_{32}H_{42}N_2O_4B_2$: C 71.12, H 7.85, N 5.19; found: C 70.93, H 8.06, N 5.29.

2j

Yield: 31% of a white solid; mp 170°C. IR (Nujol): 3361, 2927, 2856, 1610, 1581, 1523, 1462, 1375, 1360, 1317, 1270, 1240, 1211, 1140. ^{1}H NMR (in $CDCl_3$) δ 7.78 (d, *J* = 8 Hz, 2H), 7.39 (d, *J* = 8 Hz, 2H), 7.10–7.03 (ov m, 3H), 6.48 (m, 1H), 4.56 (q, *J* = 8 Hz, 1H), 4.04 (br s, 1H), 1.51 (d, *J* = 8 Hz, 3H), 1.33 (s, 24H). ^{13}C NMR δ 148.5, 146.6, 135.1, 129 (br, C-B), 128.6, 127 (br, C-B), 125.3, 123.6, 120.4, 115.3, 83.6, 53.4, 24.8, 24.7. ^{11}B NMR δ 31.9 (br). Anal. calcd. for $C_{26}H_{37}NO_4B_2$: C 69.52, H 8.30, N 3.12; found: C 70.09, H 8.21, N 3.23.

Biological testing

New boron compounds were tested for antifungal activity against pure cultures of *Aspergillus niger* and *Aspergillus flavus* supplied by Ward's Natural Science Ltd. (St. Catharines, Ontario, Canada). Cultures were maintained on Sabouraud dextrose agar (20, 21). Eight agar plugs (10 mm diameter) were cut from a 5–8 day-old colony and homogenized in distilled, sterilized water (4 mL). From this suspension, 0.5 mL was transferred aseptically to a Petri plate with Sabouraud dextrose agar (15 mL) and spread evenly over the entire surface. Each plate was provided with four evenly spaced paper disks (7 mm Whatman Number 1 filter paper) containing the boron compound (0, 25, 50, and 100 μg respectively). Each compound was applied to the disks as a solution (50 mg compound per 10 mL of acetone) where control disks were treated with neat acetone (20 μL). Test plates with fungal homogenates were incubated at 20°C for 48 h. Four replicate plates were used for each test. Antifungal activity was taken by the diameter of the clear zone surrounding the disk.

X-ray crystallography

Crystals of **1h** and **2c** were grown from methylene chloride solutions cooled to 5°C. Single crystals were mounted using a glass fibre and Paratone-N oil and frozen in the cold stream of the goniometer. Data were collected on a Bruker AXS P4/SMART 1000 diffractometer using ω and φ scans with a scan width of 0.3° and 30 s exposure times. The detector distance was 4 cm. The data were reduced (SAINT) and corrected for absorption (SADABS). The structures were solved by direct methods and refined by full-matrix least-squares on F^2(SHELXTL). All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located in Fourier difference maps and refined isotropically. Crystallographic data are summarized in Table 1 and atomic coordinates, thermal parameters, and bond lengths and angles have been deposited as supporting information.[3]

Results and discussion

We have found that attempts to prepare imines from 3-aminophenylboronic acid (3-$H_2NC_6H_4B(OH)_2$) proved exceedingly difficult owing to the ease with which boronic acids form insoluble anhydrides (6). However, protection of the boronic acid groups can be accomplished by transesterification with pinacol ($HOCMe_2CMe_2OH$) to afford quantitative formation of the organic soluble aminoboronate ester 3-$H_2NC_6H_4$Bpin (pin = 1,2-$O_2C_2Me_4$) (22). Reactions of this amine with aldehydes proceed smoothly to give the corresponding boron-containing aldimines **1a**–**i** in moderate to high yields (Fig. 1). This methodology provides an easy and general route to imines derived from aniline and benzaldehyde derivatives where the boronate ester functionality can be selectively incorporated into either or both of the aryl groups. Imines containing boronate esters are important intermediates in organic chemistry and have been used recently to prepare a number of pharmacologically important compounds (23–27). For instance, Whiting and co-workers (23) have recently used imine intermediates containing boronate esters to make enantio-enriched γ-phenyl-γ-amino alcohols. Incorporation of the boronate ester functionality in these cases is accom-

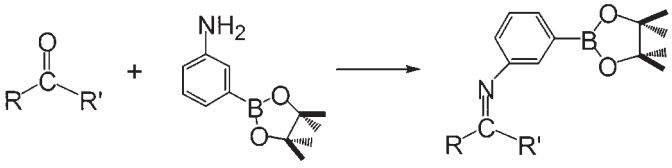
[3] Supplementary material may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0S2, Canada (http://www.nrc.ca/cisti/irm/unpub_e.shtml for information on ordering electronically). Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC nos. 160253 and 160254). Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (Fax: 44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Table 1. Crystallographic data collection parameters for **1h** and **2c**.

Complex	**1h**	**2c**
Formula	$C_{27}H_{26}BNO_2$	$C_{20}H_{26}BNO_3$
FW	407.30	339.23
Crystal system	Triclinic	Orthorhombic
Space group	$P\bar{1}$	$P2_12_12_1$
a (Å)	9.6793(4)	8.6612(4)
b (Å)	10.7397(4)	10.3794(4)
c (Å)	11.5353(4)	20.6033(9)
α (deg)	105.1890(10)	90
β (deg)	97.3030(10)	90
γ (deg)	102.1480(10)	90
V (Å^3)	1110.01(7)	1852.20(14)
Z	2	4
ρ_{calcd} (g cm^{-3})	1.219	1.217
Crystal size (mm^3)	0.125 × 0.250 × 0.275	0.150 × 0.275 × 0.350
Temperature (K)	173(1)	173(1)
Radiation	Mo Kα (λ = 0.71073)	Mo Kα (λ = 0.71073)
μ (mm^{-1})	0.075	0.080
Total reflections[a]	12 380	20 702
Total unique relections	7720	6618
No. of variables	384	331
R_{int}	0.0140	0.0188
θ range (deg)	1.86–32.50	1.98–32.50
Largest difference		
Peak/hole (e Å^{-3})	0.407/–0.155	0.374/–0.132
R^a	0.0476	0.0382
R_w	0.1301	0.0901
GoF	0.924	0.969

[a] $R = \Sigma||F_o| - |F_c||\Sigma|F_o|$; $R_w = (\Sigma[w(F_o^2 - F_c^2)^2/\Sigma[wF_o^4])^{1/2}$.

Fig. 1. Synthesis of boronated benzylideneamines.



1

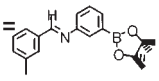
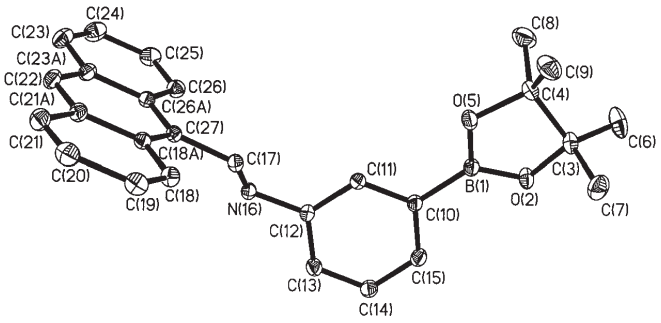
a: R = C_6H_5, R' = H
b: R = 4-$C_6H_4NO_2$, R' = H
c: R = 4-C_6H_4OMe, R' = H
d: R = 2,4,6-$C_6H_2Me_3$, R' = H
e: R = 2-C_6H_4Bpin, R' = H
f: R = 3-C_6H_4Bpin, R' = H
g: R = 4-C_6H_4Bpin, R' = H
h: R =  R' = H
i: R =  R' = H
j: R = 4-C_6H_4Bpin, R' = Me

Fig. 2. Molecular structure of **1h** with ellipsoids drawn at the 30% probability level. Hydrogen atoms were omitted for clarity.



plished by deprotonation of acetophenone-derived imines followed by alkylation with ICH_2Bpin at low temperatures. Reduction of these imines is subsequently achieved with BH_3 reagents. Likewise, boronated imines have been used in Suzuki–Miyaura cross-coupling reactions in the synthesis of 4-substituted phenylalanine derivatives (24). Carborane imines have also been prepared lately for use in boron neutron capture therapy (28).

In this study, we have found that aldimines **1a**–**i** show a signal for the N=CH methine proton between δ 8.50 and 9.70 ppm in the ^{1}H NMR spectra and a resonance at ca. 160 ppm in the ^{13}C NMR spectra corresponding to this sp^2 carbon. A broad peak at around 30 ppm in the ^{11}B NMR spectra is observed for all aldimines, indicating that the boron atom lies in a three-coordinate C-Bpin environment (29). This result is somewhat surprising for the 2-FPBpin derivative **1e** as it suggests no significant intramolecular interac-

Table 2. Selected bond lengths (Å) and angles (°) for **1h** and **2c**.

Compound **1h**		Compound **2c**	
Bond lengths (Å)			
B(1)—O(2)	1.358(1)	B(1)—O(2)	1.368(1)
B(1)—O(5)	1.365(1)	B(1)—O(5)	1.367(1)
B(1)—C(10)	1.554(1)	B(1)—C(10)	1.554(1)
O(2)—C(3)	1.465(1)	O(2)—C(3)	1.466(1)
C(4)—O(5)	1.462(1)	C(3)—C(4)	1.5651(1)
C(10)—C(15)	1.397(1)	C(4)—O(5)	1.469(1)
C(10)—C(11)	1.400(1)	C(10)—C(11)	1.392(1)
C(11)-C(12)	1.392(1)	C(11)—C(12)	1.404(1)
C(12)—C(13)	1.394(1)	C(12)—N(16)	1.385(1)
C(12)—N(16)	1.423(1)	N(16)—C(17)	1.451(2)
C(13)—C(14)	1.387(1)	C(17)—C(18)	1.511(2)
C(14)—C(15)	1.390(1)	C(18)—C(19)	1.392(2)
N(16)—C(17)	1.277(1)	C(19)—C(20)	1.380(2)
C(17)—C(27)	1.473(1)	C(20)—C(21)	1.396(2)
		C(21)—O(24)	1.370(1)
		O(24)—C(25)	1.425(1)
Bond angles (°)			
O(2)-B(1)-O(5)	113.71(8)	O(5)-B(1)-O(2)	113.51(8)
O(2)-B(1)-C(10)	124.75(8)	O(5)-B(1)-C(10)	123.68(9)
O(5)-B(1)-C(10)	121.52(7)	O(2)-B(1)-C(10)	122.81(9)
B(1)-O(2)-C(3)	106.72(7)	B(1)-O(2)-C(3)	107.37(8)
B(1)-O(5)-C(4)	107.57(7)	B(1)-O(5)-C(4)	107.10(7)
C(15)-C(10)-B(1)	121.97(8)	C(11)-C(10)-C(15)	118.78(9)
C(11)-C(10)-B(1)	119.71(8)	C(11)-C(10)-B(1)	119.49(8)
C(11)-C(12)-N(16)	122.28(8)	C(15)-C(10)-B(1)	121.73(9)
C(13)-C(12)-N(16)	118.50(8)	N(16)-C(12)-C(11)	118.56(9)
C(17)-N(16)-C(12)	117.41(7)	C(13)-C(12)-C(11)	117.77(9)
N(16)-C(17)-C(27)	123.36(8)	C(12)-N(16)-C(17)	122.63(10)
C(19)-C(18)-C(18A)	121.47(8)	N(16)-C(17)-C(18)	110.29(10)
C(26A)-C(27)-C(17)	121.68(7)	C(23)-C(18)-C(19)	117.86(10)
C(18A)-C(27)-C(17)	117.78(7)	C(23)-C(18)-C(17)	119.78(12)
		C(20)-C(19)-C(18)	121.52(10)
		O(24)-C(21)-C(22)	124.23(9)
		O(24)-C(21)-C(20)	115.83(10)
		C(21)-O(24)-C(25)	116.96(8)

tion exists between the boron atom and the imine nitrogen (30). Yet we have found that imines derived from 2-FPBpin and ethylene diamine show considerable interaction in both solution and in the solid state.[4] An X-ray diffraction study on **1h** was carried out to verify the formation of imines in these reactions. The molecular structure of **1h** is shown in Fig. 2 and crystallographic data given in Table 1. Selected bond distances and angles are shown in Table 2 and atomic coordinates are provided in Table 3. The imine C(17)—N(16) bond distance of 1.277(1) Å is comparable to azomethine compounds derived from salicylaldehyde and phenylboronic acid (25). The B—O bond distances (avg = 1.361(1) Å) are also typical for three-coordinate Bpin groups (22) and significantly shorter than those observed in chelate complexes with diphenylborinic acid (ca. 1.5 Å), where the boron atom is four-coordinate (31). Interestingly, **1h** is distorted from planarity as the anthracene ring is twisted 87.3° away from the N(16)–arene plane.

Diboronated imines will be of special interest as potential enzyme inhibitors as the corresponding amines contain two boron groups that may enhance specific binding to biomolecules. Along with aldimines **1e**–**g** we have prepared the diboronated ketimine derivative **1j** from a condensation reaction of 3-$H_2NC_6H_4$Bpin with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acetophenone. Although the methyl group for this compound shows a peak at δ 2.22 ppm in the ^{1}H NMR spectra, two different pinacol resonances are observed at 1.37 and 1.34 ppm, suggesting slightly different environments for the Bpin groups. The ^{11}B NMR spectra for **1j**, however, shows only one peak at δ 30.9 ppm as the two different boron resonances could not be differentiated.

Reduction of imines **1a**–**j** using $NaBH_4$ in methanol gave selective formation of the corresponding benzylamines **2a**–**j** in low to moderate yields. Related benzylaminoboronic acids have been reported previously (32). Indeed, benzazaborole derivatives have been prepared by condensation of 2-

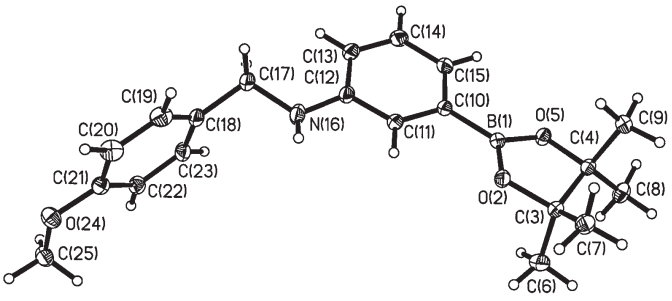
[4] L.G. Nikolcheva, C.M. Vogels, A. Decken, S.A. Westcott. Unpublished results.

Table 3. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **1h**.

	x	*y*	*z*	*U*(eq)
B(1)	2413(1)	8553(1)	9366(1)	25(1)
O(2)	1830(1)	9096(1)	10 326(1)	31(1)
C(3)	2460(1)	8731(1)	11 373(1)	30(1)
C(4)	2938(1)	7461(1)	10 749(1)	31(1)
O(5)	3165(1)	7667(1)	9577(1)	34(1)
C(6)	1342(1)	8519(2)	12 155(1)	54(1)
C(7)	3713(2)	9909(1)	12 082(1)	49(1)
C(8)	1770(2)	6174(1)	10 459(1)	53(1)
C(9)	4335(1)	7343(2)	11 409(1)	46(1)
C(10)	2301(1)	8907(1)	8141(1)	24(1)
C(11)	2675(1)	8100(1)	7128(1)	24(1)
C(12)	2675(1)	8427(1)	6037(1)	23(1)
C(13)	2275(1)	9577(1)	5949(1)	28(1)
C(14)	1904(1)	10 390(1)	6945(1)	31(1)
C(15)	1908(1)	10 057(1)	8031(1)	28(1)
N(16)	3028(1)	7606(1)	4991(1)	25(1)
C(17)	4085(1)	7097(1)	5169(1)	24(1)
C(18)	7098(1)	7411(1)	5076(1)	28(1)
C(18A)	6022(1)	6378(1)	4172(1)	23(1)
C(19)	8529(1)	7564(1)	5048(1)	33(1)
C(20)	8987(1)	6718(1)	4092(1)	35(1)
C(21)	8002(1)	5738(1)	3199(1)	32(1)
C(21A)	6490(1)	5522(1)	3209(1)	26(1)
C(22)	5480(1)	4498(1)	2312(1)	29(1)
C(23A)	4013(1)	4252(1)	2342(1)	27(1)
C(23)	3002(1)	3141(1)	1455(1)	36(1)
C(24)	1580(1)	2873(1)	1504(1)	41(1)
C(25)	1084(1)	3708(1)	2437(1)	36(1)
C(26)	2006(1)	4784(1)	3295(1)	30(1)
C(26A)	3516(1)	5107(1)	3287(1)	24(1)
C(27)	4529(1)	6179(1)	4181(1)	23(1)

Note: *U*(eq) is defined as one-third of the trace of the orthogonalized U^{ij} tensor.

Fig. 3. Molecular structure of **2c** with ellipsoids drawn at the 30% probability level. Hydrogen atoms were omitted for clarity.



(aminomethyl)benzene boronic acids (33–35). Protection of the boronic acid group by transesterification with pinacol, however, inhibits such intramolecular cyclizations from occurring in the case of **2e**. Formation of amines **2a**–**j** in these reactions is monitored by disappearance of the imine N=CH resonance in the ^{1}H NMR spectra with concomitant formation of a peak at around δ 4.3 ppm corresponding to a benzylic CH_2 resonance. Once again, the ^{11}B NMR spectra show broad peaks around δ 30 ppm, suggesting no significant intramolecular or intermolecular N → B interaction is occurring in these complexes. An X-ray diffraction study was carried out on **2c** to confirm this result. The molecular structure of **2c** is shown in Fig. 3 and selected bond distances and angles are given in Table 2. Atomic coordinates are provided in Table 4. As expected, the N(16)—C(17) bond distance of 1.451(2) Å in **2c** is significantly longer than the double bond observed for **1h**. The B—O bond distances are once again typical for three-coordinate Bpin environments at B(1)—O(5) 1.367(1) and B(1)—O(2)

Table 4. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **2c**.

	x	*y*	*z*	*U*(eq)
B(1)	8800(1)	2734(1)	1477(1)	26(1)
O(2)	9301(1)	3805(1)	1801(1)	30(1)
C(3)	10 808(1)	4156(1)	1530(1)	29(1)
C(4)	10 761(1)	3500(1)	846(1)	27(1)
O(5)	9692(1)	2423(1)	952(1)	29(1)
C(6)	12 021(2)	3595(1)	1984(1)	43(1)
C(7)	10 924(2)	5609(1)	1518(1)	38(1)
C(8)	12 286(1)	2957(1)	608(1)	40(1)
C(9)	10 030(1)	4338(1)	325(1)	34(1)
C(10)	7365(1)	1945(1)	1694(1)	26(1)
C(11)	6720(1)	2168(1)	2302(1)	28(1)
C(12)	5437(1)	1474(1)	2529(1)	30(1)
C(13)	4769(1)	574(1)	2110(1)	36(1)
C(14)	5396(1)	345(1)	1501(1)	38(1)
C(15)	6699(1)	1007(1)	1293(1)	33(1)
N(16)	4957(1)	1662(1)	3163(1)	40(1)
C(17)	3431(1)	1300(2)	3389(1)	53(1)
C(18)	3371(1)	1329(1)	4121(1)	39(1)
C(19)	2542(1)	2259(1)	4462(1)	42(1)
C(20)	2472(1)	2252(1)	5131(1)	41(1)
C(21)	3266(1)	1308(1)	5479(1)	30(1)
C(22)	4106(1)	371(1)	5151(1)	32(1)
C(23)	4140(1)	390(1)	4477(1)	39(1)
O(24)	3135(1)	1374(1)	6141(1)	38(1)
C(25)	4089(2)	530(1)	6511(1)	40(1)

Note: *U*(eq) is defined as one-third of the trace of the orthogonalized U^{ij} tensor.

Fig. 4. Reduction of boronated benzylideneamines.

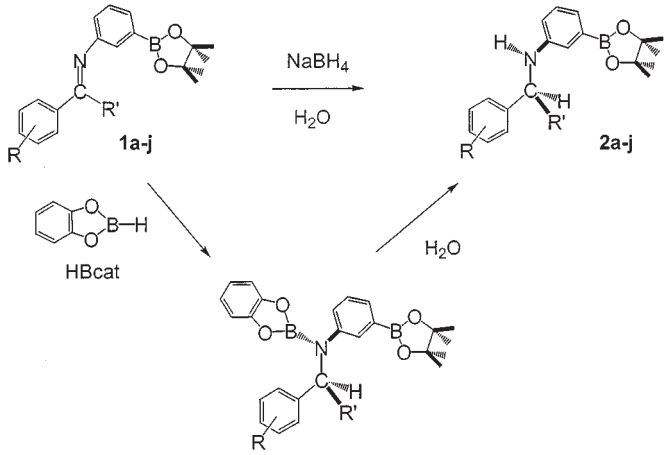


Table 5. Boron compounds tested for antifungal activity.

Entry	Compound	Dose (μg/disk)	Diameter of clear zone (mm)	
			A. niger	*A. flavus*
1	PhC(O)H	100	0	0
2	2-FPBA	25	16.2	13.4
3	2-FPBpin	25	12.0	9.4
4	3-$H_2NC_6H_4B(OH)_2$	100	0	0
5	**2b**	100	3.0	4.5
6	**2c**	100	9.0	6.3
7	**2e**	100	0	0

Note: Each compound was introduced onto a small paper disk which was placed in a culture medium. The diameter of the clear zone (the area where fungus — *A. niger* or *A. flavus* — did not grow) around each disk indicated antifungal activity.

1.368(1) Å. No significant interaction between the boron and nitrogen atoms is observed.

Interestingly, reduction of the imines could also be carried out using the gentle hydroboration reagent, catecholborane (HBcat, cat = 1,2-$O_2C_6H_4$). Reactions proceed to give the corresponding *N*-borylamine products where the hydride has added to the imine carbon and the electron deficient boryl group (BR_2) is bound to the electron rich nitrogen atom (Fig. 4). Interestingly, the ^{11}B NMR spectra for these multiply borated intermediates show broad overlapping peaks around δ 30 and 21 ppm corresponding to the C-Bpin and N-Bcat resonances, respectively. Addition of catecholborane to these bulky imines usually requires reaction times of up to 2 h. Subsequent addition of water to the *N*-borylamine intermediates afforded the benzylamines **2a**–**j** along with boric acid. Unfortunately, we were unable to affect hydroborations of these imines using pinacolborane (HBpin), even when a metal catalyst was employed (36, 37). This result is not surprising as HBpin is a significantly less reactive borane than HBcat (38).

Recent studies have shown that related heterocyclic boron compounds show appreciable antifungal activity (39–41). We therefore decided to examine these new benzylamine derivatives for their antifungal activities (42). Selected results for these compounds are shown in Table 5. Benzaldehyde was tested as a control and, as expected, showed no antifungal behaviour against either *A. niger* or *A. flavus*. Remarkably, both 2-formylphenylboronic acid (2-FPBA, Entry 2) and 2-FPBpin (Entry 3) showed considerable fungitoxicity, with the unprotected boronic acid showing slightly enhanced activity over the pinacolated derivative. These data suggest that the boron groups are responsible for the observed toxicities. Unfortunately, no activity was observed with the analogous 3- and 4-boronated derivatives (3- and 4-FPBpin) or the amine control, 3-$H_2NC_6H_4B(OH)_2$ (Entry 4). Of all the benzylamine derivatives tested, only **2b** (Entry 5) and **2c** (Entry 6) showed any appreciable activity. Higher doses of the amine, as compared with the aldehyde derivatives (100 vs. 25 μg/disk), were required. Somewhat surprising is the observation that the amine derived from 2-FPBpin (**2e**) showed no toxicity even at these higher doses (Entry 7). Further work is therefore being conducted to further our understanding of the role boron plays in fungitoxicity. The results of which will be reported in due course.

Conclusion

We have prepared a number of new imines containing boronate ester groups via condensation reactions with 3-$H_2NC_6H_4$Bpin (pin = 1,2-$O_2C_2Me_4$) and readily available aldehydes. A novel diboronated ketimine derived from 3-$H_2NC_6H_4$Bpin and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acetophenone was also prepared. Reduction of these imines with catecholborane generated the corresponding amines, upon aqueous workup. This methodology provides an easy and efficient route to secondary benzylamines containing boronate esters where the boron functionality can be selectively incorporated into either or both of the amine aryl rings. We have also found that several of these boron containing compounds display antifungal behaviour against both *A. niger* and *A. flavus*.

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References

1. C. Morin. Tetrahedron, **50**, 12 521 (1994).
2. V.S. Stroll, B.T. Eger, R.C. Hynes, V. Martichonok, J.B. Jones, and E.F. Pai. Biochemistry, **37**, 451 (1998).
3. Z.-Y. Zhang and B.D. Smith. J. Am. Chem. Soc. **120**, 7141 (1998).
4. G.S. Weston, J. Blázquez, F. Baquero, and B.K. Shoichet. J. Med. Chem. **41**, 4577 (1998).
5. D. Bao, W.P. Huskey, C.A. Kettner, and F. Jordan. J. Am. Chem. Soc. **121**, 4684 (1999).
6. V. Martichonok and J.B. Jones. J. Am. Chem. Soc. **118**, 950 (1996).
7. E. Skordalakes, R. Tyrell, S. Elgendy, C.A. Goodwin, D. Green, G. Dodson, M.F. Scully, J.-M.H. Freyssinet, V.V. Kakkar, and J.J. Deadman. J. Am. Chem. Soc. **119**, 9935 (1997).

8. J.D. Cox, N.N. Kim, A.M. Traish, and D.W. Christianson. Nat. Struct. Biol. **6**, 1043 (1999).
9. Z.-Q. Tian, B.B. Brown, D.P. Mack, C.A. Hutton, and P.A. Bartlett. J. Org. Chem. **62**, 514 (1997).
10. C.A. Kettner and A.B. Shenvi. J. Biol. Chem. **259**, 15106 (1984).
11. N. Miyaura and A. Suzuki. Chem. Rev. **95**, 2457 (1995).
12. S. Sakuma, M. Sakai, R. Itooka, and N. Miyaura. J. Org. Chem. **65**, 5951 (2000).
13. H. Eggert, J. Frederiksen, C. Morin, and J.C. Norrild. J. Org. Chem. **64**, 3846 (1999).
14. R.J. Snow, W.W. Bachovchin, R.W. Barton, S.J. Campbell, S.J. Coutts, D.M. Freeman, W.G. Gutheil, T.A. Kelly, C.A. Kennedy, D.A. Krolikowski, S.F. Leonard, C.A. Pargellis, L. Tong, and J. Adams. J. Am. Chem. Soc. **116**, 10 860 (1994).
15. C.S. Brosz, J.C. Calabrese, and C.A. Kettner. Tetrahedron: Asymmetry, **8**, 1435 (1997).
16. C.J. Ward, P. Patel, P.R. Ashton, and T.D. James. Chem. Commun. 229 (2000).
17. J.J.S. Lamba and J.M. Tour. J. Am. Chem. Soc. **116**, 11 723 (1994).
18. A. Dicko, M. Montury, and M. Baboulene. Synth. Commun. **18**, 459 (1988).
19. J.M. Jego, B. Carboni, and M. Vaultier. J. Organomet. Chem. **435**, 1 (1992).
20. E. Block, R. DeOrazio, and M. Thiruvazhi. J. Org. Chem. **5**9 2273 (1994).
21. F.J. Baerlocher, R.F. Langler, M.U. Frederiksen, N.M. Georges, and R.D. Witherell. Aust. J. Chem. **52**, 167 (1999).
22. C.M. Vogels, H.L. Wellwood, K. Biradha, M.J. Zawortko, and S.A. Westcott. Can. J. Chem. **77**, 1196 (1999), and refs. therein.
23. H.E. Sailes, J.P. Watts, and A. Whiting. Tetrahedron Lett. **41**, 2457 (2000).
24. F. Firooznia, C. Gude, K. Chan, N. Marcopulos, and Y. Satoh. Tetrahedron Lett. **40**, 213 (1999).
25. H. Höpfl, M. Sánchez, N. Farfán, and V. Barba. Can. J. Chem. **76**, 1352 (1998).
26. M.P. Hughes and B.D. Smith. J. Org. Chem. **62**, 4492 (1997).
27. M.P. Groziak, A.D. Ganguly, and P.D. Robinson. J. Am. Chem. Soc. **116**, 7597 (1994).
28. I.B. Sivaev, A.B. Bruskin, V.V. Nesterov, M. Yu. Antipin, V.I. Bregadze, and S. Sjöberg. Inorg. Chem. **38**, 5887 (1999).
29. H. Nöth and B. Wrackmeyer. *In* Nuclear magnetic resonance spectroscopy of boron compounds. Springer–Verlag, Berlin. 1978.
30. H. Höpfl, M. Sánchez, V. Barba, N. Farfán, S. Rojas, and R. Santillan. Inorg. Chem. **37**, 1679 (1998).
31. J. Grünefeld, W. Kliegel, S.J. Rettig, and J. Trotter. Can. J. Chem. **77**, 439 (1999).
32. A.M. Genaev, S.M. Nagy, G.E. Salnikov, and V.G. Shubin. Chem. Comm. 1587 (2000).
33. P.T. Hawkins and A.U. Blackham. J. Org. Chem. **32**, 597 (1967).
34. H.E. Dunn, J.C. Catlin, and H.R. Synder. J. Org. Chem. **33**, 4483 (1968).
35. M. Lauer and G. Wulff. J. Organomet. Chem. **256**, 1 (1986).
36. I. Beletskaya and A. Pelter. Tetrahedron, **53**, 4957 (1997).
37. R.T. Baker, J.C. Calabrese, and S.A. Westcott. J. Organomet. Chem. **498**, 109 (1995).
38. S. Pereira and M. Srebnik. Tetrahedron Lett. **37**, 3283 (1996).
39. T. Pandey and R.V. Singh. Main Group Met. Chem. **23**, 345 (2000).
40. T. Pandey and R.V. Singh. Synth. React. Inorg. Met. Org. Chem. **30**, 855 (2000), and refs. therein.
41. T. Pandey and R.V. Singh. Met. Based Drugs, **7**, 7 (2000).
42. F.J. Baerlocher, M.O. Baerlocher, C.L. Chaulk, R.F. Langler, and S.L. MacQuarrie. Aust. J. Chem. **53**, 399 (2000).