Heteroatom Chemistry
Volume 15, Number 5, 2004

Synthesis and Reactivity of Sulfonamides Containing Boronate Esters

Xiao-Feng He,[1] Haiwen Zhang,[1] Christopher M. Vogels,[1]
Andreas Decken,[2] and Stephen A. Westcott[1]

[1] *Department of Chemistry, Mount Allison University, Sackville, New Brunswick E4L 1G8, Canada*

[2] *Department of Chemistry, University of New Brunswick, Fredericton, New Brunswick E3B 5A3, Canada*

Received 11 November 2003; revised 24 March 2004

ABSTRACT: *Sulfonamides containing pinacol protected boronate ester groups have been prepared by the addition of $H_2NC_6H_4Bpin$ (pin = $O_2C_2Me_4$) to sulfonyl chlorides* p-$RC_6H_4SO_2Cl$ *(R = CH_3, NO_2). Hydrogenation of the nitro derivatives afford the corresponding sulfanilamides without compromising the aryl-Bpin bond. The sulfanilamides were further functionalized to afford novel platinum complexes containing boranosulfonamides.* © 2004 Wiley Periodicals, Inc. Heteroatom Chem 15:369–375, 2004; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20025

INTRODUCTION

Compounds containing boronic acids ($RB(OH)_2$) or boronate esters ($RB(OR')_2$) have received considerable attention in catalyzed carbon-carbon bond formation reactions [1], solid-phase synthesis [2], macrocyclic chemistry [3], organometallic and organic synthesis [4], and as glucose sensors for diabetes therapy [5]. Interest in these compounds also arises from their potent biological activities [6–15]. For instance, sulfonamides containing boronic acids have been examined for their ability to inhibit β-lactamases, enzymes responsible for the widespread resistance mechanisms of β-lactam antibiotics. These properties, along with the ability of boronic acid groups to transport water insoluble reagents through membranes [16], prompted us to investigate the use of boronate ester sulfonamide compounds as carrier ligands for biologically-active metal complexes.

Cisplatin, *cis*-$[PtCl_2(NH_3)_2]$, and a few related platinum-based complexes are currently used as anticancer agents against testicular and ovarian malignancies [17–20]. There are several limitations to platinum therapy, however, such as neural and kidney toxicity as well as intrinsic and acquired resistance of tumor cells to the drugs [17]. These complications have provided incentive for further research in the development of platinum-based complexes with increased solubilities in physiological media that show enhanced specificity toward cancer cells. Recent studies have shown that *cis*-amminedichloro (2-methylpyridine)platinum(II) (AMD473 or ZD0473, Fig. 1) shows considerable cytotoxicity in cisplatin resistant cell lines [21,22]. Steric crowding from the methyl group is believed to decrease the rates of hydrolysis and substitution reactions of AMD473 thereby permitting high selectivity in binding with

---

Correspondence to: S. A. Westcott; e-mail: swestcott@mta.ca.

Contract grant sponsor: Natural Science and Engineering Research Council (Canada).
Contract grant number: 184044.
Contract grant sponsor: NSERC.
Contract grant sponsor: American Chemical Society-Petroleum Research Fund.
Contract grant number: 37824-B1.
Contract grant sponsor: Canada Research Chairs program/Canadian Foundation for Innovation/Atlantic Innovation Fund.
Contract grant sponsor: Mount Allison University.
© 2004 Wiley Periodicals, Inc.

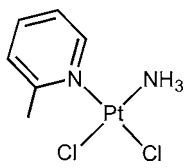


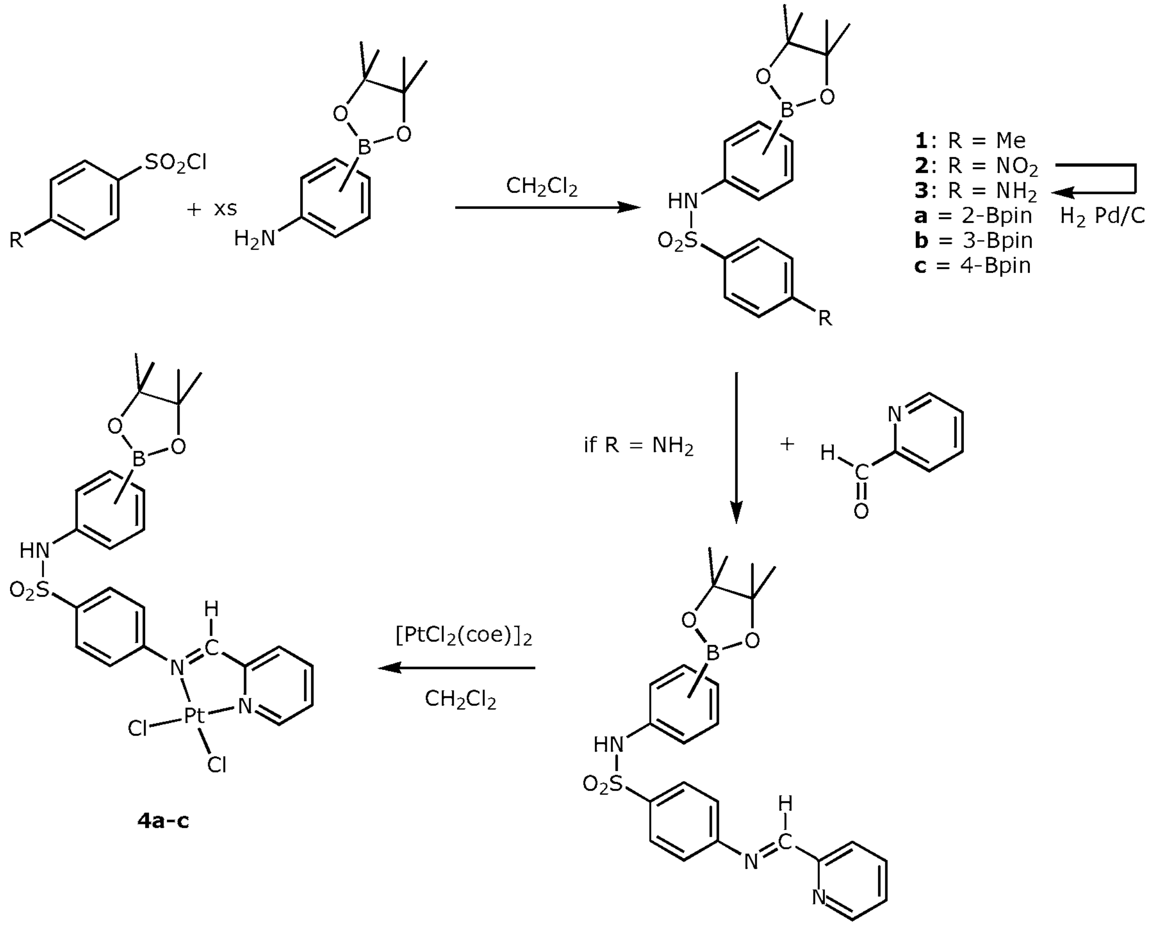
FIGURE 1 AMD473.

DNA [23]. The primary mechanism of action in these platinum drugs is believed to arise, at least in part, from the metal's interaction with DNA.

We have begun to develop AMD473 analogues by replacing the NH_3 group with a pendant imine group. Previous studies have shown that the platinum complex derived from aniline has shown considerable activity against the hormone independent human mammary carcinoma cell line MDA-MB 231 [24]. Varying the aniline functionality allows us to design compounds with a wide range of physical and chemical properties that may provide steric congestion around the platinum atom. As well, the use of bidentate ligands prevents trans labilization and undesired displacement of the ligands by sulfur and nitrogen donors in biomolecules, interactions believed responsible for some of the adverse side effects associated with cisplatin [17]. We report herein our results on the synthesis of *cis*-dichloro(pyridin-2-ylcarboxaldimine)platinum(II) compounds containing sulfonamide boronate esters.

RESULTS AND DISCUSSION

N-Aryl sulfonamides are an important class of pharmaceutically important compounds [25,26]. Our interest in preparing novel boron compounds prompted us to investigate the synthesis of sulfonamides containing boronate esters [13,27,28]. Protection of the boronic acid groups in aminophenylboronic acids ($H_2NC_6H_4B(OH)_2$) by transesterification with pinacol ($HOCMe_2CMe_2OH$), to prevent unwanted formation of anhydrides [29], gives quantitative formation of the corresponding organic soluble aminoboronate ester $H_2NC_6H_4Bpin$ (pin = $O_2C_2Me_4$) [30]. Addition of these amines to sulfonyl chlorides gave the desired sulfonamides in low to moderate yields (28–62%, Scheme 1).



SCHEME 1 Sulfonamides containing boronate esters.

The IR spectra for the sulfonamides **1a–c** display absorption bands ranging from 3282–3234 cm^{-1} assigned to ν(N—H). The ^1H NMR spectra for **1a** shows a broad singlet at δ 8.56 ppm for the NH peak, while this resonance is observed at δ 6.68 and 7.01 ppm for **1b** and **1c**, respectively. This result is interesting as it suggests that a weak interaction of the amide hydrogen with the neighbouring boron atom may be occurring. However, the ^{11}B NMR spectrum for **1a** shows a broad peak at δ 29 ppm, signifying that the boron atom lies in a trigonal environment [31]. An X-ray diffraction study on **1a** was conducted to confirm the formation of these sulfonamides (Fig. 2) and to see if any significant N—H$\cdots$B interaction was occurring in the solid state. Crystallographic data are given in Table 1 and selected bond distances and angles shown in Table 2. A distance of N—H(16)$\cdots$B of 2.550(18) Å indicates an interaction between the amine hydrogen and the boron atom. The trigonal environment of the boron atom suggests, however, that this interaction is weak and testifies to the reduced Lewis acidity of the Bpin groups compared to other boronate ester appendages [13]. The B—O bond distances of 1.3514(17) and 1.3649(16) Å are typical for those observed in other three coordinate Bpin complexes [13]. The OBO plane is roughly coplanar with the aromatic ring of the sulfonamide (12.4°), indicating that significant overlap is occurring with the π–system of the ring and the empty p orbital of the boron atom.

TABLE 1 Summary of Data Collection and Refinement for **1a**

	1a
Formula	$C_{19}H_{24}BNO_4S$
M	373.26
T (K)	198(2)
Cryst. syst.	Monoclinic
Space group	P2(1)/c
a (Å)	9.8379(10)
b (Å)	11.4745(12)
c (Å)	16.4414(16)
β (°)	90.685(2)
V (Å^3)	1855.9(3)
Z	4
μ (mm^{-1})	0.199
d ($g\ cm^{-3}$)	1.336
λ (Å)	0.71073
R1[a]	0.0370
wR2[b]	0.1098

[a] $R1 = \sum ||Fo| - |Fc|| / \sum |Fo|$.

[b] All data, $wR2\ (F^2) = (\sum[w(Fo^2 - Fc^2)^2] / \sum[Fo^4])^{1/2}$, Weight $= 1/[\sigma^2 (F_o{}^2) + (0.0671 * P)^2 + (0.263 * P)]$ where $P = (\max(F_o{}^2, 0) + 2 * F_c{}^2)/3$

The pinacol protected boronic acid derivatives of aniline added readily to $4\text{-}O_2NC_6H_4SO_2Cl$ to give the putative nitro sulfonamides **2a–c**, which were readily reduced with dihydrogen using 10% Pd/C to give the sulfanilamides **3a–c**. These compounds are of singular interest owing to their resemblance to the

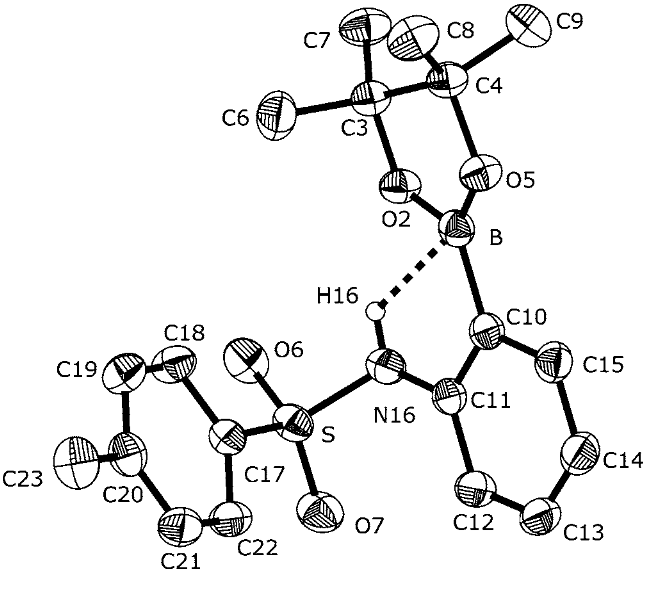


FIGURE 2 The molecular structure of **1a** with ellipsoids drawn at 30% probability level. Hydrogen atoms have been omitted for clarity with the exception of H(16).

TABLE 2 Selected Bond Lengths (Å) and Angles (°) for **1a**

B–O(5)	1.3514(17)		
B–O(2)	1.3649(16)		
B–C(10)	1.5491(19)		
O(2)–C(3)	1.4630(15)		
C(4)–O(5)	1.4587(15)		
C(11)–N(16)	1.4169(16)		
N(16)–S	1.6369(11)		
S–O(7)	1.4214(10)		
S–O(6)	1.4223(10)		
S–C(17)	1.7480(13)		
B–H(16)	2.550(18)		
O(5)–B–O(2)	113.55(11)	O(7)–S–O(6)	120.31(7)
O(5)–B–C(10)	122.07(11)	O(7)–S–N(16)	108.35(6)
O(2)–B–C(10)	124.32(12)	O(6)–S–N(16)	104.05(6)
B–O(2)–C(3)	107.05(10)	O(7)–S–C(17)	108.11(6)
O(2)–C(3)–C(7)	108.39(11)	O(6)–S–C(17)	109.03(6)
O(2)–C(3)–C(6)	106.09(11)	N(16)–S–C(17)	106.13(6)
O(2)–C(3)–C(4)	102.48(9)	C(22)–C(17)–S	120.69(10)
O(5)–C(4)–C(8)	107.93(11)	C(18)–C(17)–S	118.78(10)
O(5)–C(4)–C(9)	106.96(11)		
O(5)–C(4)–C(3)	102.31(10)		
B–O(5)–C(4)	108.01(10)		
C(11)–C(10)–B	124.58(11)		
C(15)–C(10)–B	117.95(12)		
C(12)–C(11)–N(16)	120.35(12)		
C(10)–C(11)–N(16)	118.79(11)		
C(11)–N(16)–S	124.55(9)		

antibiotics sulfapyridine and sulfadimidine [32]. Related boranosulfonamides have recently been examined as potential β-lactamase inhibitors [33]. Once again, a significant downfield shift is observed in the ^{1}H NMR data for the amide NH bond in **3a** (δ 8.54 ppm) compared to **3b** (6.33 ppm) and **3c** (6.44 ppm). The ^{11}B NMR spectra for all three compounds are at ca δ 30 ppm, meaning the boron retains its trigonal planar configuration.

As part of our investigation into preparing biologically active boron-metal complexes, we decided to examine the use of boranosulfonamides (**3a–c**) as ligands for platinum dichloride complexes. Addition of 2-pyridinecarboxaldehyde to **3a–c** afforded the iminopyridyl ligands, which reacted further with organic soluble $[PtCl_2(coe)]_2$ (coe = *cis*-cyclooctene) [34] to give **4a–c** in moderate yields (38–67%, Scheme 1). Complexes **4a–c** have been characterized by a number of physical methods, including multinuclear NMR spectroscopy. A significant downfield shift in the ^{1}H NMR spectra is observed for the imine sp^2 proton upon coordination of the ligand to the metal center. For instance, the singlet at δ 8.54 ppm for the 3-Bpin derivative shifts to 9.38 ppm in complex **4b**. Platinum satellites are also observed for this resonance ($J_{\text{H-Pt}} = 81$ Hz) upon complexation of the ligand to the metal. Similar trends are observed for the pyridine hydrogen alpha to the nitrogen atom as the chemical shift changes from δ 8.73 to 9.46 ppm ($J_{\text{H-Pt}} = 43$ Hz). Unfortunately, attempts to produce single crystals of these complexes for X-ray diffraction studies proved unsuccessful. Related metal complexes derived from iminopyridyl ligands containing sulfonamide appendages have been reported [35]. We will examine the biological activity of these novel metal complexes for their efficacy to act as anticancer agents and will report our findings in due course.

CONCLUSION

We have prepared a number of sulfonamides containing pinacol protected boronate ester groups, which can be used to generate a wide range of new sulfonamides using the Suzuki–Miyaura cross-coupling reaction. A weak interaction of the amide N—H bond with the neighboring ortho boron atom is observed in solution and in the solid state as evident by ^{1}H NMR spectroscopy and X-ray crystallography. The sulfanilamides were further functionalized with 2-pyridinecarboxaldehyde to give pyridyl imine ligands, which were subsequently used to give the corresponding platinum complexes.

EXPERIMENTAL

Reagents and solvents used were obtained from Aldrich Chemicals. K_2PtCl_4 was purchased from Precious Metals Online Ltd. 2-$H_2NC_6H_4$Bpin [36], 3-$H_2NC_6H_4$Bpin [30], and $[PtCl_2(coe)]_2$ [34,37] were prepared as described in the literature. NMR spectra were recorded on a JEOL JNM-GSX270 FT NMR spectrometer. ^{1}H NMR chemical shifts are reported in ppm and are referenced to residual protons in deuterated solvent at 270 MHz. ^{11}B NMR chemical shifts are referenced to external $BF_3{\cdot}OEt_2$ at 87 MHz. ^{13}C NMR chemical shifts are referenced to solvent carbon resonances as internal standards at 68 MHz. Multiplicities are reported as singlet (s), doublet (d), triplet (t), multiplet (m), broad (br), and overlapping (ov). Infrared spectra were obtained using a Mattson Genesis II FT-IR spectrometer and are reported in cm^{-1}. Melting points were measured uncorrected with a Mel-Temp apparatus. Microanalyses for C, H, and N were carried out at Guelph Chemical Laboratories Ltd. (Guelph, ON).

Synthesis of Sulfonamides **1a–c**

The appropriate {4,4,5,5-tetramethyl-[1,3,2]-dioxaborolan-2-yl}phenylamine (200 mg, 0.91 mmol) in CH_2Cl_2 (3 ml) was added to a CH_2Cl_2 (3 ml) solution of *p*-toluenesulfonyl chloride (86 mg, 0.45 mmol) and the reaction mixture was heated at reflux for 18 h. Extraction with CH_2Cl_2 (3 × 5 ml) from H_2O (10 ml) followed by removal of the solvent under vacuum afforded compounds **1a–c**.

Sulfonamide **1a**. Yield: 56 mg (33%) of an off-white solid; mp 164–166°C. Anal. Calcd for $C_{19}H_{24}NBO_4S$: C, 61.12; H, 6.49; N, 3.75. Found: C, 61.58; H, 6.43; N, 3.84%. ^{1}H NMR ($CDCl_3$): δ 8.56 (br s, 1H, NH), 7.63–7.58 (ov m, 4H, Ar), 7.38 (t d, $J = 7, 2$ Hz, 1H, Ar), 7.14 (d, $J = 8$ Hz, 2H, Ar), 7.03 (t, $J = 7$ Hz, 1H, Ar), 2.32 (s, 3H, CH_3Ar), 1.28 (s, 12H, $O_2C_2(CH_3)_4$); ^{11}B NMR ($CDCl_3$): δ 29.4 (br); ^{13}C NMR (acetone-d_6): δ 143.9, 136.5, 132.9, 130 (br, C-B), 129.6, 129.1, 127.3, 124.8, 123.8, 119.6, 84.8, 24.3, 20.5. IR (Nujol): 3282, 2931, 2858, 1604, 1577, 1493, 1458, 1377, 1346, 1319, 1265, 1169, 1138, 1090, 1070, 1039, 962, 912, 854, 825, 758, 669, 565.

Sulfonamide **1b**. Yield: 47 mg (28%) of an off-white solid; mp 144–146°C. Anal. Calcd for $C_{19}H_{24}NBO_4S$: C, 61.12; H, 6.49; N, 3.75. Found: C, 61.67; H, 6.89; N, 3.99%. ^{1}H NMR ($CDCl_3$): δ 7.64 (d, $J = 8$ Hz, 2H, Ar), 7.51 (d, $J = 7$ Hz, 1H, Ar), 7.33–7.18 (ov m, 5H, Ar), 6.68 (br s, 1H, NH), 2.35 (s, 3H, CH_3Ar), 1.29 (s, 12H, $O_2C_2(CH_3)_4$); ^{11}B NMR

($CDCl_3$): δ 29.8 (br); ^{13}C NMR (acetone-d_6): δ 143.6, 137.6, 137.3, 130.7, 130 (br, C-B), 129.6, 128.6, 127.2, 126.9, 123.5, 83.8, 24.4, 20.5. IR (Nujol): 3253, 2926, 2856, 1454, 1377, 1358, 1338, 1207, 1165, 1146, 1092, 968, 937, 850, 820, 791, 706, 673, 569, 544.

Sulfonamide **1c**. Yield: 104 mg (62%) of an off-white solid; mp 201–202°C. Anal. Calcd for $C_{19}H_{24}NBO_4S$: C, 61.12; H, 6.49; N, 3.75. Found: C, 60.88; H, 6.10; N, 3.63%. ^1H NMR ($CDCl_3$): δ 7.67 (d, $J = 8$ Hz, 2H, Ar), 7.64 (d, $J = 8$ Hz, 2H, Ar), 7.19 (d, $J = 8$ Hz, 2H, Ar), 7.06 (d, $J = 8$ Hz, 2H, Ar), 7.01 (br s, 1H, NH), 2.34 (s, 3H, CH_3Ar), 1.29 (s, 12H, $O_2C_2(CH_3)_4$); ^{11}B NMR ($CDCl_3$): δ 30.1 (br); ^{13}C NMR (acetone-d_6): δ 143.8, 140.9, 137.2, 135.8, 130 (br, C-B), 129.6, 127.2, 118.8, 83.6, 24.4, 20.5. IR (Nujol): 3234, 2918, 2860, 1608, 1460, 1373, 1336, 1146, 1092, 922, 854, 819, 571.

Synthesis of Sulfonamides **3a–c**

A solution of the appropriate {4,4,5,5-tetramethyl-[1,3,2]-dioxaborolan-2-yl}phenylamine (200 mg, 0.91 mmol) in CH_2Cl_2 (3 ml) was added to a solution of *p*-nitrobenzenesulfonyl chloride (100 mg, 0.45 mmol) in CH_2Cl_2 (3 ml). The reaction mixture was heated at reflux for 18 h. Extraction with CH_2Cl_2 (3 × 5 ml) from H_2O (10 ml) followed by removal of the solvent under vacuum afforded compounds **2a–c**. Compounds **3a–c** were prepared by dissolving the appropriate sulfonamide **2a–c** in EtOH (5 ml) in the presence of a catalytic amount of Pd/C (10%). The mixture was shaken under an atmosphere of H_2 for 4 h, at which point, the catalyst was removed by suction filtration and the solvent removed under vacuum. The products were isolated by crystallization from a solution of CH_2Cl_2 (2 ml) and hexane (3 ml) stored at 5°C.

Sulfonamide **3a**. Yield: 62 mg (37%) of a white solid; mp 138–140°C. Anal. Calcd for $C_{18}H_{23}N_2BO_4S$: C, 57.75; H, 6.21; N, 7.49. Found: C, 57.31; H, 6.18; N, 7.42%. ^1H NMR ($CDCl_3$): δ 8.54 (br s, 1H, NH), 7.61 (t, $J = 8$ Hz, 2H, Ar), 7.53 (d, $J = 8$ Hz, 2H, Ar), 7.37 (t d, $J = 7$, 2 Hz, 1H, Ar), 7.01 (t d, $J = 7$, 2 Hz, 1H, Ar), 6.61 (d, $J = 8$ Hz, 2H, Ar), 4.05 (br s, 2H, NH_2), 1.30 (s, 12H, $O_2C_2(CH_3)_4$); ^{11}B NMR ($CDCl_3$): δ 29.4 (br); ^{13}C NMR (acetone-d_6): δ 152.8, 144.5, 136.4, 132.7, 130 (br, C-B), 129.3, 125.5, 123.2, 119.3, 112.9, 84.6, 24.3. IR (Nujol): 3483, 3383, 3255, 2924, 2854, 1628, 1579, 1495, 1456, 1377, 1358, 1315, 1265, 1147, 1120, 1088, 928, 833, 766, 677, 567.

Sulfonamide **3b**. Yield: 94 mg (56%) of a white solid; mp 160–162°C. Anal. Calcd for $C_{18}H_{23}N_2BO_4S$: C, 57.75; H, 6.21; N, 7.49. Found: C, 57.85; H, 6.33; N, 7.60%. ^1H NMR ($CDCl_3$): δ 7.52 (d, $J = 8$ Hz, 2H, Ar), 7.32–7.20 (ov m, 4H, Ar), 6.56 (d, $J = 8$ Hz, 2H, Ar), 6.33 (br s, 1H, NH), 4.06 (br s, 2H, NH_2), 1.30 (s, 12H, $O_2C_2(CH_3)_4$); ^{11}B NMR ($CDCl_3$): δ 30.5 (br); ^{13}C NMR (acetone-d_6): δ 152.8, 138.3, 130.1, 130 (br, C-B), 129.2, 128.4, 126.6, 126.3, 123.1, 113.0, 83.8, 24.4. IR (Nujol): 3460, 3369, 3228, 2912, 2864, 1633, 1595, 1462, 1377, 1155, 1090, 968, 945, 849, 721.

Sulfonamide **3c**. Yield: 69 mg (41%) of a white solid; mp 220–224°C. Anal. Calcd for $C_{18}H_{23}N_2BO_4S$: C, 57.75; H, 6.21; N, 7.49. Found: C, 57.51; H, 6.37; N, 7.46%. ^1H NMR ($CDCl_3$): δ 7.65 (d, $J = 8$ Hz, 2H, Ar), 7.54 (d, $J = 8$ Hz, 2H, Ar), 7.03 (d, $J = 8$ Hz, 2H, Ar), 6.56 (d, $J = 8$ Hz, 2H, Ar), 6.44 (br s, 1H, NH), 4.05 (br s, 2H, NH_2), 1.30 (s, 12H, $O_2C_2(CH_3)_4$); ^{11}B NMR ($CDCl_3$): δ 28.6 (br); ^{13}C NMR ($CDCl_3$): δ 150.8, 139.7, 136.0, 130 (br, C-B), 129.5, 127.2, 119.4, 114.0, 83.9, 24.9. IR (Nujol): 3444, 3361, 3232, 2926, 2856, 1651, 1597, 1458, 1375, 1362, 1269, 1144, 1090, 962, 918, 833, 706.

Synthesis of Platinum Complexes **4a–c**

Compounds **3a–c** were added to a CH_2Cl_2 solution of 2-pyridinecarboxaldehyde (1 equivalent) in the presence of activated molecular sieves. The reaction was allowed to proceed for 5 days, at which point, the molecular sieves were removed by suction filtration and the solvent removed under vacuum. The desired pyridinyl-carboxaldimine (2 equivalents), used without further purification, was added drop-wise to a stirred CH_2Cl_2 solution of $[PtCl_2(coe)]_2$. Solvent was removed after 2 h under vacuum to afford an orange residue. Compounds **4a–c** were crystallized from saturated THF solutions which were stored overnight at 5°C.

Platinum Complex **4a**. Yield: 28 mg (38%) of a yellow solid; mp 230°C (decomp.). Anal. Calcd for $C_{24}H_{26}N_3BCl_2O_4PtS \cdot THF$: C, 41.95; H, 4.28; N, 5.24. Found: C, 41.23; H, 4.26; N, 5.37%. ^1H NMR (DMSO-d_6): δ 9.46 (br m, 1H, Ar), 9.36 (br m, 1H, Ar), 9.12 (br s, 1H, NH), 8.44 (br m, 1H, Ar), 8.24 (br m, 1H, Ar), 8.00 (br m, 1H, Ar), 7.79 (br m, 2H, Ar), 7.58 (br m, 3H, Ar), 7.43 (br m, 1H, Ar), 7.28 (br m, 1H, Ar), 7.14 (br m, 1H, Ar), 1.31 (s, 12H, $O_2C_2(CH_3)_4$); ^{11}B NMR (DMSO-d_6): δ 30.3 (br); ^{13}C NMR (DMSO-d_6): δ 174.2, 157.5, 150.5, 149.7, 142.7, 141.3, 139.5, 136.6, 133.0, 130.7, 130.5, 130 (br, C-B), 129.4, 127.6, 125.9, 125.2, 121.3, 112.9, 84.9, 25.2. IR (Nujol): 3257, 3238, 2924, 2856, 1608, 1556, 1485, 1435, 1348, 1267, 1169, 1142, 1070, 920, 856, 773, 706, 669, 627.

Platinum Complex **4b**. Yield: 49 mg (67%) of a yellow solid; mp 250°C (decomp.). Anal. Calcd for $C_{24}H_{26}N_3BCl_2O_4PtS$: C, 39.51; H, 3.60; N, 5.76. Found: C, 39.10; H, 3.49; N, 5.52%. ^{1}H NMR (DMSO-d_6): δ 10.43 (s, 1H, NH), 9.46 (d, $J_{\text{H-Pt}} = 43$ Hz, $J = 5$ Hz, 1H, Ar), 9.38 (s, $J_{\text{H-Pt}} = 81$ Hz, 1H, C(H)N), 8.44 (t, $J = 7$ Hz, 1H, Ar), 8.19 (d, $J = 7$ Hz, 1H, Ar), 8.00 (t, $J = 7$ Hz, 1H, Ar), 7.86 (d, $J = 8$ Hz, 2H, Ar), 7.62 (d, $J = 8$ Hz, 2H, Ar), 7.46 (s, 1H, Ar), 7.36 (t, $J = 5$ Hz, 1H, Ar), 7.28–7.26 (ov m, 2H, Ar), 1.27 (s, 12H, $O_2C_2(CH_3)_4$); ^{11}B NMR (DMSO-d_6): δ 32.2 (br); ^{13}C NMR (DMSO-d_6): δ 174.5, 157.5, 150.4, 149.8, 141.3, 140.1, 137.6, 130.9, 130.6, 130 (br, C-B), 129.5, 129.4, 127.4, 126.8, 126.0, 123.6, 84.4, 25.2. IR (Nujol): 3248, 2933, 2868, 1581, 1556, 1460, 1414, 1377, 1267, 1155, 1090, 968, 947, 891, 850, 773, 721, 627.

Platinum Complex **4c**. Yield: 28 mg (38%) of a yellow solid; mp 280°C (decomp.). Anal. Calcd for $C_{24}H_{26}N_3BCl_2O_4PtS$: C, 39.51; H, 3.60; N, 5.76. Found: C, 39.51; H, 3.16; N, 5.67%. ^{1}H NMR (DMSO-d_6): δ 10.71 (s, 1H, NH), 9.45 (d, $J_{\text{H-Pt}} = 43$ Hz, $J = 5$ Hz, 1H, Ar), 9.38 (s, $J_{\text{H-Pt}} = 85$ Hz, 1H, C(H)N), 8.44 (t, $J = 8$ Hz, 1H, Ar), 8.18 (d, $J = 8$ Hz, 1H, Ar), 8.00 (t, $J = 5$ Hz, 1H, Ar), 7.90 (d, $J = 8$ Hz, 2H, Ar), 7.62 (d, $J = 7$ Hz, 2H, Ar), 7.54 (d, $J = 7$ Hz, 2H, Ar), 7.15 (d, $J = 8$ Hz, 2H, Ar), 1.24 (s, 12H, $O_2C_2(CH_3)_4$); ^{11}B NMR (DMSO-d_6): δ 32.7 (br); ^{13}C NMR (DMSO-d_6): δ 174.4, 157.5, 150.5, 149.7, 141.3, 140.9, 139.9, 136.2, 130.5, 130 (br, C-B), 129.3, 129.0, 127.4, 126.0, 122.3, 119.2, 118.2, 113.1, 84.2, 25.2. IR (Nujol): 3178, 2931, 2858, 1608, 1558, 1456, 1362, 1340, 1300, 1273, 1159, 1140, 1090, 1020, 916, 849, 775, 733, 662, 637, 600, 561.

X-Ray Data

Crystals of **1a** were grown from a saturated solution of THF at 5°C. Single crystals were coated with Paratone-N oil, mounted using a glass fibre, and frozen in the cold stream of the goniometer. A hemisphere of data were collected on a Bruker AXS P4/SMART 1000 diffractometer using ω and ϕ scans with a scan width of 0.3° and 10 s exposure times. The detector distance was 5 cm. The data were reduced (SAINT) [38] and corrected for absorption (SADABS) [39]. The structure was solved by direct methods and refined by full-matrix least squares on F^2 (SHELXTL) [40]. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located in Fourier difference maps and refined isotropically.

ACKNOWLEDGMENTS

We thank Dan Durant and Roger Smith for expert technical assistance and an anonymous reviewer for helpful comments.

REFERENCES

[1] Miyaura, N.; Suzuki, A. Chem Rev 1995, 95, 2457.

[2] Carboni, B.; Pourbaix, C.; Carreaux, F.; Deleuze, H.; Maillard, B. Tetrahedron Lett 1999, 40, 7979.

[3] Farfan, N.; Höpfl, H.; Barba, V.; Ochoa, M. E.; Santillan, R.; Gomez, E.; Gutierrez, A. J Organomet Chem 1999, 581, 70.

[4] Tailor, J.; Hall, D. G. Org Lett 2000, 2, 3715.

[5] Eggert, H.; Frederiksen, J.; Morin, C.; Chr. Norrild, J. J Org Chem 1999, 64, 3846.

[6] James, T. D.; Linnane, P.; Shinkai, S. J Chem Soc, Chem Commun 1996, 281.

[7] Yang, W.; Gao, X.; Wang, B. Med Res Rev 2003, 23, 346.

[8] Morin, C. Tetrahedron 1994, 50, 12521.

[9] Cama, E.; Colleluori, D. M.; Emig, F. A.; Shin, H.; Kim, S. W.; Kim, N. N.; Traish, A. M.; Ash, D. E.; Christianson, D. W. Biochemistry 2003, 42, 8445.

[10] Stolowitz, M. L.; Ahlem, C.; Hughes, K. A.; Kaiser, R. J.; Kesicki, E. A.; Li, G.; Lund, K. P.; Torkelson, S. M.; Wiley, J. P. Bioconjugate Chem 2001, 12, 229.

[11] Kullberg, E. B.; Bergstrand, N.; Carlsson, J.; Edwards, K.; Johnsson, M.; Sjöberg, S.; Gedda, L. Bioconjugate Chem 2002, 13, 737.

[12] Soloway, A. H.; Tjarks, W.; Barnum, B. A.; Rong, F.-G.; Barth, R. F.; Codogni, I. M.; Wilson, J. G. Chem Rev 1998, 98, 1515.

[13] Decken, A.; Singh, A.; Vogels, C. M.; Westcott, S. A. Acta Cryst 2002, E58, o1213.

[14] Gronowitz, S.; Dalgren, T.; Namtvedt, J.; Roos, C.; Sjöberg, B.; Forsgren, U. Acta Pharm Suecica 1971, 8, 377.

[15] Powers, R. A.; Shoichet, B. K. J Med Chem 2002, 45, 3222.

[16] Westmark, P. R.; Smith, B. D. J Am Chem Soc 1994, 116, 9343.

[17] Jamieson, E. R.; Lippard, S. J. Chem Rev 1999, 99, 2467.

[18] Reedijk, J. Chem Rev 1999, 99, 2499.

[19] Wong, E.; Giandomenico, C. M. Chem Rev 1999, 99, 2451.

[20] Ho, Y.-P.; Au-Yeung, S. C. F.; To, K. K. W. Med Res Rev 2003, 23, 633.

[21] Butour, J. L.; Macquet, J.-P. Biochemistry 1977, 78, 455.

[22] Neplechová, K.; Kašpárková, J.; Vrána, O.; Nováková, O.; Habtemariam, A.; Watchman, B.; Sadler, P. J.; Brabec, V. Mol Pharmacol 1999, 56, 20.

[23] Hotze, A. C. G.; Chen, Y.; Hambley, T. W.; Parsons, S.; Kratochwil, N. A.; Parkinson, J. A.; Munk, V. P.; Sadler, P. J Eur J Inorg Chem 2002, 1035.

[24] Brunner, H.; Schmidt, M.; Schönenberger, H. Inorg Chim Acta 1968, 123, 201.

[25] Romero, D. L.; Morge, R. A.; Genin, M. J.; Biles, C.; Busso, M.; Resnick, L.; Althaus, I. W.; Reusser, F.; Thomas, R. C.; Tarpley, W. G. J Med Chem 1993, 36, 1505.

[26] Turner, S. R.; Strohbach, J. W.; Tommasi, R. A.; Aristoff, P. A.; Johnson, P. D.; Skulnick, H. I.; Dolak, L. A.; Seest, E. P.; Tomich, P. K.; Bohanon, M. J.; Horng, M. M.; Lynn, J. C.; Chong, K.-T.; Hinshaw, R. R.; Watenpaugh, K. D.; Janakiraman, M. N.; Thaisrivongs, S. J Med Chem 1998, 41, 3467.

[27] Gallop, P. M.; Paz, M. US Patent 4 496 722, 1985.

[28] Calderwood, D. J.; Johnston, D. N.; Rafferty, P.; Twigger, H. L.; Munschauer, R.; Arnold, L. US Patent 6 001 839, 1999.

[29] Martichonok, V.; Jones, J. B. J Am Chem Soc 1996, 118, 950.

[30] Kennedy, J. W. J.; Hall, D. G. J Organomet Chem 2003, 680, 263.

[31] Medina, J. R.; Cruz, G.; Cabrera, C. R.; Soderquist, J. A. J Org Chem 2003, 68, 4631 and references therein.

[32] Mann, J.; Crabbe, J. C. Bacteria and Antibacterial Agents: Biochemical and Medicinal Chemistry Series; Spektrum Academic Publishers: Oxford, 1996.

[33] Powers, R. A.; Shoichet, B. K. J Med Chem 2002, 45, 3222.

[34] Otto, S.; Roodt, A.; Elding, L. I. Dalton Trans 2003, 2519.

[35] Congreve, A.; Kataky, R.; Knell, M.; Parker, D.; Puschmann, H.; Senanayake, K.; Wylie, L. New J Chem 2003, 27, 98.

[36] Baudoin, O.; Guénard, D.; Guéritte, F. J Org Chem 2000, 65, 9268.

[37] Vogels, C. M.; Wellwood, H. L.; Hennigar, T. L.; Biradha, K.; Zaworotko, M. J.; Westcott, S. A. Can J Chem 1999, 77, 1196.

[38] SAINT 6.02, Bruker AXS, Inc., Madison, Wisconsin, USA, 1997–1999.

[39] Sheldrick, G. M. SADABS, Bruker AXS, Inc., Madison, Wisconsin, USA, 1999.

[40] Sheldrick, G. M. SHELXTL 5.1, Bruker AXS, Inc., Madison, Wisconsin, USA, 1997.