Synthesis and characterization of new platinum(II) complexes containing thiazole and imidazole donors III*. Dichlorobis(styrylbenzazole)platinum(II) complexes

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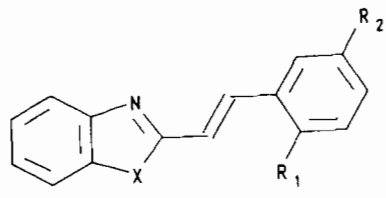
Abstract

Platinum(II) complexes of the type *cis*-$[Pt(L)_2Cl_2]$, where L is a styrylbenzazole, have been prepared. The benzazoles included derivatives of imidazole, thiazole and oxazole. The ligands and the complexes were characterized by their melting points, elemental analyses, NMR, UV–Vis and IR spectra. The benzazole ligands are all coordinated to the Pt through N. The assignment of *cis* geometry for the complexes was based on the method of synthesis, comparison with a styrylbenzazole complex of known geometry, and far-IR spectral data.

Introduction

The discovery of the antitumor activity of *cis*-dichlorodiammineplatinum(II) (*cis*-DDP) by Rosenberg *et al.* [3–5] aroused great interest in the synthesis and screening of new complexes of Pt(II) which might have improved activity or lowered toxicity compared to *cis*-DDP [6]. Several complexes with N-heterocyclic ligands such as imidazole, thiazole and benzoxazole have been reported [7–13]. Recently, new anionic complexes $[NEt_4][Pt(L)Br_3]$ and mixed ligand complexes *cis*-$[Pt(NH_3)(L)Cl_2]$ containing thiazole, benzothiazole and imidazole derivatives were prepared, and some of these showed significant cytotoxicity [1, 13]. Several Schiff bases derived from thiazoles and benzothiazoles [14] and derivatives of styrylbenzothiazoles [15] have shown biological activity. Therefore, it seemed of interest to prepare and characterize complexes of the type *cis*-$[Pt(L)_2Cl_2]$ for comparison with *cis*-DDP.

The ligands used were: 2-(2′-chloro-5′-nitrostyryl)benzothiazole (nsb, **1**, X = S, R_1 = Cl, R_2 = NO_2), 2-(2′-chloro-5′-nitrostyryl)benzoxazole (nsbo, **1**, X = O, R_1 = Cl, R_2 = NO_2), 2-(2′-hydroxystyryl)benzothiazole (ohsb, **1**, X = S, R_1 = OH, R_2 = H, 2-(2′-acetoxystyryl)benzothiazole (asb, **1**, X = S, R_1 = $CH_3CO_2^-$, R_2 = H), 2-(2′-chlorostyryl)benzothiazole (csb, **1**, R_1 = Cl, R_2 = H), 2-(2′,5′-dimethoxystyryl)benzoxazole (dmsesbo, **1**, X = O, R_1 = R_2 = OCH_3), 2-(2′-chloro-5′-nitrostyryl)benzimidazole (nsbiz, **2**, R_1 = H, R_2 = NO_2), 2-(2′-chloro-5′-nitrostyryl)-1-methylbenzimidazole (mensbiz, **2**, R_1 = CH_3, R_2 = NO_2), 2-(2′-chloro-5′-nitrostyryl)-1-ethylbenzimidazole (et-nsbiz, **2**, R_1 = C_2H_5, R_2 = NO_2), 2-(2′-chloro-5′-nitrostyryl)-1-isopropylbenzimidazole (ipr-nsbiz, **2**, R_1 = iso-C_3H_7, R_2 = NO_2), 2-(2′-chlorostyryl)-1-ethylbenzimidazole (et-csbiz, **2**, R_1 = C_2H_5, R_2 = H), 2-(2′-chloro-4′-nitrostyryl)-6-meth-



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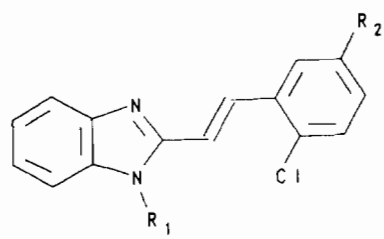

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*For Part II see ref. 1. Presented in part, see ref. 2.
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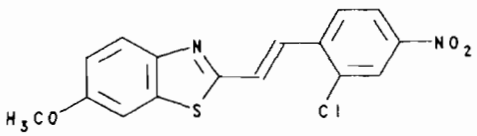
oxybenzothiazole (me-4-nsb, **3**, and 2-(2',3'-dimethoxystyryl)benzothiazole (dmesbt, **4**).



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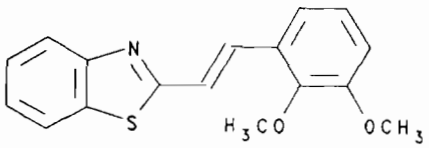

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Experimental

Physical measurements

UV–Vis spectra were recorded using a Hewlett Packard 8452A, Cary 14, Hitachi Perkin-Elmer 200 or Perkin-Elmer 552 UV–Vis spectrophotometer. IR spectra for complexes were recorded for KBr pellets or Nujol mulls between polyethylene discs and for ligands in KBr pellets using a Nicolet 6000 Series 80 FT-IR spectrometer. ^1H and ^{13}C NMR spectra were recorded with a GE QE-300, GN-300 NMR, JEOL FX 90Q NMR, or Varian EM-360 (Iowa University) spectrometer using internal tetramethylsilane as standard. Melting points are uncorrected and were measured in capillary tubes with a Mel-Temp apparatus. Elemental analyses were performed by Atlantic Microlabs, Inc., Atlanta, GA.

Materials

The following compounds were purchased from Aldrich Chemical Company and were used as received: 2,3-dimethoxybenzaldehyde, *o*-anisaldehyde, 2-methylbenzothiazole, 6-methoxy-2-methylbenzothiazole, 2-methylbenzoxazole, 2-methylbenzimidazole, 1-ethyl-2-methylbenzimidazole, 2-chlorobenzaldehyde, isopropylbromide, DMSO-d_6, $CDCl_3$ and sodium hydride. Solvents and K_2PtCl_4 (Strem Chemical Co.) were used as received. 2-Chloro-4-nitrobenzaldehyde was prepared as described [16].

Syntheses of ligands

(*E*)-2-(2'-Chloro-5'-nitrostyryl)benzothiazole (nsb) and (*E*)-2-(2'-chloro-5'-nitrostyryl)benzoxazole (nsbo) were prepared and characterized by Cox *et al.* [15].

General alkylation procedure for the synthesis of 1-substituted 2-methylbenzimidazoles from 2-methylbenzimidazole

To a mixture of powdered potassium hydroxide in DMSO, stirred for 5 min, were added first 2-methylbenzimidazole and then the alkyl halide. The mixture was stirred for 24 h, after which time the mixture was poured into water and extracted with methylene chloride. The organic extracts were then combined and washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated under a vacuum to afford a product which was purified by vacuum distillation or fractional recrystallization.

1-Isopropyl-2-methylbenzimidazole (ipr-mebiz)

Following the general procedure, 2-methylbenzimidazole (42 g, 0.32 mol) was alkylated with isopropyl bromide (79 g, 0.64 mol) and potassium hydroxide (73 g, 1.3 mol) in DMSO to afford 3.1 g (79%) or ipr-mebiz: b.p. 140 °C (1 mm); ^1H NMR ($CDCl_3$, 90 MHz) δ 7.64–7.16 (m, 4H, aromatic), 4.46 (d, $J=7.3$ Hz, 1 H, $CH(CH_3)_2$, 2.51 (s, 3 H, 2-CH_3), 1.53 (d, $J=6.9$ Hz, $CH(CH_3)_2$); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 13.3, 19.7, 46.4, 109.7, 117.8, 119.9, 120.2, 132.4, 142.0, 149.5; IR (KBr) 3040, 2960, 2920, 2880, 1614, 1597, 1518, 1462, 1438, 1284, 1408, 1388, 1362, 1309, 1246, 1180, 1163, 1131, 1107, 1088, 1004, 771, 746 cm^{-1}. The compound was converted to the corresponding 2-(2'-chloro-5'-nitrostyryl)benzimidazole and this, in turn, to the corresponding 7-isopropyl-3-nitrobenzimidazolo[3,2*a*]-quinolinium chloride and analyzed as such.

1,2-Dimethylbenzimidazole (me-mebiz)

A 60% sodium hydride and mineral oil dispersion (2.00 g; 1.20 g NaH, 49.6 mmol) was added to dry THF (distilled from sodium and benzophenone) (160 ml) and stirred at 0 °C under an argon atmosphere. The 2-methylbenzimidazole (4.00 g, 30.3 mmol) was then added in portions. A yellow color was evident in the reaction mixture. The reaction mixture was then left stirring at 0 °C for 20 min, and then at 25 °C for an additional 20 min. The methyl iodide (4.40 g, 31.0 mmol) was then added in portions and left stirring at ambient temperature for 24 h. The resulting reaction mixture was cooled to 0° with an ice-water bath and water was then added. It was extracted with chloroform (4×80 ml), dried over anhydrous magnesium sulfate, filtered and concentrated under vacuum to afford 3.1 g (70%) of me-mebiz: m.p. 110–112 °C (lit.[17] m.p. 111–112 °C); ^1H NMR ($CDCl_3$, 90 MHz) δ 2.48 (s, 3 H), 3.54 (s, 3 H), 7.14–7.7 (m, 4 H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 13.35, 29.38, 108.64, 118.55, 121.48, 121.69, 135.45, 142.17, 151.54; IR (KBr) 3040, 1671, 1617, 1515, 1483, 1451, 1429, 1402, 1331, 1290, 1242, 1152, 1126,

1041, 1004, 879, 861, 761, 737, 668, 587, 570, 540, 436 cm^{-1}.

General procedure for the synthesis of 2-styrylbenzazole derivatives

Procedure A. A solution of an equimolar amount of a substituted benzaldehyde and a substituted 2-methylbenzazole in the appropriate volume of acetic anhydride was refluxed for 5 h. The reaction mixture was allowed to cool room temperature and the precipitated solid was collected by vacuum filtration. The product was then purified by recrystallization from a suitable solvent.

Procedure B. This procedure follows that described by Dryanska and Ivanov [18]. To a solution of the corresponding benzaldehyde and a 2-methylbenzazole derivative in 10 ml of dimethyl sulfoxide were added dropwise with constant stirring 3 ml of 50% sodium hydroxide solution. A change in color from dark brown to yellow was observed with concomitant formation of a solid. The reaction was allowed to stand at room temperature for 2–24 h. Then water was added (50 ml) and the precipitated solid was collected by vacuum filtration, washed with water and recrystallized from a suitable solvent.

(E)-2-(2'-Acetoxystyryl)benzothiazole (asb)

Following general procedure A this compound was obtained in 75% yield from the condensation of 2-methylbenzothiazole and *o*-anisaldehyde. The product was recrystallized from cyclohexane to afford pale yellow crystals: m.p. 136–138 °C; ^{1}H NMR (90 MHz, $CDCl_3$) 8.06–7.08 (complex pattern 10 H, aromatic and CH=CH), 2.42 (s, 3H, CH_3CO); ^{13}C NMR 169.1, 166.6, 153.8, 148.7, 134.3, 130.9, 130.5, 130.1, 128.0, 127.1, 126.3, 126.0, 125.5, 124.2, 123.1, 122.7, 121.5, 20.9. *Anal.* Calc. for $C_{17}H_{13}NO_2S$:C, 69.15; H, 4.41; N, 4.74. Found: C, 69.13; H, 4.45; N, 4.73%.

(E)-(2'-Hydroxystyryl)benzothiazole (ohsb)

This compound was obtained in 90% yield from the saponification of asb with ethanolic potassium hydroxide. The product was recrystallized from aqueous methanol to afford a white solid: m.p. 236–238 °C; ^{1}H NMR 8.1–6.8 (complex pattern 10 H, aromatic and CH=CH), 9.1 (s, 1H, OH); ^{13}C NMR 167.2, 156.1, 153.5, 133.8, 133.2, 130.7, 128.1, 126.4, 125.2, 122.4, 122.1, 121.8, 121.2, 119.5, 116.1. *Anal.* Calc. for $C_{15}H_{11}NOS$: C, 71.12; H, 4.38; N, 5.53. Found: C, 71.00; H, 4.36; N, 5.38%.

(E)-2-(2'-Chlorostyryl)benzothiazole (csb)

Following general procedure A this compound was obtained in 73% yield from 2-chlorobenzaldehyde and 2-methylbenzothiazole as white crystals: m.p. 100–101 °C (lit. [18] m.p. 100–101 °C); ^{1}H NMR ($CDCl_3$, 90 MHz) 8.03–7.10 (m, complex pattern, 10 H, aromatic); ^{13}C NMR ($CDCl_3$, 90 MHz) 166.6, 154.1, 134.7, 134.4, 133.8, 133.6, 130.2, 129.4, 128.4, 127.2, 126.4, 125.6, 124.8, 123.3, 121.5; FT-IR (KBr) 1441, 1434, 1315, 1223, 1209, 1051, 1038, 958, 789, 729 cm^{-1}.

(E)-2-(2'-Chloro-5'-nitrostyryl)benzothiazole (me-4-nsb)

Following the general procedure A this compound was prepared in 40% yield from the condensation of 2-chloro-4-nitrobenzaldehyde and 6-methoxy-2-methylbenzothiazole. The crude product was recrystallized from toluene to give pure me-4-nsb as an orange solid: m.p. 206–208 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) δ ppm 8.32–8.30 (d, 2.07 Hz, 1H), 8.24–7.09 (m, arom and CH=CH, 7H), 3.91 (s, OCH_3); ^{13}C NMR 162.3, 158.5, 148.4, 147.6, 140.0, 136.3, 134.1, 129.4, 128.3, 127.2, 125.1, 123.9, 121.9, 116.2, 104.1, 55.7. *Anal.* Calc. for $C_{16}H_{11}ClN_2O_3S$: C, 55.40; H, 3.20; N, 8.08. Found: C, 55.46; H, 3.23; N, 8.01%.

(E)-2-(2'-Chloro-5'-nitrostyryl)benzimidazole (nsbiz)

Following the general procedure A, 2-methylbenzimidazole (1.0 g, 3.3 mmol) was condensed with 2-chloro-5-nitrobenzaldehyde (0.62 g, 3.3 mmol) to give 0.5 g of a solid. Recrystallization from $CHCl_3$ afforded 0.4 g (27%) of nsbiz: m.p. 194–196 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 8.675 (d, J=3.0 Hz, 1 H, aromatic), 8.16 (dd, J=9.0, 3.0 Hz, 1 H, aromatic), AB pattern at 7.99, 7.93, 7.53 and 7.47 (J=18.0 Hz, *trans* CH=CH), 7.82 (d, J=9.0 Hz, 1 H), 7.61–7.58 (m, 2 H, aromatic), 7.24–7.21 (m, 4 H, aromatic); ^{13}C NMR (DMSO-d_6, 300 MHz) δ 121.8, 122.7, 123.2, 124.3, 125.8, 127.9, 130.4, 131.6, 135.4, 138.0, 139.3, 140.8, 146.4, 147.1, 149.9; IR (KBr) 3425, 3100, 2900, 2850, 1724, 1532, 1457, 1385, 1369, 1342, 1292, 1192, 1124, 1048, 961, 827, 738, 676, 592 cm^{-1}. *Anal.* Calc. for $C_{15}H_{10}ClN_3O_2$: C, 60.11; H, 3.36; N, 14.02. Found: C, 59.98; H, 3.30; N, 13.91%.

(E)-2-(2'-Chloro-5'-nitrostyryl)-1-methylbenzimidazole (me-nsbiz)

Following general procedure A, 1,2-dimethylbenzimidazole (5.0 g, 34 mmol) was condensed with 2-chloro-5-nitrobenzaldehyde (6.3 g, 34 mmol) to yield 6.5 g (61%) of crude product. Recrystallization from $CHCl_3$ afforded 2.7 g (25%) of me-nsbiz: m.p. 265–266 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.60 (d, J=2.8 Hz, 1 H), 8.49–7.19 (m, 8 H), 3.98 (s, 3 H, 1-Me); ^{13}C NMR (DMSO-d_6, 300 MHz) δ 30.0, 90.0, 110.5, 112.0, 114.0, 117.0, 119.0, 119.5, 120.0, 122.5, 123.0, 124.5, 124.8, 126.0, 126.5, 126.8, 127.0, 128.0, 129.0, 129.5, 130.2, 131.2, 132.1, 133.0, 133.5, 135.4, 136.5, 138.0, 139.5, 144.2, 145.0, 150.0; IR (KBr) 3100, 3080, 1632, 1607,

1568, 1524, 1496, 1459, 1396, 1548, 1315, 1289, 1258, 1238, 1194, 1157, 1125, 1045, 967, 923, 893, 853, 825, 766, 750, 736, 689, 573, 518, 436 cm^{-1}. *Anal.* Calc. for $C_{16}H_{12}ClN_3O_2$: C, 61.25; H, 3.86; N, 13.39. Found: C, 60.95; H, 3.94; N, 13.24%.

(E)-2-(2'-Chlorostyryl)-1-ethylbenzimidazole (et-csbiz)

Following general procedure A this compound was prepared in 83% yield by the condensation of 2-chlorobenzaldehyde and 1-ethyl-2-methylbenzimidazole. The product was recrystallized from hexane to afford a pale yellow solid: m.p. 103–104 °C; ^1H NMR ($CDCl_3$) 8.29, 8.23, 7.09, 7.04 (AB quartet, CH=CH, 2H, $J = 15.9$ Hz), 7.84–7.24 (m, complex pattern, 8H, aromatic), 4.26 (q, 2H, CH_2, $J = 7.2$ Hz), 4.25 (t, 3H, CH_3, $J = 7.2$ Hz). *Anal.* Calc. for $C_{17}H_{15}ClN_2$: C, 72.19; H, 5.35; N, 9.91. Found: C, 72.30; H, 5.37; N, 10.10%.

2-(2'-Chloro-5'-nitrostyryl)-1-ethylbenzimidazole (et-nsbiz)

Following the general procedure A, 1-ethyl-2-methylbenzimidazole (2.0 g, 12 mmol) was condensed with 2-chloro-5-nitrobenzaldehyde (2.3 g, 12 mmol) to yield 2.5 g (61%) of et-nsbiz: m.p. 150–152 °C; ^1H NMR ($CDCl_3$, 90 MHz) δ 8.49 (d, $J = 2.5$ Hz, 1 H, aromatic), AB pattern at 8.33, 8.15, 7.55 and 7.38 ($J = 15.8$ Hz, *trans* CH=CH), 8.00 (dd, $J = 9.0$, 2.4 Hz, 1 H, aromatic), 7.81–7.74 (m, 1 H, aromatic), 7.55–7.45 (d, $J = 8.9$ Hz, 1 H, aromatic), 7.21–7.25 (m, 3 H, aromatic), 4.31 (q, $J = 7.2$ Hz, CH_2CH_3), 1.45 (t, $J = 7.2$ Hz, CH_2CH_3); ^{13}C NMR (DMSO-d_6, 90 MHz) δ 15.8, 21.1, 38.6, 109.6, 118.1, 119.7, 121.7, 123.4, 123.6, 123.8, 131.1, 131.3, 134.8, 135.8, 140.7, 142.6, 146.9, 148.7; IR (KBr) 3091, 3078, 3024, 1689, 1641, 1607, 1568, 1519, 1434, 1350, 1318, 1278, 1198, 1149, 1050, 964, 899, 862, 826, 735, 434 cm^{-1}. *Anal.* Calc. for $C_{17}H_{14}ClN_3O_2$: C, 62.29; H, 4.31; N, 12.82. Found: C, 62.01; H, 4.48; N, 12.60%.

2-(2'-Chloro-5'-nitrostyryl)-1-isopropylbenzimidazole (ipr-nsbiz)

Following general procedure A, 1-isopropyl-2-methylbenzimidazole (3.1 g, 28 mmol) was condensed with 2-chloro-5-nitrobenzaldehyde (5.3 g, 28 mmol) to afford 3.1 g (32%) of crude product, which was recrystallized from $CHCl_3$/hexane (1:1) to afford 2.6 g (27%) of ipr-nsbiz: m.p. 148–150 °C; ^1H NMR ($CDCl_3$, 300 Hz) δ 8.58 (d, $J = 2.7$ Hz, 1 H, aromatic), AB pattern at 8.26, 8.21, 7.36 and 7.31 ($J = 15.6$ Hz, *trans* CH=CH), 8.065 (dd, $J = 9.0$, 2.7 Hz, 1 H, aromatic), 7.57 (d, $J = 8.7$ Hz, 1 H, aromatic), 7.30–7.22 (m, 3 H, aromatic) 1.73 (d, $J = 6.9$ Hz, 6 H, $CHMe_2$), 4.99 (d, $J = 6.9$ Hz, 1 H, $CHMe_2$); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 21.7, 48.1, 111.7, 119.0, 119.9, 121.7, 122.8, 123.0, 123.6, 131.0, 131.6, 133.7, 135.8, 140.5, 143.0, 146.8, 148.7; IR (KBr) 3080, 3060, 2960, 2920, 1699, 1527, 1463, 1451, 1415, 1386, 1348, 1265, 1200, 1093, 1041, 972, 827, 749 cm^{-1}. *Anal.* Calc. for $C_{18}H_{16}ClN_3O_2$: C, 63.25; H, 4.22; N, 12.29. Found: C, 63.40; H, 4.30; N, 12.20%.

2-(2',5'-Dimethoxystyryl)benzoxazole (dmesbo)

Following general procedure B this compound was prepared in 80% yield by the condensation of 2,5-dimethoxybenzaldehyde (8.3 g, 50 mmol) and 2'-methylbenzoxazole (6.7 g, 50 mmol). The product was recrystallized from hexane/ethyl acetate to afford yellow crystals: m.p. 83–85 °C; ^1H NMR ($CDCl_3$) 8.2–6.6 (m, complex pattern, 9H, CH=CH, and aromatic), 3.905 (s, 3H, OCH_3), 3.829 (s, 3H, OCH_3). *Anal.* Calc. for $C_{17}H_{15}NO_3$: C, 75.58; H, 5.37; N, 4.98. Found: C, 75.85; H, 5.40; N, 5.02%.

2-(2',3'-Dimethoxystyryl)benzothiazole (dmesbt)

Following general procedure B this compound was prepared by the condensation of 2,3-dimethoxybenzaldehyde (6.61 g, 40 mmol) and 2'-methylbenzothiazole (6.4 ml, 49 mmol). The crude product was recrystallized from hexane/chloroform (3:1) to give beige crystals (15.8 g, 49% yield): m.p. 87–89 °C (lit. [19] m.p. 90–91 °C; ^1H NMR ($CDCl_3$) 8.08 (d, $J = 8.4$ Hz), 7.98 (d, $J = 8.1$ Hz), AB pattern at 7.84, 7.79, 7.63 and 7.58 ($J = 16.5$ Hz, *trans* CH=CH), complex pattern from 7.54 to 7.40 and 7.20 to 6.90, 3.81 (s, OCH_3), 3.84 (s, OCH_3).

Syntheses of complexes

cis-Dichlorobis[2-(2'-chloro-5'-nitrostyryl)-benzothiazole]platinum(II), cis[Pt(nsb)$_2$Cl$_2$]

An acetone solution (90 ml) of 0.153 g (0.483 mmol) of 2-(2'-chloro-5'-nitrostyryl)benzothiazole was added slowly to 30 ml of an aqueous solution of 0.100 g (0.241 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plate at about the boiling point for 5 h, and then left to cool to room temperature. The solid obtained was filtered, washed several times with water, then washed with ether and dried. The yellow powder was obtained in 51% yield, 0.111 g: m.p. > 200 °C dec.

cis-Dichlorobis[2-(2'-acetoxystyryl)benzothiazole]-platinum(II), cis-[Pt(asb)$_2$Cl$_2$]

An acetone solution (20 ml) of 0.142 g (0.482 mmol) of 2-(2'-acetoxystyryl)benzothiazole was added slowly to 10 ml of an aqueous solution of 0.100 g (0.241 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plate at about the boiling point for 3 h, and then left to cool to room temperature. The solid obtained was filtered, washed several times with water, then washed with THF, ethanol, ether and dried.

The yellow powder was obtained in 58% yield, 0.121 g: m.p. 180 °C.

cis-Dichlorobis[2-(2'-chlorostyryl)benzothiazole]-platinum(II), cis-[Pt(csb)$_2$Cl$_2$]

A THF/ethanol solution (4 ml) of 0.131 g (0.482 mmol) of 2-(2'-chlorostyryl)benzothiazole was added slowly to 4 ml of an aqueous solution of 0.100 g (0.241 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plate at about the boiling point for 1 h, and then left to cool to room temperature. The solid obtained was filtered, washed several times with water, then washed with THF, ethanol, ether and dried. The pale yellow powder was obtained in 12% yield, 0.025 g: m.p. > 200 °C dec.

cis-Dichlorobis[2-(2'-hydroxystyryl)benzothiazole]-platinum(II), cis-[Pt(ohsb)$_2$Cl$_2$]

An acetone solution (10 ml) of 0.122 g (0.480 mmol) of 2-(2'-hydroxystyryl)benzothiazole was added slowly to 10 ml of an aqueous solution of 0.100g (0.241 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plane at about the boiling point for 1 h, and then left to cool to room temperature. The solid obtained was filtered, washed several times with water, then washed with ether and dried. The yellow–brown powder was obtained in 38% yield, 0.072 g: m.p. 160 °C dec.

cis-Dichlorobis[2-(2'-chloro-4'-nitrostyryl)-6-methoxybenzothiazole]platinum(II), cis-[Pt(me-4-nsb)$_2$Cl$_2$]

An acetone solution (50 ml) of 0.128 g (0.369 mmol) of 2-(2'-chloro-4'-nitrostyryl)-6-methoxybenzothiazole was added slowly to 10 ml of an aqueous solution of 0.060 g (0.144 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plate at about the boiling point for 2 h, and then stirred 1 h more while it cooled to room temperature. The solid obtained was filtered, washed several times with water, then washed with THF, ethanol, ether and dried. The yellow powder was obtained in 16% yield, 0.111 g: m.p. > 210 °C dec.

cis-Dichlorobis[2-(2'-chloro-5'-nitrostyryl)-benzoxazole]platinum(II), cis-[Pt(nsbo)$_2$Cl$_2$]

An acetone solution (40 ml) of 0.145 g (0.469 mmol) of 2-(2'-chloro-5'-nitrostyryl)benzoxazole was added slowly to 20 ml of an aqueous solution of 0.100 g (0.241 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plate at about the boiling point for 3 h, and then left to cool to room temperature. The solid obtained was filtered, washed several times with water, then washed with THF, ethanol, ether and dried. The colorless powder was obtained in 51% yield, 0.106 g: m.p. > 200 °C dec.

cis-Dichlorobis[2-(2',5'-dimethoxystyryl)-benzoxazole]platinum(II), cis-[Pt(dmesbo)$_2$Cl$_2$]

An acetone solution (10 ml) of 0.160 g (0.280 mmol) of 2-(2',5'-dimethoxystyryl)benzoxazole was added to 3 ml of an aqueous solution of 0.0600 g (0.140 mmol) of K_2PtCl_4. The reaction mixture was stirred for 10 min and the solvent was left to evaporate at room temperature. The solid was filtered and washed with water, acetone and ether. The yellow solid was recrystallized from acetone to give 0.0606 g of product, 51% yield: m.p. > 200 °C.

cis-Dichlorobis[2-(2',3'-dimethoxystyryl)-benzothiazole]platinum(II), cis-[Pt(dmesbt)$_2$Cl$_2$]

An acetone solution (2 ml) of 0.0675 g (0.227 mmol) of 2-(2',3'-dimethoxystyryl)benzothiazole was added to 0.5 ml of an aqueous solution of 0.050 g (0.120 mmol) of K_2PtCl_4. The reaction mixture was stirred and heated on a hot plate at the boiling point for 1.5 h. Acetone (1 ml) was added occasionally to keep a relatively constant volume. A yellow solid precipitated, which was filtered, washed with water (3 ml), acetone (3 ml), and then ether (20 ml), and dried. The yellow powder was obtained in 74% yield, 0.0763 g: m.p. > 200 °C dec.

cis-Dichlorobis[2-(2'-chloro-5'-nitrostyryl)-benzimidazole]platinum(II), cis-[Pt(nsbiz)$_2$Cl$_2$]

An acetone solution (15 ml) of 0.079 g (0.264 mmol) of 2-(2'-chloro-5'-nitrostyryl)benzimidazole was added slowly to 5 ml of an aqueous solution of 0.050 g (0.120 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plate at about the boiling point for 1 h, and then stirred for another hour while it cooled to room temperature. The solvent was evaporated and the solid obtained washed several times with water, then washed with THF, ethanol, ether and dried. The yellow powder was obtained in 71% yield, 0.0788 g; m.p. > 200 °C dec.

cis-Dichlorobis[2-(2'-chloro-5'-nitrostyryl)-1-isopropylbenzimidazole]platinum(II), cis-[Pt(ipr-nsbiz)$_2$Cl$_2$]

An acetone solution (10 ml) of 0.0823 g (0.241 mmol) of 2-(2'-chloro-5'-nitrostyryl)-1-isopropylbenzimidazole was added slowly to 5 ml of an aqueous solution of 0.050 g (0.120 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plate at about the boiling point for 0.5 h, and then stirred for 1.5 h more, while it cooled to room temperature. The solvent was evaporated and the solid obtained washed several times with water, then washed with ether and dried. The orange powder was obtained in 57% yield, 0.0650 g: m.p. > 200 °C dec.

cis-Dichlorobis[2-(2'-chloro-5'-nitrostyryl)-1-ethylbenzimidazole]platinum(II), cis-[Pt(et-nsbiz)$_2$Cl$_2$]

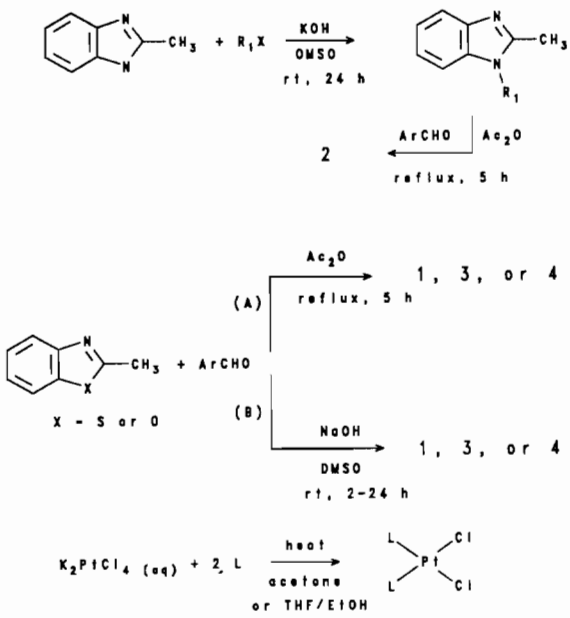
An acetone solution (45 ml) of 0.158 g (0.482 mmol) of 2-(2'-chloro-5'-nitrostyryl)-1-ethylbenzimidazole was added slowly to 20 ml of an aqueous solution of 0.100 g (0.241 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plate at about the boiling point for 2 h, and then left to cool to room temperature. The solvent was evaporated and the solid obtained washed with water, then washed with ether and dried. The colorless powder was obtained in 38% yield, 0.0836 g: m.p. > 200 °C dec.

cis-Dichlorobis[2-(2'-chlorostyryl)-1-ethylbenzimidazole]platinum(II), cis-[Pt(et-csbiz)$_2$Cl$_2$]

An acetone solution (15 ml) of 0.136 g (0.481 mmol) of 2-(2'-chlorostyryl)-1-ethylbenzimidazole was added slowly to 5 ml of an aqueous solution of 0.100 g (0.241 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plate at about the boiling point for 1 h, and then stirred for 1 h while it cooled to room temperature. The solvent was evaporated and the solid obtained was washed several times with water, then washed with ether and dried. The orange powder was obtained in 68% yield, 0.140 g: m.p. 115 °C dec.

cis-Dichlorobis[2-(2'-chloro-5'-nitrostyryl)-1-methylbenzimidazole]platinum(II), cis-[Pt(me-nsbiz)$_2$Cl$_2$]

An acetone solution (110 ml) of 0.151 g (0.481 mmol) of 2-(2'-chloro-5'-nitrostyryl)-1-methylbenzimidazole was added slowly to 50 ml of an aqueous solution of 0.100 g (0.241 mmol) of $K_2[PtCl_4]$. The reaction mixture was stirred and heated on a hot plate at about the boiling point for 3 h, and then left to cool to room temperature. The solid obtained was filtered, washed several times with water, then washed with THF, ethanol, ether and dried. The yellow powder was obtained in 52% yield, 0.116 g: m.p. > 200 °C dec.



Scheme 1.

TABLE 1. Chemical shifts and coupling constants of the AB pattern for the ethylene moiety in selected 2-styrylbenzazole ligands[a]

Ligand	δ_A	δ_B[b, c]	J (Hz)
nsb	7.53	7.88	16.4
Z-nsb[b]	6.98	7.13	12.0
nsbo	7.21	8.09	16.2
nsbiz	7.50	7.96	18.0
me-nsbiz	7.40	8.30	15.8
et-nsbiz	7.48	8.23	15.8
ipr-nsbiz	7.34	8.23	15.6
et-csbiz	7.06	8.26	15.9
dmesbt	7.61	7.81	16.5

[a]Solvent $CDCl_3$, 300 MHz. [b]Referenced from TMS in ppm. [c]The downfield signal is assigned to the hydrogen adjacent to the aryl nucleus using 2D NMR techniques [21]. [d]This is the *Z*-isomer of nsb whose spectrum was also analyzed by 2D NMR techniques [21].

Results and discussion

Ligands

The 2-styrylbenzazole ligands used in this study were prepared by the condensation of the corresponding aromatic aldehyde with a 2-methylbenzazole derivative in boiling acetic anhydride (Procedure A) [15] or in the presence of sodium hydroxide in aqueous DMSO [18] (Procedure B), as shown in Scheme 1. These procedures give the *E*-isomer (**1–4**) as the major product as determined by X-ray structural analysis [20], FT-IR, UV–Vis and ^1H and ^{13}C NMR spectroscopy.

The protons attached to the ethylene moiety of the 2-styrylbenzazoles appear as an AB quartet which is clearly discernible in the ligands included in this study. The low field doublet is assigned to the proton closer to the aryl nucleus based on chemical and 2D-NMR techniques [21]. The signals of this AB pattern (see Table 1) display an upfield shift in the *Z*-isomer, where the low field doublet experiences the largest upfield shift. The proton–proton coupling constants for the *E*-isomers are 16–18 Hz, characteristic of *trans* olefins [22]. On the other hand that for *Z*-nsb is 12 Hz [21].

The UV–Vis spectra of all *E*-ligands show the characteristic spectrum of stilbenes and related systems [23] (see Table 2). In general there are at least two major bands, and in some cases the longwave band shows vibrational peaks. In *Z*-nsb the longwave band appears

TABLE 2. UV–Vis spectral data for 2-styrylbenzazole ligands (L) and for *cis*-$Pt(L)_2Cl_2$

Ligand	Wavelength, nm (10^{-3} ϵ) for ligand in 95% EtOH	Wavelength, nm (10^{-3} ϵ) for complex in DMF
nsb	214 (16.8), 333 (28.4)	340 (22), 400 (5.4) sh, 450 (0.62) sh
Z-nsb	205 (41.9), 217 (38.7), 281 (24.4), 288 (24.4)	
nsbo	202 (1.2), 325 (18.9)	315
ohsb	218 (50.0), 237 (23.4), 313 (34.9), 362 (55.6)	330 (33), 390 (8.5) sh, 445 (0.79) sh
asb	215 (34.4), 270 (28.1), 312 (8.36), 323 (29.8)	350 (62), 374 (51) sh, 422 (1.1) sh[a]
csb	217 (16.6), 264 (54.3), 332 (18.8)	345 (22), 398 (7.2) sh, 420 (3.6) sh
dmesbo	209 (15.1), 314 (18.0), 317 (18.1), 365 (14.9)	280 (8.10, 320 (7.8), 400 (6.8), 450 (3.0)
nsbiz	204 (2.16), 241 (2.61), 259 (3.11), 337 (5.36)	340 (20), 410 sh
me-nsbiz	224 (4.63), 262 (3.07), 338 (4.63)	320 (35), 390 (5.2) sh, 420 (0.72) sh
et-nsbiz	207 (50.0), 230 (23.0) sh, 260 (33.0), 289 (22.0) sh, 342 (51.0)	320 (31), 391 (9), 450 (0.18) sh
ipr-nsbiz	206 (16.0), 259 (9.30), 288 (6.60), 337 (13.0)	318 (20), 355 (10) sh, 400 (4) sh, 454 (0.2)
et-csbiz	218 (10.8), 260 (9.22), 312 (11.5), 327 (12.7), 352 (11.3)	326 (10), 390 (2) sh, 434 (0.4) sh
me-4-nsb	208 (20.6), 281 (7.91), 287 (7.8), 350 (8.23)	370 (21), 400 (14) sh, 430 (5.1) sh, 480 (0.45) sh
dmesbt	205 (7.43), 211 (7.3), 215 (7.34), 226 (8.46), 250 (9.36), 335 (29.7)	298 (30) sh, 354 (40)

[a]Solvent: DMSO.

at considerably shorter wavelength and is less intense than that of the *E*-isomer, as is usual in stilbenes and related systems [23].

Complexes

The *cis*-dichloro complexes of Pt(II) were synthesized directly from K_2PtCl_4 by reaction with the heterocyclic ligands in stoichiometric amounts (Scheme 1). Because of the differing solubilities of the starting complex and the ligands, all the reactions were carried out in mixtures of water and organic solvents. In most cases, the neutral product precipitated from the reaction mixture and was isolated by filtration. According to the kinetic *trans* effect [24], this method is expected to yield complexes with *cis* geometry. With few exceptions, the complexes were insoluble in common organic solvents such as ethanol and acetone. All the complexes are partially soluble in DMF or DMSO. Those ligands which were very soluble in acetone or in THF/ethanol mixtures (asb, ohsb and most of the benzimidazole derivatives) gave complexes which were partially soluble in the reacting media. In these cases, the solvent was evaporated from the reaction mixture and the solid obtained was purified by washing with appropriate solvents. The formulas and results of elemental analyses for the complexes obtained are listed in Table 3. The low solubilities of the complexes precluded purification by recrystallization, but careful washing gave material with reasonably good agreement between calculated and experimental compositions, with the exception of the dmesbo complex.

The color of the styrylbenzazole complexes varies greatly depending on the ligand. The colorless ligand nsbo gave a nearly colorless complex, while dmesbo and those alkylbenzimidazole ligands with considerable absorption ($\epsilon \sim 100$) in the visible region gave bright yellow complexes.

TABLE 3. Formulas and elemental analyses for new platinum(II) complexes

Formula[a]	Found (calc.) (%)	
	C	H
cis-$Pt(nsb)_2Cl_2$	40.3 (40.1)	2.4 (2.0)
cis-$Pt(nsbo)_2Cl_2$	41.3 (41.5)	2.2 (2.1)
cis-$Pt(ohsb)_2Cl_2$	46.8 (46.6)	3.2 (2.9)
cis-$Pt(asb)_2Cl_2 \cdot 0.5H_2O$	47.2 (47.2)	3.2 (3.1)
cis-$Pt(csb)_2Cl_2 \cdot 2.5H_2O$[b]	42.0 (42.2)	2.9 (2.9)
cis-$Pt(dmesbo)_2Cl_2$	49.3 (49.4)	3.6 (4.1)
cis-$Pt(nsbiz)_2Cl_2$	41.7 (41.6)	2.6 (2.3)
cis-$Pt(me\text{-}nsbiz)_2Cl_2 \cdot 2H_2O$	41.6 (41.5)	3.0 (3.0)
cis-$Pt(et\text{-}nsbiz)_2Cl_2$	44.1 (44.3)	3.1 (3.1)
cis-$Pt(ipr\text{-}nsbiz)_2Cl_2$[c]	45.4 (45.5)	3.4 (3.4)
cis-$Pt(et\text{-}csbiz)_2Cl_2 \cdot H_2O$	48.0 (48.0)	3.5 (3.7)
cis-$Pt(me\text{-}4\text{-}nsb)_2Cl_2$	40.3 (40.0)	2.5 (2.8)
cis-$Pt(dmesbt)_2Cl_2$	47.3 (47.4)	3.5 (3.5)

[a]Molecules of solvent were included as justified by the analytical results. [b]S: calc., 7.4; found, 7.5%. Cl: calc., 16.6; found, 16.6%. [c]N: calc., 8.8; found 8.8%.

Data from the UV–Vis spectra of the complexes are summarized in Table 2, and can be compared with the data in Table 2 for the pure ligands, although the solvents differ as noted in the Table. Each ligand has an absorption band in the region between 323 and 365 nm with molar absorptivity of the order of 10^4. The corresponding complex also has a band of nearly identical form in the region from 318 to 370 nm, with similar ϵ and a shift in λ of from 10 to 30 nm. This band in the complex was assigned as belonging to a ligand–ligand transition. At wavelengths greater than 370 nm, the ligands show much weaker absorption ($\epsilon < 200$) than do the complexes. This suggests that the bands at longest wavelength in the complexes are either d–d or charge transfer transitions, or possibly both. The intensities would support assignment as charge

transfer. The spectra of the complexes below 318 nm consist of overlapping ligand–ligand and charge transfer bands. No attempt was made to distinguish these and they were omitted from Table 2.

The mode of coordination for the benzimidazole ligands obviously must be through N, but for the ligands asb, csb, nsb, ohsb, me-4-nsb, and nsbo, which contain one N and one other heteroatom (S or O), the coordinating atom in the ligand needs to be assigned. The single-crystal X-ray structure determination of the complex *cis*-$Pt(asb)_2Cl_2$ has been reported [25] and the coordination is through the N of asb and not through the S. This is consistent with several complexes of the type $[Pt(L)Br_3]^-$ (L = nsb [26], asb [27], csb [1], me-4-nsb [1]) for which X-ray structural studies have shown coordination through N rather than through S. Given the similarity of the spectra of all the related complexes in Table 2, it is reasonable to assume that all the complexes are coordinated through N. However, given the apparent overlap of ligand bands with d–d bands or charge transfer bands, this assignment cannot be made with certainty solely on the basis of these spectra.

IR data were obtained for several complexes: two styrylbenzothiazoles (asb and csb), a styrylbenzimidazole (et-nsbiz) and a benzoxazole (dmesbo). The vibrational frequencies of the styrylbenzazole ligands in the mid-IR region (see 'Experimental') do not change substantially upon complexation. More notable changes occur for bands in the 900–600 cm^{-1} region. These are commonly related to ring vibrations of the benzazole moiety.

The far-IR spectra of the complexes show ligand vibrations, Pt–Cl stretching vibrations, and Pt–X stretching vibrations (X = N, S, O or Se). The Pt–Cl stretching bands are very strong compared to the weak absorptions of the Pt–X and ligand bands. Even when there is overlap, there is little doubt about the assignment of the ν(Pt–Cl) bands. However, in most cases the metal–nitrogen stretching bands could not be distinguished from other weak absorptions present in the spectra.

The presence of two Pt–Cl stretching frequencies in the spectra of the compounds is consistent with *cis* geometry. It has been reported that the *cis*-$Pt(imidazole)_2Cl_2$ complex shows bands at 329 and 322 cm^{-1}, while the *trans* isomer shows only one strong band at 350 cm^{-1} [10]. The styrylbenzimidazole complex et-nsbiz shows ν(Pt–Cl) bands at 338 and 326 cm^{-1}, which is consistent with *cis* rather than *trans* geometry.

Styrylbenzothiazole complexes have two ν(Pt–Cl) bands, in the regions 335 to 339 and 327 to 329 cm^{-1}. This is consistent with the frequencies reported for *cis*-$Pt(thiazole)_2Cl_2$ and *cis*-$Pt(4\text{-methylthiazole})_2Cl_2$, which are 328, 321 cm^{-1} and 336, 326 cm^{-1}, respectively [28]. The dmesbo and nsbo complexes have two strong bands at 337 and 320 cm^{-1} and at 334 and 319 cm^{-1}, respectively. These bands, assigned to ν(Pt–Cl), are consistent with *cis* geometry for these complexes.

Conclusions

Twelve new styrylbenzazole ligands and thirteen new complexes of the type $Pt(L)_2Cl_2$ have been prepared. The geometry has been assigned as *cis* based on *trans* effect predictions of the products from the synthetic method used, the splitting of the ν(Pt–Cl) band observed in the far-IR spectra of the complexes and the previously reported X-ray diffraction study of *cis*-$Pt(asb)_2Cl_2$. Although two potential donor atoms are present in styrylbenzothiazoles and in styrylbenzoxazoles, these ligands all bind to Pt(II) through the N of the azole ring. The UV–Vis spectra of the complexes are very similar to those of the pure ligands, except for the presence of charge transfer and/or d–d transitions in the visible region.

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