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FULL PAPER

Terpyridyl derivatives as bifunctional chelates: synthesis and crystal structures of 4′-[2-(1,3-dioxolan-2-yl)ethylsulfanyl]-2,2′:6′,2″-terpyridine and chloro(4′-methylsulfanyl-2,2′:6′,2″-terpyridine)gold(III) bis(trifluoromethanesulfonate) †

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A variety of 2,2′:6′,2″-terpyridine (terpy) derivatives modified at the 4′ position has been synthesized to generate bifunctional chelates. A particularly convenient route to these bifunctional chelates, based on nucleophilic substitution of 4′-chloroterpyridine is described. The crystal structure of 4′-[2-(1,3-dioxolan-2-yl)ethylsulfanyl]-2,2′:6′,2″-terpyridine has been determined. The palladium(II) and gold(III) complexes of the analog with an SMe group at the 4′ position have been synthesized and characterized. The crystal structure of the latter has been determined.

Introduction

Functional mimics of naturally occurring bioinorganic molecules are of increasing interest as catalysts for asymmetric synthesis and as potential catalytic drugs. One of our groups (the JKB group) has focused for some time on the construction and optimization of functional mimics of ribozymes, synthetic molecules that are sequence-specific RNA cleavage agents.[1–7] These molecules have the potential to serve as catalytic antisense drugs and to destroy harmful messenger RNA (such as viral mRNA) in a gene-specific manner.[1,8–12] A large part of this work has involved the identification of catalysts that cleave RNA by the biocompatible transesterification/hydrolysis pathway,[7,13,14] and then the elucidation of strategies for incorporating these catalysts into DNA building blocks.[4,15–18] Terpyridine ethers, thioethers and related compounds have played a prominent role in the production of sequence-specific RNA cleavage reagents.[1–7,19–21] The resulting reagents are suitable for solid-phase DNA synthesis, and can be incorporated into any DNA sequence of interest. In the course of this program we have prepared a variety of bifunctional chelates that allow metal complexes to be covalently linked to biomolecules. Most recently, we employed such chelates for the pinpoint cleavage of a portion of HIV mRNA.[2] Bifunctional chelates of polypyridine ligands are generally applicable to a wide range of chemistry, including supramolecular chemistry, dendrimers, and molecular electronics.[22–44] As described in this paper, a collaboration has sprung up between our groups (JKB and SSJ) to explore some of these additional areas, especially those related to diagnostic and therapeutic radiopharmaceuticals. We also follow up recent communications by providing herein the full details for preparation of key terpy derivatives.[2,5,6]

† *Supplementary data available*: reactions of compound **8** with oxyanionic substrates. For direct electronic access see http://www.rsc.org/suppdata/dt/1999/2049/, otherwise available from BLDSC (No. SUP 57533, 3 pp.) or the RSC Library. See Instructions for Authors, 1999, Issue 1 (http://www.rsc.org/dalton).

Metal complexes have found applications in the development of diagnostic and therapeutic pharmaceuticals[45–48] and for investigating DNA and RNA structures,[49–54] cleavage,[53,55–59] and repair.[60] A current focus in the development of diagnostic and therapeutic pharmaceuticals involves the use of bifunctional chelates that are capable of simultaneously co-ordinating to a metal and covalently bonding to a biological carrier for targeting specific diseases. Bifunctional chelates can also be used to deliver radiometals to specific biological targets. Numerous reviews discuss the merits of various radiometals for the development of diagnostic and therapeutic radiopharmaceuticals.[61–63] Of course, no discussion of this area would be complete without citing the pioneering work of Meares on bifunctional chelates, their use in the delivery of radiometals, and the whole field of bioconjugates.[64–71]

It is clear that for diagnostic applications ^{99m}Tc and ^{111}In are the most useful radionuclides at this time.[45,47] However, for radiotherapeutic applications, various radioisotopes such as ^{199}Au, ^{188}Re, ^{90}Sr, ^{153}Sm, ^{105}Rh, ^{67}Cu, and ^{177}Lu may be useful when tumor size, whole body radiation dose, and pharmacokinetics of the radiolabeled compound are taken into account.[46,47,72]

Terpyridine and its derivatives are well established chelates for transition metals, particularly the d^8 metals that form square planar complexes.[73–76] Gold(III) and Pd^{II} are known to form stable complexes with terpyridine, and both have radioisotopes, ^{199}Au and ^{109}Pd, with nuclear properties suitable for radiotherapy: ^{199}Au emits a 0.453 MeV beta particle, has a 3.14 d half-life, and is available in high specific activity from a ^{198}Pt target; ^{109}Pd is a 1.03 MeV beta particle emitter, has a 13.5 h half-life and is available from an enriched ^{108}Pd target.

We wished to synthesize (and characterize) a number of terpyridine (terpy) derivatives that were functionalized in the 4′ position. The target ligands had amino, hydroxy, halogeno and carboxylate groups pendant to the 4′ position to allow attachment to a biotargeting moiety. Three different methods were used to prepare these bifunctional ligands. In Method 1, 4′-alkylsulfanyl derivatives were synthesized from

acetylpyridine, CS_2, and alkyl halides. In Method 2, deprotonation of 4′-methylterpyridine was followed by reaction with alkyl halides. Method 3, which we found to be the most convenient procedure, employed the reaction of 4′-chloro-2,2′:6,6″-terpyridine, with alkoxides to give an ether linkage. This involves nucleophilic aromatic substitution of the electron deficient terpyridine moiety *via* oxyanionic attack. It can take place in the presence of other nucleophiles such as amines and carboxylates, showing good selectivity for the alkoxide nucleophile.

In related work, the production of ether-linked 1,10-phenanthroline ligands *via* nucleophilic aromatic substitution at the 2 position has been previously reported by Halcrow and Kermack.[77] Constable *et al.*[78] reported nucleophilic attack on 4′-halogenoterpyridines in their search for control of charge separation in the ground or photoaccessible states of co-ordination compounds. The literature also provides various other important techniques for the production of substituted terpyridines.[24,25,27,36–38,79–86]

The reaction of terpyridyl ligands with d^8 transition metals (*e.g.*, Pt^{II}, Au^{III}) results in square planar complexes with a monodentate ligand in the 4th co-ordination site. We synthesized and characterized the complexes of Au^{III} and Pd^{II} with 4′-methylsulfanyl terpyridine, and the expected complexes were obtained. In addition to the terpy ligand and metal complex syntheses and characterization, the crystal structures of a terpyridine–dioxolane derivative and of the gold complex are reported.‡

Experimental

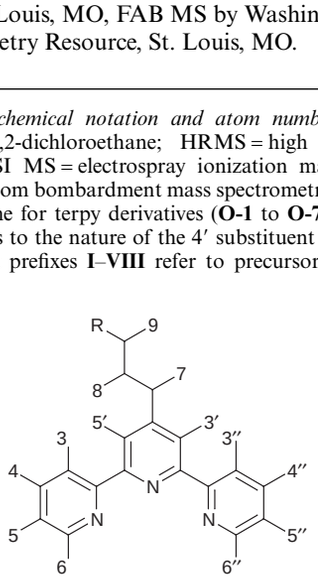
Materials

Compound **S-8** was available from a literature preparation,[87] $PdCl_2$ and $NaAuCl_4$ were purchased from Aesar Chemical Co. All other chemicals were reagent grade and used as received unless otherwise specified.

Physical measurements

The ^1H NMR spectra were run on a Bruker 250 MHz or a Varian 300 MHz spectrometer (as indicated) in the solvent described with TMS as the internal standard. Elemental analyses were performed by Quantitative Technologies Inc. (QTI) in Whitehouse, NJ, or by Galbraith Laboratories Inc. in Knoxville, TN. ESI MS was performed by Mallinckrodt Medical in St. Louis, MO, FAB MS by Washington University Mass Spectrometry Resource, St. Louis, MO.

‡ *Abbreviations, chemical notation and atom numbering scheme for NMR.* DCE = 1,2-dichloroethane; HRMS = high resolution mass spectrometry; ESI MS = electrospray ionization mass spectrometry; FAB MS = fast atom bombardment mass spectrometry. The compound numbering scheme for terpy derivatives (**O-1** to **O-7, S-1** to **S-8**, and **C-1** to **C-6**) refers to the nature of the 4′ substituent (**O**, **S**, or **C**). The numbers without prefixes **I**–**VIII** refer to precursors and **1**–**3** to the metal complexes.



Spectroscopy numbering system: standard numbering is used for the terpy ring system. The 4′ substituent is numbered consecutively, starting with 7 at the first carbon. An example is illustrated above for a hydrocarbon substituent at 4′.

Standard methods

The TLC measurements were made on Selecto Scientific Alumina Oxide Basic plates (200 μm) unless otherwise stated. Flash chromatography was conducted with Selecto Scientific Alumina Oxide Basic (20–80 μm) unless otherwise stated. Standard conditions are defined to be extraction between CH_2Cl_2 and saturated $NaHCO_3$ three times, and drying by addition of Na_2SO_4, filtration, followed by concentration by rotary evaporation under reduced pressure.

Method 1

4′-Phthalimidopropylsulfanyl-2,2′:6′,2″-terpyridine S-1. A 500 mL three necked flask under N_2 was charged with KO(*t*-Bu) (39.2 mmol, 4.4 g) and dry THF (43 mL). To the stirred suspension was added 2-acetylpyridine **I** (17.5 mmol, 2.13 g, 2.3 mL), and a creamy suspension of the enolate was formed. The enolate was trapped with anhydrous CS_2 (17.5 mmol, 1.34 g, 1.06 mL). The orange suspension was treated with a solution of *N*-(3-iodopropyl)phthalimide (35.1 mmol, 11.1 g) [made *via* a Finklestein reaction of *N*-(3-bromopropyl)phthalimide with NaI] in THF (18 mL) and stirred for 5.5 h which turned the reaction mixture brownish green. This was diluted with dry THF (43 mL) and charged with **I** (17.5 mmol, 2.13 g, 2.3 mL) and KO(*t*-Bu) (39.2 mmol, 4.4 g). The red reaction mixture was stirred overnight (12–16 h) at room temperature. To the reaction mixture was then added NH_4OAc (1.3 g) followed by glacial acetic acid (27 mL). The THF was removed from the olive green reaction mixture by distillation in a hood (stench) and a dark purple residue obtained. The residue was extracted under standard conditions, and the excess of acid neutralized with addition of solid $NaHCO_3$. The organic layer was separated and the aqueous layer further extracted with CH_2Cl_2. The combined organic layers were dried to a dark brown oil. This residue was chromatographed with 25% EtOAc–hexane followed by 50% EtOAc–hexane to give compound **S-1** (≈40% yield from carbon disulfide), mp 170–171 °C; TLC R_f 0.41 (50:50 hexane–ethyl acetate) ^1H NMR (300 MHz, $CDCl_3$): δ 2.19 (m, 2 H, H8, J = 7.02); 3.24 (t, 2 H, H7, J = 7.17); 3.91 (t, 2 H, H9, J = 6.90); 7.34 (ddd, 2 H, H5 and H5″, J = 6.45,4.86,1.23); 7.71 (dd, 2 H, H4 and H4″, J = 5.46, 3.03); 7.85 (m, 2 H, H10 and H13); 8.32 (s, 2 H, H3′ and H5′); 8.59 (m, 2 H, H3 and H3″, J = 7.77); 8.67 (m, 2 H, H6 and H6″, J = 4.60 Hz). ^{13}C NMR (75.1 MHz, $CDCl_3$): δ 27.7, C8; 28.3, C7; 37.0, C9; 117.8, C3 and C3″; 121.4, C3′ and C5′; 123.3, C11 and C12; 123.8, C5 and C5″; 132.0, C10 and C13; 134.0, C14 and C15; 136.9, C4 and C4″; 149.0, C6 and C6″; 150.7, C4′; 154.9, C2 and C2″; 155.7, C2′ and C6′. IR (solid film on 3M card): 1393.5, 1558.4 and 1713.6 cm^{-1}. HRMS EI: *m*/*z* calc. for $C_{26}H_{20}N_4O_2S$: 452.1307, found 452.1293. MS EI: *m*/*z* (%) 452 (11), 419 (3.3), 405 (9.3), 294 (6), 293 (19.1), 292 (100), 281 (5.6), 280 (18.4), 279 (99.6), 278 (8.7), 265 (13.9), 233 (13.1), 221 (7.5), 160 (11.6) and 130 (4.6) [Calc. (Found) for $C_{26}H_{20}N_4O_2S$: C, 69.01 (69.23); H, 4.45 (4.58); N, 12.38 (12.61); S, 7.09 (7.07)%].

4′-(2-dioxaneylethylsulfanyl)-2,2′:6′,2″-terpyridine S-2. A three neck flask was filled with a nitrogen inlet and a stir bar. The apparatus was flame dried and charged with KO(*t*-Bu) (17.6 g, 157 mmol) and anhydrous THF (130 mL). 2-Acetylpyridine (10.2 mL, 91 mmol) was added dropwise, followed by CS_2 (5.1 mL, 84.8 mmol) and 2-(2-bromoethyl)-1,3-dioxane (21 mL, 154 mmol). The mixture was stirred at room temperature for 5.5 h and additional THF (190 mL), KO(*t*-Bu) (17.6 g, 157 mmol), and 2-acetylpyridine (9.9 mL, 89 mmol) were then added. The reaction mixture was stirred for 14 h at room temperature and subsequently charged with ammonium acetate (64 g) and glacial acetic acid (105 mL). The THF was then distilled off over a 4 h period. The mixture was cooled to room temperature, poured over ice and taken up in a large separatory funnel with dichloromethane. The excess acid was neutralized with

solid sodium hydrogencarbonate. The organic layers were dried. The thick dark liquid was chromatographed twice on basic alumina with hexanes and ethyl acetate to yield a light-yellow liquid which crystallized on standing to give pink–yellow crystals (7.18 g, 22.2%) mp 126.5–127.5 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.33 [1H, m, J = 13.99, H12(eq.)]; 2.07 [3H, m, H12(ax.), H8]; 3.28 (2H, m, J = 7.49, H7); 3.76 [2H, ddd, J = 12.49, 12.49, 4.49, H10 and H11(ax.)]; 4.11 (2H, ddd, J = 11.49, 4.99, 1.00, H10 and H11(eq.)]; 4.74 (1H, t, J = 4.75, H9); 7.33 (2H, m, J = 7.99, H5 and H5″); 7.85 (2H, m, J = 7.99, 7.49, 1.99, H4, H4″); 8.35 (2H, s, H3′, H5′); 8.60 (2H, m, J = 7.99, H3, H3″); 8.69 (2H, J = 4.99, 1.49, 1.00 Hz, H6, H6″) ^{13}C NMR ($CDCl_3$, 125 MHz): δ 25.04, C12; 25.46, C8; 33.83, C7; 66.79, C10 and C11; 100.31, C9; 117.82, C3 and C3″; 121.49, C3′ and C5′; 123.97, C5 and C5″; 136.99, C4 and C4″; 149.23, C6 and C6″; 151.44, C4′; 155.17, C2 and C2″; 156.09, C2′ and C6′. HRMS: *m*/*z* calc. for $C_{21}H_{21}N_3O_2S$: 379.1354, found 379.1356.

4′-(3-Aminopropylsulfanyl)-2,2′:6′,2″-terpyridine (S-4). A two necked pear shaped flask was charged with compound **S-1** (0.712 mmol, 322 mg) and ethanol (10 mL). To this solution was added anhydrous hydrazine (0.718 mmol, 23 mg, 23 mL) and the reaction mixture refluxed for 6 h. After cooling to room temperature, saturated NaCl (aqueous 20 mL) was added and a white suspension formed. After the addition of about 5 drops of 50% NaOH (aq), the suspension was extracted with CH_2Cl_2 (2×) The organic layers were dried to a yellow oil **S-4** (220 mg, >95%). R_f 0.26 (15% MeOH–CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.93 (q, 2 H, H8); 2.90 (t, 2 H, H9); 3.24 (t, 2 H, H7); 7.32 (ddd, 2 H, H5 and H5″); 7.84 (ddd, 2 H, H4 and H4″); 8.33 (s, 2 H, H3′ and H5′); 8.59 (m, 2 H, H3 and H3″); and 8.68 (m, 2 H, H6 and H6″) ^{13}C NMR (75.1 MHz, $CDCl_3$): δ 18.3, C8; 28.1, C7; 32.0, C9; 117.6, C3 and C3″; 121.3, C3′ and C5′; 123.8, C5 and C5″; 136.8, C4 and C4″; 148.9, C6 and C6″; 151.3, C4′; 154.8, C2 and C2″; and 155.7, C2′ and C6′; HRMS EI: *m*/*z* calc. for $C_{18}H_{18}N_4S$ 322.1252, found 322.1258; MS EI: *m*/*z* (%) 322 (8), 292 (72), 279 (46), 265 (100), 233 (15), 221 (18), 137 (8), 81 (32), 69 (61), 57 (30) and 55 (26).

4′-[2-(1,3-dioxolan-2-yl)ethylsulfanyl]-2,2′:6′,2″-terpyridine S-3. The procedure for compound **S-1** was followed with neat 2-(2-bromoethyl)-1,3-dioxolane added to the enolate. After drying the residue was twice chromatographed with 0–5% EtOAc–hexane to give pure **S-3** (6.43 g, 21.3% from CS_2). Pale yellow crystals suitable for X-ray diffraction were obtained by slow cooling of a hexane solution. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.14 (ddd, 2 H, H8, J = 7.67, 7.67, 4.66), 3.29 (dd, 2 H, H7, J = 7.49, 7.49), 3.89–4.02 (m, 4 H, H10 and H11), 5.08 (dd, 1 H, H9, J = 4.48, 4.48), 7.32 (ddd, 2 H, H5 and H5″, J = 7.46, 4.79, 1.06), 7.84 (ddd, 2 H, H4 and H4″, J = 7.71, 7.71, 1.72), 8.35 (s, 2 H, H3′ and H5′), 8.59 (m, 2 H, H3 and H3″, J = 8.09), 8.69 (ddd, 2 H, H6 and H6″, J = 4.55, 1.67, 0.85 Hz). ^{13}C NMR (75.1 MHz, $CDCl_3$): δ 25.0, C8; 32.7, C7; 65.0, C10 and C11; 103.0, C9; 117.8, C3 and C3″; 121.5, C3′ and C5′; 124.0, C5 and C5″; 137.0, C4 and C4″; 149.3, C6 and C6″; 151.4, C4′; 155.3, C2 and C2″; 156.1, C2′ and C6′. IR (solid film on 3M card): 680.8, 790.8, 1131.2, 1392.5, 1435.9, 1465.8, 1540.1, 1558.4, 1569.0, 1576.7, 2848.7, 2887.3, 2896.9 and 2915.2 cm^{-1}. HRMS EI: *m*/*z* calc. for $C_{20}H_{19}N_3O_2S$ 365.1198, found 365.1201. MS EI: *m*/*z* (%) 365 (5.8), 322 (9.3), 320 (7.4), 292 (9.5), 266 (39.3), 265 (100), 221 (20.9), 128 (9.7), 116 (12.5), 100 (28.3), 99 (28.1), 78 (31.2), 73 (49.2) and 51 (9.6) [Calc. (Found) for $C_{20}H_{19}N_3O_2S$: C, 65.73 (65.79); H, 5.24 (5.26); N, 11.50 (11.61); S, 8.77 (8.05)%].

4′-(2-Formylethylsulfanyl)-2,2′:6′,2″-terpyridine S-5. A 25 mL two necked flask fitted with a reflux condenser was charged with compound **S-3** (0.1688 mmol, 61.7 mg) and 1 M HCl (aqueous 6 mL). The stirred reaction mixture was heated to 70–75 °C for 24 h, then cooled and extracted. The organic layer was dried to give **S-5** (52.6 mg, 97%). A single compound was observed by ^{1}H and ^{13}C NMR. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.97 (ddd, 2 H, H8, J = 7.10, 7.10, 0.82); 3.46 (dd, 2 H, H7, J = 7.10, 7.10); 7.32 (ddd, 2 H, H5 and H5″, J = 7.40, 4.76, 1.10); 7.86 (ddd, 2 H, H4 and H4″, J = 7.66, 7.66, 1.77); 8.32 (s, 2 H, H3′ and H5′); 8.56 (ddd, 2 H, H3 and H3″, J = 8.00, 1.02, 1.02); and 8.67 (ddd, 2 H, H6 and H6″, J = 3.96, 1.89, 0.91 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 23.0, C7; 42.5, C8; 117.6, C3 and C3″; 121.3, C3′ and C5′; 123.9, C5 and C5″; 136.8, C4 and C4″; 149.0, C6 and C6″; 150.0, C4′; 155.1, C2 and C6′; and 199.5, COH.

4′-(3-Hydroxypropylsulfanyl)-2,2′,2′:6′,2″-terpyridine S-6. A flame dried two necked flask under nitrogen was charged with compound **S-5** (1.0 mmol, 321 mg), DCE (10 mL) and finally with glacial acetic acid (5.0 mL) and stirred. After 5 min *n*-butylamine (3.0 mmol, 220 mg, 0.3 mL) was added and the reaction stirred for 10 min. Then, sodium cyanotrihydroborate (3.0 mmol, 190 mg) was added in 3 portions under a positive pressure of nitrogen. An additional 3 mmol of reducing agent were added and the reaction mixture stirred for 1 h. The TLC showed one spot and no starting material. The reaction mixture was extracted and dried. The crude extract was chromatographed on reversed phase silica gel using 50% MeCN–acetone to give pure alcohol **S-6** (70 mg, 21.6%), R_f 0.43 (acetone) ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.03 (m, 2 H, H8, J = 5.91, 7.11); 3.29 (t, 2 H, H7, J = 7.11); 3.82 (t, 2 H, H9, J = 5.91); 7.32 (ddd, 2 H, H5 and H5″, J = 7.68, 4.95, 1.41); 7.84 (ddd, 2 H, H4 and H4″, J = 7.76, 7.76, 1.77); 8.32 (s, 2 H, H3′ and H5′); 8.57 (m, 2 H, H3 and H3″, J = 7.86) and 8.66 (m, 2 H, H6 and H6″, J = 4.72 Hz). ^{13}C NMR (75.1 MHz, $CDCl_3$): δ 27.0, C7; 31.7, C8; 60.8, C9; 117.6, C3 and C3″; 121.4, C3′ and C5′; 123.9, C5 and C5″; 136.9, C4 and C4″; 148.9, C6 and C6″; 151.4, C4′; 154.8, C2 and C2″; 155.8, C2′ and C6′. HRMS EI: *m*/*z* calc. for $C_{18}H_{16}N_3OS$ [M − H]: 322.1014, found 322.0999: MS-EI: *m*/*z* (%) 322 (2), 292 (7), 279 (5), 265 (100), 233 (8), 221 (31), 205 (3), 155 (4), 143 (11), 116 (12), 89 (7), 78 (41) and 51 (13).

4′-(2-Chloroethylsulfanyl)-2.2′:6,′2″-terpyridine S-7. A flame dried two necked flask under N_2 was charged with compound **S-6** (0.73 mmol, 236 mg), *n*-butylamine (1.0 mmol, 74 mg), and dichloroethane (2.0 mL) and stirred for 17 h. Glacial acetic acid (6.0 mmol, 400 mg, 0.4 mL) was added dropwise, and the solution turned red. The reaction was stirred for 3 h, and then sodium triacetoxyhydroborate (1.5 mmol, 320 mg) added. The TLC showed one spot, and the reaction mixture was extracted and dried. The crude extract was chromatographed using 1% EtOH in $CHCl_3$ to give pure product **S-7** (154 mg, 64.3%). R_f 0.88 (1:20 EtOH–$CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.41 (dd, 2 H, H7, J = 9.06, 8.04); 3.69 (dd, 2 H, H8 J = 9.06, 8.04); 7.23 (ddd, 2 H, H5 and H5″ J = 7.71, 4.95, 1.11); 7.73 (ddd, 2 H, H4 and H4″, J = 7.73, 7.73, 1.77); 8.25 (s, 2 H, H3′ and H5′); 8.48 (m, 2 H, H3 and H3″, J = 7.95) and 8.58 (m, 2 H, H6 and H6″, J = 4.63 Hz). ^{13}C NMR (75.1 MHz, $CDCl_3$): δ 32.9, C8; 41.9, C7; 117.9, C3 and C3″; 121.3, C3′ and C5′; 124.0, C5 and C5″; 136.8, C4 and C4″; 149.0, 149.0, C4′; C6 and C6″; 155.3, C2 and C2″; and 155.4, C2′ and C6′. HRMS EI: *m*/*z* calc. for $C_{17}H_{14}ClN_3S$: 327.0597, found 327.0591. MS EI: *m*/*z* (%) 327 (8), 292 (18), 265 (47), 221 (24), 143 (14), 128 (8), 116 (9), 89 (6), 78 (33), 63 (4) and 51 (10).

Method 2

4′-(3-Formylpropyl)-2,2′:6′,2″-terpyridine C-2. A 100 mL three necked flask, equipped with a rubber septum, a Teflon coated stir bar and a gas inlet adapter, was flushed with N_2. A dry THF solution (10 mL) of 4′-methyl-2,2′:6′,2″-terpyridine **C-1** (0.494 g, 2 mmol) was added by syringe into the flask. The reaction mixture was cooled to −78 °C and lithium diisopropylamide (LDA) (1.6 mL, 2.4 mmol) added *via* syringe. The resulting dark brown mixture was stirred for 2 h at −78 °C. 2-(2-

Bromoethyl)-1,3-dioxolane (0.434 mL, 2.4 mmol) was added; the reaction was stirred for 1 h at −78 °C and allowed to warm to room temperature overnight. The mixture was poured over 10 mL of brine and the aqueous layer extracted with CH_2Cl_2. The extracts were dried to yield the crude acetal. The acetal was hydrolysed with 1 M HCl (10 mL) by heating to 50–60 °C for 2 h. The solution was then neutralized with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The extracts were dried to yield the crude aldehyde. Purification by flash chromatography (neutral alumina, CH_2Cl_2 elution) gave pure aldehyde **C-2** (0.339 g, 1.12 mmol, 56%). ^{1}H NMR ($CDCl_3$): δ 2.50 (t, 2 H, H9); 2.1 (m, 2 H, H8); 2.80 (m, 2 H, H7); 8.70 (m, 2 H, H6, H6″); 8.60 (d, 2 H, H3, H3″); 8.30 (s, 2 H, H3′, H5′); 7.85 (m, 2 H, H4, H4′); 7.35 (m, H5, H5″); and 9.50 (br s, 1 H, H10). ^{13}C NMR ($CDCl_3$): δ 22.8, C8; 34.9, C7; 43.2, C9; 121.7, C3 and C3″; 121.9, 3′ and C5′; 124.2, C5 and C5″; 136.9, C4 and C4″; 149.2, C6 and C6″; 152.4, C4′; 155.6, C2′ and C2″; 156.3, C2′ and C6′; and 201.8, C10. FAB MS: *m*/*z* 310, $(M + Li)^+$; exact mass found 310.1570, calculated for $C_{19}H_{19}LiN_3O$ 310.1532.

4′(4-Hydroxybutyl)-2,2″:6′,2″-terpyridine C-3. The aldehyde **C-2** (0.303 g, 1 mmol) was dissolved in absolute ethanol (5 mL), and $NaBH_4$ (0.05 g, 1 mmol) added at room temperature. After stirring for 30 min the mixture was poured into 10 mL of brine and extracted with CH_2Cl_2 (3 × 10 mL). The extracts were dried to yield the desired alcohol **C-3** (0.264 g, 0.86 mmol, 86%). ^{1}H NMR ($CDCl_3$): δ 1.70 (m, 2 H, H9); 1.90 (m, 2 H, H8); 2.30 (br s, 1 H, H11); 2.80 (t, 2 H, H7); 3.70 (t, 2 H, H10); 7.35 (m, H5, H5″); 7.85 (m, 2 H, H4, H4″); 8.30 (s, 2 H, H3′, H5′); 8.60 (d, 2 H, H3, H3″); and 8.70 (m, 2 H, H6, H6″). ^{13}C NMR ($CDCl_3$): δ 27.1, C8; 32.8, C9; 35.9, C7; 62.9, C10; 121.7, C3 and C3″; 121.9, C3′ and C5′; 124.2, C5 and C5″; 137.4, C4 and C4″; 149.5, C6 and C6″; 153.9, C4′; 155.8, C2′ and C2″; 156.9, C2′ and C6′. FAB MS: *m*/*z* 312, $(M + Li)^+$; exact mass found 312.1733, calculated for $C_{19}H_{19}LiN_3O$ 312.1688.

4′-(4-Bromobutyl)-2,2′:6′,2″-terpyridine C-4. The alcohol **C-3** (0.200 g, 0.65 mmol) was dissolved in 5 mL HBr (48%) and refluxed for 6 h. After cooling to room temperature the mixture was poured over 20 g of crushed ice, treated with a saturated aqueous solution of Na_2CO_3 and extracted with CH_2Cl_2. The extracts were dried to yield the bromo derivative **C-4** (0.186 g, 0.51 mmol, 78%). ^{1}H NMR ($CDCl_3$): δ 1.90 (m, 2 H, H9); 1.90 (m, 2 H, H8); 2.80 (t, 2 H, H7); 3.45 (t, 2 H, H10); 7.35 (m, H5, H5″); 7.85 (m, 2 H, H4, H4″); 8.30 (s, 2 H, H3′, H5′); 8.60 (d, 2 H, H3, H3″); and 8.70 (m, 2 H, H6, H6″). ^{13}C NMR ($CDCl_3$): δ 29.4, C8; 32.8, C9; 33.8, C10; 35.3, C7; 121.5, C3 and C3″; 121.8, 3′ and C5′; 124.2, C5 and C5″; 137.4, C4 and C4″; 149.6, C6 and C6″; 153.3, C4′; 155.9, C2′ and C2″; 156.8, C2′ and C6′. FAB MS: *m*/*z*: 374, $(M + Li)^+$; exact mass found 374.0881, calculated for $C_{19}H_{18}BrLiN_3$ 374.0844.

4′-(4-Phthalimidobutyl)-2,2′:6′,2″-terpyridine C-5. The bromo compound **C-4** (0.186 g, 0.51 mmol) in DMF (2 mL) was added to a suspension of potassium phthalimide (0.095 g, 0.51 mmol) in DMF (1 mL) and the mixture stirred for 2 h at 50–60 °C. After cooling, the reaction mixture was poured into water (10 mL) and the resulting mixture thoroughly extracted with $CHCl_3$ (3 × 25 mL). The organic layers were combined, washed with 20 mL of 0.2 M NaOH, water (20 mL) and dried to give a thick oil. Recrystallization from ethanol gave a white crystalline solid (0.208 g, 0.48 mmol, 95%), mp 128 °C. ^{1}H NMR ($CDCl_3$): δ 1.80 (m, 2 H, H9); 1.80 (m, 2 H, H8); 2.85 (t, 2 H, H7); 3.75 (t, 2 H, H10); 7.30 (m, H5, H5″); 7.85 (m, 2 H, H4, H4″); 8.30 (s, 2 H, H3′, H5′); 8.60 (d, 2 H, H3, H3″); and 8.70 (m, 2 H, H6, H6″). ^{13}C NMR ($CDCl_3$): δ 28.3, C8; 28.9, C9; 35.8, C7; 38.2, C10; 121.6, C3 and C3″; 121.8, C3′ and C5′; 124.2, C5 and C5″; 137.3, C4 and C4″; 149.5, C6 and C6″; 153.5, C4′; 155.9, C2′ and C2″; 156.8, C2′ and C6′. FAB MS: *m*/*z* 441, $(M + Li)^+$; exact mass found 441.1932, calculated for $C_{27}H_{22}LiN_4O_2$ 441.1903.

4′-(4-Aminobutyl)-2,2′:6′,2″-terpyridine C-6. The phthalimide derivative **C-5** (0.208 g, 0.48 mmol) was suspended in 7 mL EtOH and treated with hydrazine hydrate (88 mg, 0.48 mmol). The mixture was refluxed for 6 h. It was cooled to room temperature, poured into brine (10 mL) and adjusted to pH 12 with 50% w/w NaOH. The mixture was thoroughly extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were dried to give compound **C-6** (0.130 g, 0.43 mmol, 89%). ^{1}H NMR ($CDCl_3$): δ 1.30 (br s, 2 H, H11); 1.55 (m, 2 H, H9); 1.80 (m, 2 H, H8); 2.75 (t, 2 H, H10); 2.85 (t, 2 H, H7); 7.30 (m, H5, H5″); 7.85 (m, 2 H, H4, H4″); 8.30 (s, 2 H, H3′, H5′); 8.60 (d, 2 H, H3, H3″); and 8.70 (m, 2 H, H6, H6″). ^{13}C NMR ($CDCl_3$): δ 28.3, C8; 34.1, C9; 36.1, C7; 42.5, C10; 121.6, C3 and C3″; 121.8, C3′ and C5′; 124.2, C5 and C5″; 137.3, C4 and C4″; 149.5, C6 and C6″; 154.0, C4′; 155.9, C2′ and C2″; and 156.9, C2′ and C6′. FAB MS: *m*/*z* 311, $(M + Li)^+$; exact mass found 311.1848, calculated for $C_{19}H_{20}LiN_4$ 311.1848.

Method 3

4′-(3-Carboxypropoxy)-2,2′:6′,2″-terpyridine O-1. To a suspension of powdered KOH (3.16 g, 0.0412 mol) and 4-hydroxybutyric acid sodium salt (1.09 g, 8.64 mmol) in dry DMSO (70 mL) was added 4′-chloro-2,2′:6,2″-terpyridine **VIII** (2.31 g, 8.63 mmol). After stirring at RT for 1 h, the reaction mixture was allowed to stand for 40 h at 50 °C. The mixture was quenched with ice–water (30 mL), then acidified to pH 6 with a 10% aqueous solution of HCl. The white precipitate was filtered off and washed with cold water to give compound **O-1** (2.27 g, 78.4%). R_f 0.05 (2% MeOH–CH_2Cl_2). ^{1}H NMR (300 MHz, d^6-DMSO): δ 2.07 (tt, 2 H, H8); 2.47 (t, 2 H, H9); 4.30 (t, 2 H, H7); 7.50 (dd, 2 H, H5, H5″); 7.98 (s, 2 H, H3′, H5′); 8.00 (m, 2 H, H4, H4″); 8.61 (d, 2 H, H3 and H3″); and 8.74 (dd, 2 H, H6 and H6″). ^{13}C NMR (75 MHz, d^6-DMSO): δ 24.1, C8; 30.1, C9; 67.2, C7; 106.7, C3′ and C5′; 120.9, C5 and C5″; 124.5, C3 and C3″; 137.4, C4 and C4″; 149.2, C6 and C6″; 154.2, C2 and C2″; 156.7, C2′ and C6′; 166.6, C4′; and 174.1, C12. HRMS FAB: *m*/*z* $C_{19}H_{18}N_3O_3$, $(M + H)^+$: calculated 336.1348, found 336.1338.

4′-(3-Aminopropoxy)-2,2′:6′,2″-terpyridine O-2. A suspension of powdered KOH (0.634 g, 11.33 mmol) and 3-amino-1-propanol (0.772 g, 0.786 mL, 10.30 mmol) in dry DMSO (75 mL) was formed under nitrogen gas. 4′-Chloro-2,2′:6′,2″-terpyridine (2.5 g, 9.36 mmol) was added and the mixture stirred for 1 h at room temperature. The mixture was allowed to stand for 40 h at 55 °C. The reaction was quenched with cold water (35 mL) and then reduced to dryness under vacuum. The product was chromatographed using a solvent gradient of 2 to 10% methanol in chloroform. Following drying, a slightly brown solid **O-2** was obtained (1.661 g, 5.43 mmol, 58%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.97 (tt, 2 H, H8); 2.92 (t, 2 H, H9); 4.29 (t, 2 H, H7); 7.29 (dd, 2 H, H5, H5″); 7.81 (m, 2 H, H4, H4″); 7.98 (s, 2 H, H3′, H5′); 8.58 (d, 2 H, H3 and H3″); and 8.61 (d, 2 H, H6 and H6″). ^{13}C NMR (75 MHz, $CDCl_3$): δ 32.0, C11; 39.0, C15; 66.0, C9; 107.0, C3′ and C5′; 121.0, C5 and C5″; 123.0, C3 and C3″; 136.0, C4 and C4″; 148.0, C6 and C6″; 156.0, C2 and C2″; 157.0, C2′ and C6′; and 167.0, C4′. IR (Neat): 2741, 2803, 1515, 1497, 1404, 1380, 1298, 1144 and 741 cm^{-1}. HRMS FAB: calculated for $C_{18}H_{19}N_4O$ *m*/*z* 307.1559, found 307.1567 $(M + H)^+$.

4′-(3-Hydroxypropoxy)-2,2′:6′,2″-terpyridine O-3. To a 50 mL round bottom flask under a nitrogen atmosphere, 1,3-propanediol (56.0 mmol, 4.26 g) was added to 25 mL of dry DMSO. While stirring the solution, KOH (56.0 mmol, 3.14 g) was added, and the mixture heated to 60 °C for 10 min. Compound **VIII** (11.2 mmol, 3.00 g) was added and the temperature maintained at 60 °C for 2 d. The reaction mixture was then poured into 20 mL of ice–water, and the pH adjusted to 6. The white precipitate formed was collected by filtration and

recrystallized from methanol giving 85% yield. R_f 0.13 (2:98 methanol–chloroform). ^{1}H NMR (300 MHz, d^6-DMSO): δ 1.95 (m, 2 H, H8); 3.61 (q, 2 H, H9); 4.28 (t, 2 H, H7); 4.60 (t, 1 H, H10); 7.45 (dd, 2 H, H5, H5″); 7.95 (m, 4 H, H3′, H5′, H4, H4″); 8.61 (d, 2 H, H3 and H3″); and 8.73 (d, 2 H, H6 and H6″). ^{13}C NMR (75 MHz, d^6-DMSO): δ 31.8, C8; 57.1, C9; 65.2, C7; 106.7, C3′ and C5′; 120.8, C5 and C5″; 124.5, C3 and C3″; 137.3, C4 and C4″; 149.2, C6 and C6″; 154.8, C2 and C2″; 156.6, C2′ and C6′; and 166.7, C4′. HRMS FAB: $(M + H)^+$, calculated for $C_{18}H_{18}N_3O_2$ *m/z* 308.1321, found 308.1399.

4′-(4-Hydroxybutoxy)-2,2′:6′,2″-terpyridine O-4. The same general procedure shown above for compound **O-3** was followed giving a 79% yield. R_f 0.18 (2:98 methanol–chloroform). ^{1}H NMR (300 MHz, d^6-DMSO): δ 1.65 (m, 2 H, H9); 1.82 (m, 2 H, H8); 3.45 (m, 2 H, H10); 4.27 (t, 2 H, H7); 4.41 (t, 1 H, H11); 7.45 (dd, 2 H, H5, H5″); 7.82 (s, 2 H, H3′, H5′); 8.00 (m, 2 H, H4, H4″); 8.61 (d, 2 H, H3 and H3″); and 8.73 (d, 2 H, H6 and H6″). ^{13}C NMR (75 MHz, d^6-DMSO): δ 26.8, C9; 30.3, C8; 65.0, C10; 72.1, C7; 106.7, C3′ and C5′; 120.7, C5 and C5″; 124.5, C3 and C3″; 137.4, C4 and C4″; 148.3, C6 and C6″; 154.6, C2 and C2″; 156.6, C2′ and C6′; and 166.8, C4′. HRMS FAB: $(M + H)^+$, calculated for $C_{19}H_{20}N_3O_2$ *m/z* 322.1477, found 322.1485.

4′-(6-Hydroxyhexyloxy)-2,2′:6′,2″-terpyridine O-5. The same procedure was followed as shown above for compound **O-3** giving a 76% yield. R_f 0.20 (2:98 methanol–chloroform). ^{1}H NMR (300 MHz, d^6-DMSO): δ 1.45 (m, 6 H, H9, H10, H11); 1.82 (m, 2 H, H8); 3.41 (m, 2 H, H12); 4.23 (t, 2 H, H7); 4.32 (t, 1 H, H13); 7.45 (dd, 2 H, H5, H5″); 7.95 (m, 4 H, H3′, H4, H4″, H5′); 8.61 (d, 2 H, H3 and H3″); and 8.73 (d, 2 H, H6 and H6″). ^{13}C NMR (75 MHz, d^6-DMSO): δ 25.59, C9; 25.63, C10; 28.81, C11; 32.81, C8; 60.95, C12; 68.29, C7; 107.4, C3′ and C5′; 121.2, C5 and C5″; 124.9, C3 and C3″; 137.7, C4 and C4″; 149.6, C6 and C6″; 155.2, C2 and C2″; 157.0, C2′ and C6′; and 167.1, C4′ HRMS FAB: $(M + H)^+$, calculated for $C_{21}H_{24}N_3O_2$ *m/z* 350.1790, found 350.1868.

4′-(8-Hydroxyoctyloxy)-2,2′:6′,2″-terpyridine O-6. The procedure for compound **O-3** gave a 75% yield. R_f 0.24 (2:98 methanol–chloroform) ^{1}H NMR (75 MHz, d^6-DMSO): δ 1.40 (m, 10 H, H9, H10, H11, H12 and H13); 1.82 (m, 2 H, H8); 3.42 (m, 2 H, H14); 4.23 (t, 2 H, H7); 4.32 (t, 1 H, H15); 7.45 (dd, 2 H, H5, H5″); 7.95 (m, 4 H, H3′, H4, H4″, H5′); 8.61 (d, 2 H, H4); and 8.73 (d, 2 H, H6 and H6″). ^{13}C NMR (300 MHz, d^6-DMSO): δ 25.4, C9; 25.5, C10; 28.4, C11; 28.8, C12; 28.9, C13; 32.6, C8; 60.7, C14; 67.9, C7; 106.7, C3′ and C5′; 120.8, C5 and C5″; 124.4, C3 and C3″; 137.3, C4 and C4″; 149.2, C6 and C6″; 154.9, C2 and C2″; 156.6, C2′ and C6′; and 166.7, C4′ HRMS FAB: $(M + H)^+$, calculated for $C_{23}H_{28}N_3O_2$ *m/z* 378.2103, found 378.2181.

4-(Hydroxydecyloxy)-2,2′:6′,2″-terpyridine O-7. The procedure for compound **O-3** gave a 65% yield. R_f 0.28 (2:98 methanol–chloroform): ^{1}H NMR (75 MHz, d^6-DMSO): δ 1.40 (m, 14 H, H9, H10, H11, H12, H13, H14 and H15); 1.84 (m, 2 H, H8), 3.41 (m, 2 H, H16), 4.25 (t, 2 H, H7); 4.34 (t, 1 H, H17); 7.45 (dd, 2 H, H5, H5″); 7.95 (m, 4 H, H3′, H4, H4″, H5′); 8.61 (d, 2 H, H3 and H3″); 8.73 (d, 2 H, H6 and H6″). ^{13}C NMR (300 MHz, d^6-DMSO): δ 25.9, C9; 26.1, C10; 28.2, C11; 28.4, C12; 28.8, C13; 28.9, C14; 30.2, C15; 34.0, C8; 64.4, C16; 74.1, C7; 105.2, C3′ and C5′; 120.5, C5 and C5″; 124.1, C3 and C3″; 136.9, C4 and C4″; 149.7, C6 and C6″; 153.2, C2 and C2″; 158.9, C2′ and C6′; and 170.7, C4′ HRMS FAB: $(M + H)^+$ calculated for $C_{25}H_{32}N_3O_2$ *m/z* 406.2416, found 406.2425.

[AuCl(S-8)][O$_3$SCF$_3$]$_2$ (1). Compound **S-8** (0.040 g, 0.143 mmol) and $KAuCl_4$ (0.054 g, 0.143 mmol) were combined with 20 mL of water and the pH of the resultant suspension adjusted to 3 with 1 M HCl. The mixture was refluxed for 2 h during which time the **S-8** went into solution. The colour gradually changed from the yellow of tetrachloroaurate to the red-brown of the product. The reaction mixture was cooled and the volume reduced to *ca*. 7 mL by rotary evaporation. On addition of an excess of $LiPF_6$ the immediate formation of an orange precipitate was observed. The product was collected by filtration, washed with diethyl ether, and air dried; mass spectra were obtained on the PF_6 salt. If $NH_4CF_3SO_3$ was added to the reaction mixture in place of $LiPF_6$ the orange trifluoromethanesulfonate (triflate) salt of the product precipitated from solution. Slow ether diffusion into an acetonitrile solution of the triflate salt afforded crystals suitable for X-ray diffraction analysis. Yield: 0.0875 g (80%). [Calc. (Found) for $C_{16}H_{13}AuClF_{12}N_3P_2S$: C, 23.97 (24.05); H, 1.63 (1.63); Cl, 4.42 (4.43); N, 5.24 (5.20); S, 4.00 (4.64)%]. ESI MS: *m/z* 255.8 corresponding to the doubly charged species of *M* 511–512 and having the appropriate isotope pattern for the cation. ^{1}H NMR (CD_3CN): δ 2.89 (s, CH_3, 3 H), 8.08 (m, 2 H), 8.23 (s, 2 H), 8.59(m, 4 H) and 9.13 (m, 2 H).

[PdCl(S-8)]PF$_6$ (2). Compound **S-8** (0.070 g, 0.143 mmol) and $PdCl_2$ (0.044 g, 0.143 mmol) were combined with 30 mL of water and the pH of the resultant suspension was adjusted to 3 with 1 M HCl. The mixture was refluxed for 2 h during which time the **S-8** went into solution which gradually changed from the yellow of tetrachloropalladate to the red-brown of the product. The reaction mixture was cooled and the volume reduced to *ca*. 10 mL by rotary evaporation. On addition of an excess of $LiPF_6$ the immediate formation of a yellow precipitate was observed. The product was collected by filtration, washed with diethyl ether, and air dried. The solid was slightly soluble in acetonitrile and quite soluble in DMSO. Yield: 0.1194 g (85%) [Calc. (Found) for $PdC_{16}H_{13}ClF_6N_3PPd$: C, 33.94 (33.61); H, 2.31 (2.29); Cl, 6.26 (5.98);N, 7.42 (7.11); S, 5.66 (4.72)%]. ESI MS: *m/z* 418 to 426 with the appropriate isotope pattern for the cation. ^{1}H NMR (CD_3CN): δ 2.76 (s, CH_3, 3 H), 7.73 (m, 2 H), 7.95 (s, 2 H), 8.28 (m, 4 H) and 8.75 (m, 2 H).

X-Ray diffraction analysis

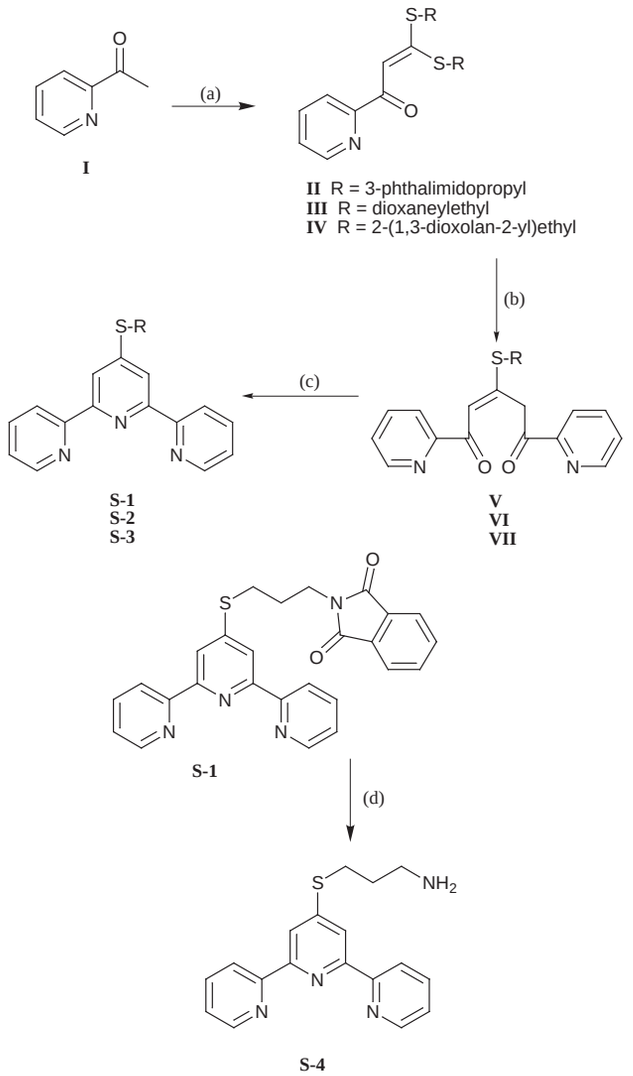
Yellow crystals of the trifluoromethanesulfonate salt of $[AuCl(\mathbf{S\text{-}8})]^{2+}$ and pale yellow crystals of **S-3** were obtained as described above. Intensity data were obtained on an Enraf-Nonius CAD 4 automatic diffractometer, using the ω–2θ scan mode with Cu-Kα radiation from a graphite monochromator (λ = 1.5412 Å) for **S-3**. For **1** data were collected on a Siemens SMART CCD system using Mo-Kα radiation (λ = 0.71073 Å) and the ω-scan method. Intensities were corrected for Lorentz-polarization effects. Equivalent reflections were merged, and semiempirical absorption corrections applied. Space group, lattice parameters and other relevant information are given in Table 1. The structures were solved by direct methods with full-matrix least-squares refinement, employing the NRCVAX package.[88–92] Scattering factors, including f' and f'', were taken from ref. 93. All non-hydrogen atoms were refined with anisotropic thermal parameters. The hydrogen atoms were placed at calculated positions and included in the refinement using a riding model, with fixed isotropic *U*. The final difference maps had no features of chemical significance.

CCDC reference number 186/1412.

Results and discussion

Synthesis of terpyridines *via* Methods 1 and 2

In Method 1 (Schemes 1 and 2), terpy thioether derivatives were the desired targets, and the reactions were analogous to the preparation of **S-8** reported by Potts *et al*.[87] In our case, we replaced MeI used by Potts with 2-bromoethyl-1,3-dioxolane, 2-(2-bromoethyl)-1,3-dioxane and *N*-3-iodopropylphthalimide

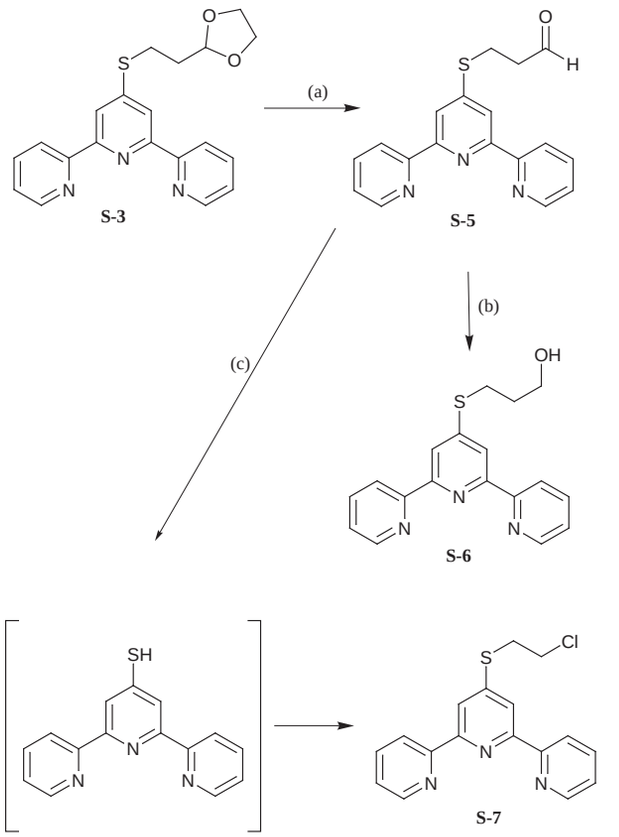


Scheme 1 Method 1: (a) KO(*t*-Bu), THF, CS_2, RX (X = halide); (b) KO(*t*-Bu), 2-acetylpyridine; (c) NH_4OAc, HOAc; (d) NH_2NH_2, EtOH.

to introduce the desired functionality directly into the terpyridine. Since thioether groups may not always be desirable, we also pursued Method 2 (Scheme 3), in which **S-8** was cross-coupled with methyl Grignard in a nickel-catalysed reaction analogous to the work of Potts *et al.*,[87] and similar to that of Pridgen and Killmer.[94] As shown in Scheme 3, this versatile starting material was then lithiated with lithium diisopropylamide and treated with 2-(2-bromoethyl)-1,3-dioxolane at −78 °C. After deprotection with 1 M HCl and flash chromatography, the desired aldehyde **C-2** was obtained (56%). Sodium tetrahydroborate reduction in ethanol gave the corresponding alcohol **C-3** (86%). To provide additional terpy reagents of general utility, the alcohol was treated with HBr, giving the corresponding 4-bromobutyl derivative **C-4** in 78% yield. In a two-step procedure, **C-6** was prepared *via* its phthalimidobutyl precursor. The purified yield of **C-5** was 95%, and this was converted into the amine in 89% yield on treatment with hydrazine hydrate. It was previously shown that the analogous amine 4-(4-aminobutyl)-4′-methyl-2,2′-bipyridine, is a useful reagent for incorporating bipyridine into nucleosides.[18,95] As reported by Schepartz and Cuenoud,[96] the cross-coupling of **S-8** with functionalized Grignard reagents is more direct than Method 2. However, not all Grignard reagents coupled efficiently enough in our hands for this reaction to be universally useful.

Synthesis of ether linked terpyridine ligands (Method 3)

Compound **VIII** was prepared through standard literature techniques.[97] An alcohol was allowed to react with a suspension of base (KOH or NaH) in solvent (DMSO or DMF), and then **VIII** was introduced (Scheme 4). Table S0 (SUP 57533) shows the effects of solvent, base and reaction stoichiometry. One equivalent of base was used for the diol reactions to avoid formation of di-terpyridine side products (terpy-O$(CH_2)_n$-O-terpy). In reactions not involving diols a large excess of base was used without generating much 4′-hydroxyterpyridine. Reaction of **VIII** with KOH gives nucleophilic substitution of chloride by hydroxide, if no competing alcohols are present.

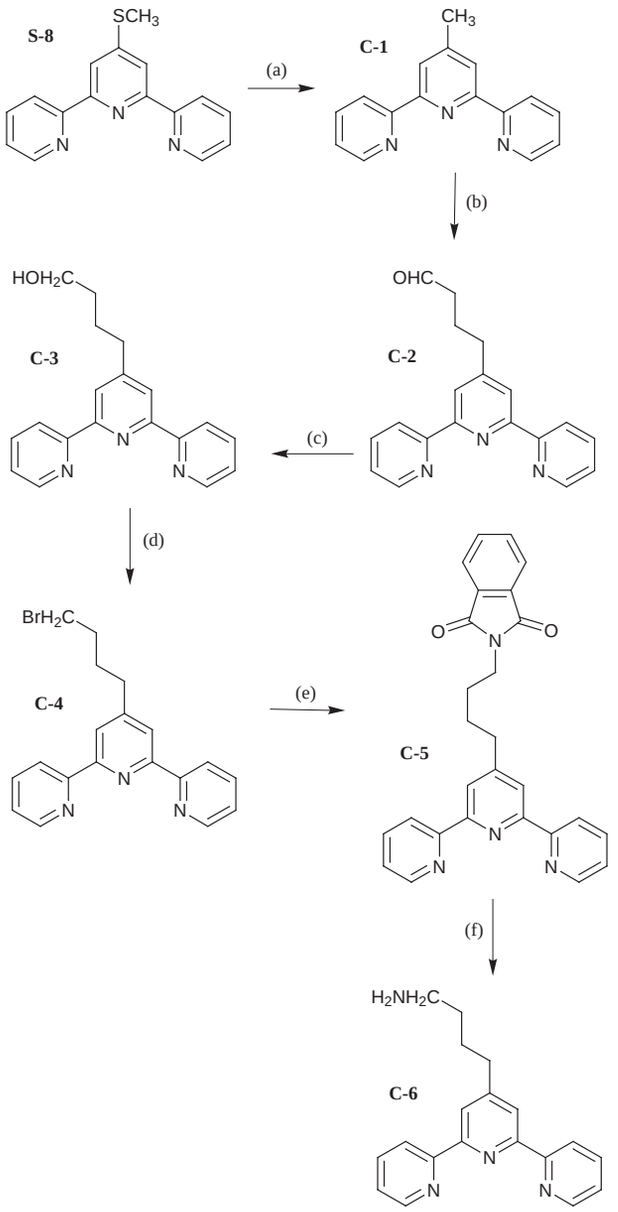


Scheme 2 Method 1: (a) 1 M HCl; (b) DCE, HOAc, *n*-Butylamine, $NaBH_3CN$; (c) *n*-butylamine, DCE, HOAc, sodium triacetoxyhydroborate.

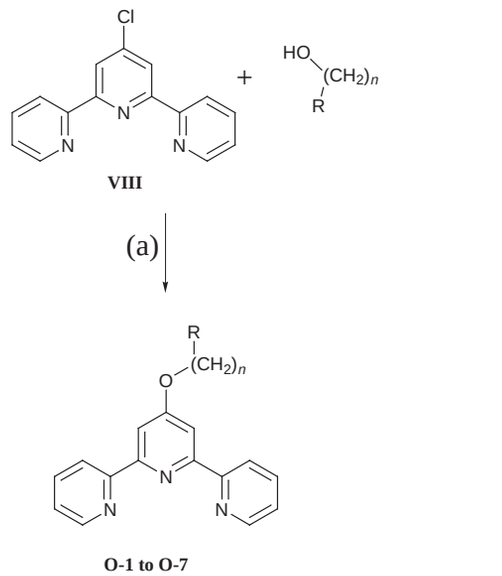
Amino- and carboxy-alcohols react selectively at the alcohol to form the ethers under our conditions. Mass spectral analysis of the partially purified product of reaction of 3-amino-1-propanol with compound **VIII** did show a parent ion assignable to the product of nucleophilic attack by both the amine and the hydroxide, (terpy-O$(CH_2)_3$NH-terpy). This product was present in less than 5% yield as determined by proton NMR. Fukui *et al.*[98] previously demonstrated that amines, in phenol at 100 °C, can act as good substrates for direct nucleophilic aromatic substitution on 4′-substituted pyridine rings. Constable *et al.*[78] achieved metal-mediated attack of 4′-halogeno-terpyridine by an amine. Under the conditions investigated here, the reactivity of electrophilic 4′-halogenopyridine rings correlates directly with the strength of the nucleophile.

Metal complexes of terpyridine

The reactions of Pd^{II} and Au^{III} with **S-8** yielded the expected four-co-ordinate complexes with a chloride in the fourth co-ordination site. These complexes were easily prepared in high yield by refluxing the metal salts in pH 3 aqueous media and isolated as the hexafluorophosphate salts. Complexes of terpy with both of these metals have been reported[73,76] and the present complexes are analogous. The ^1H NMR spectra were consistent with the proposed structures with the terpyridyl resonances most affected by co-ordination to the metal, with



Scheme 3 Method 2: (a) $[NiCl_2(PPh_3)_2]$ MeMgBr; (b) LDA, 2-(2-bromoethyl)-1,3-dioxolane, THF, HCl; (c) $NaBH_4$, EtOH; (d) HBr; (e) potassium phthalimide, DMF; (f) Hydrazine hydrate, EtOH.



Scheme 4 Method 3: Synthesis of ether derivatives. (a) Reaction conditions listed in the Experimental section and Table S0 (SUP 57533).

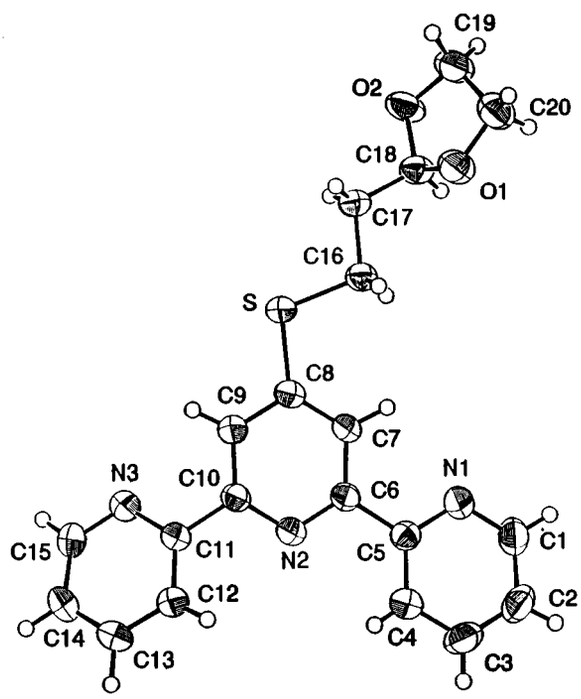


Fig. 1 An ORTEP representation (50% probability ellipsoids) of compound **S-3**.

the gold(III) center more deshielding than the Pd^{II} for all protons. Two sets of terpyridyl protons are shielded relative to those of the "free" ligand, the unique protons on the central pyridyl ring. The ESI mass spectrum of $[AuCl(\mathbf{S\text{-}8})][PF_6]_2$ **3** the $(PF_6)_2$ analog of **1**, showed a signal consistent with the doubly charged parent ion at *m*/*z* 255–256 having the appropriate isotope pattern. A significantly weaker signal was observed at *m*/*z* 511–512 for the deprotonated molecular ion. The parent ion of $[PdCl(\mathbf{S\text{-}8})]PF_6$ **2** with the appropriate isotope pattern was observed at *m*/*z* 421–422 in the ESI mass spectrum.

We were interested in the palladium(II) and gold(III) complexes for the potential radiotherapeutic applications of their radioisotopes ^{109}Pd and ^{199}Au. In addition, both of these d^8 metals will only co-ordinate to one terpyridine per metal. This latter property is important in that the attachment of only one targeting vector per radiometal complex is desired to insure better biological clearance properties *in vivo*.

Crystal structures

Single crystal structures were determined for the ligand **S-3** and the complex **1**. The ORTEP[99] representations of these two molecules are shown in Figs. 1 and 2, respectively. Table 1 lists the experimental details of the structural analyses while Table 2 lists selected bond distances and angles for the two structures.

The gold atom in the $[AuCl(\mathbf{S\text{-}8})]^{2+}$ cation is distorted slightly from square planar co-ordination geometry. The steric constraints of the tridentate terpyridine ligand prevent the formation of N–Au–N bond angles of 90°, leading to an average of 81.3(2)°. The Au atom sits 0.010(3) Å from the least squares plane defined by the chlorine and three nitrogen atoms [average deviation 0.014(8) Å]. The dihedral planes between the three pyridyl rings show the constraints of the square planar geometry about the gold(III) center. These angles between rings 1 and 2, 2 and 3, and 1 and 3 (with 2 being the central ring) are 1.7(3), 1.8(3) and 3.4(4)°, respectively. In the uncomplexed terpy ligand, **S-3**, the same dihedral angles are 14.5(2), 28.4(1) and 21.8(1)°, respectively, clearly showing the effects of metal complexation. Two oxygen atoms, one from each triflate anion,

Table 1 Crystal data, data collection and refinement parameters for compounds **S-3** and **1**

	S-3	**1**
Empirical formula	$C_{20}H_{19}N_3O_2S$	$C_{18}H_{13}AuClF_6N_3O_6S_3$
M	365.45	809.90
T/K	295	296
Crystal system	Triclinic	Orthorhombic
Space group	$P\bar{1}$	*Pbca*
a/Å	6.3451(8)	13.9095(7)
b/Å	10.966(2)	14.1597(7)
c/Å	13.098(4)	26.097(1)
α/°	87.96(2)	
β/°	88.86(2)	
γ/°	76.55(2)	
V/Å^3	885.73(3)	5140.0(4)
Z	2	8
D_c/Mg m^{-3}	1.370	2.093
μ/mm^{-1}	0.63	6.13
F(000)	384	3092
Crystal size/mm	0.25 × 0.15 × 0.20	0.15 × 0.25 × 0.40
Reflections collected	2901	27647
Independent reflections, *p*	2626	5622
Reflections with $F_o^2 > 2\sigma F_o^2$	2497	3963
Data, parameters (*n*)	292	343
Goodness of fit on F^2, *S*	2.63	1.53
*R*1	0.046	0.059
*wR*2	0.076	0.074
Largest difference map peak and hole/e Å^{-3}	0.340 and −0.440	1.900 and −1.260

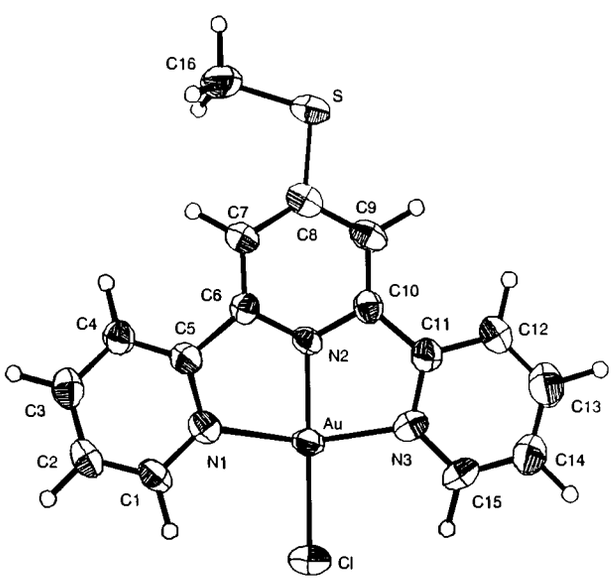


Fig. 2 An ORTEP representation (50% probability ellipsoids) of [AuCl(**S-8**)]$^{2+}$.

are loosely bonded [2.938(9) and 3.08(1) Å] in the 5th and 6th co-ordination sites about the Au atom. These distances are shorter than the nonbonding contacts (3.6 Å for Au···O),[100] but longer than Au–O single bonds (1.975–2.23; average 2.02 Å).[101,102] A similar situation was reported for [AuCl(terpy)]Cl_2·$3H_2O$[73] and [AuCl(dien)]Cl[ClO_4][100] in which an axial chloride and an axial oxygen atom were loosely bonded to the Au atom in the square planar cations. The Au–N bond lengths are comparable to those found in other gold(III) four-co-ordinate complexes (1.969–2.17; average 2.05 Å) as is the Au–Cl bond length (2.253–2.38; average 2.28 Å).[73,100,101] The bond distances and bond angles observed about the gold(III) atom in this structure are nearly identical to those found in [AuCl(terpy)]Cl[ClO_4].[73] The greatest difference is observed in the Au–N2 bond distances [1.945(7) here *vs.* 1.931(7) Å]; the average Au–N bond distances are identical [2.074(6) here *vs.* 2.073(5) Å].[73] The bond angles observed for these two structures are almost identical, with the greatest difference found in Cl–Au–N2 [178.9(2) here *vs.* 176.9(2)].[73] The crystal structure of compound **1** clearly shows that the co-ordinated terpy could act as a bifunctional chelate and that the metal should not hinder its ability to do so.

Table 2 Selected bond angles (°) and distances (Å)

	S-3	**1**
Au–Cl		2.259(3)
Au–N1		2.025(8)
Au–N2		1.945(7)
Au–N3		2.018(8)
Au–O1		3.08(1)
Au–O6		2.938(9)
S1–C8	1.748(2)	1.733(10)
S1–C16	1.809(2)	1.811(12)
N1–C1	1.330(3)	1.353(12)
N1–C5	1.338(3)	1.359(13)
N2–C6	1.346(2)	1.351(12)
N2–C10	1.336(3)	1.357(11)
N3–C11	1.347(3)	1.383(12)
N3–C15	1.331(3)	1.347(13)
C1–C2	1.379(4)	1.367(15)
C2–C3	1.369(4)	1.407(16)
C3–C4	1.360(3)	1.394(14)
C4–C5	1.386(3)	1.372(14)
C5–C6	1.486(3)	1.486(13)
C6–C7	1.400(3)	1.364(13)
C7–C8	1.385(3)	1.417(13)
C8–C9	1.400(3)	1.413(15)
C9–C10	1.385(3)	1.378(13)
C10–C11	1.488(3)	1.450(13)
C11–C12	1.387(3)	1.396(14)
C12–C13	1.380(3)	1.361(18)
C13–C14	1.383(3)	1.369(18)
C14–C15	1.366(4)	1.387(16)
Cl–Au–N1		98.8(2)
Cl–Au–N2		178.9(2)
Cl–Au–N3		98.7(2)
N1–Au–N2		81.4(3)
N1–Au–N3		162.5(3)
N2–Au–N3		81.2(3)

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References

1 B. N. Trawick, A. T. Daniher and J. K. Bashkin, *Chem. Rev.*, 1998, **98**, 939.
2 A. T. Daniher and J. K. Bashkin, *Chem. Commun.*, 1998, 1077.
3 J. K. Bashkin, *Chem. Rev.*, 1998, **98**, 937.
4 J. K. Bashkin, J. Xie, A. T. Daniher, U. Sampath and J. L.-F. Kao, *J. Org. Chem.*, 1996, **61**, 2314.
5 J. K. Bashkin, E. I. Frolova and U. Sampath, *J. Am. Chem. Soc.*, 1994, **116**, 5981.
6 J. K. Bashkin, in *Bioinorganic Chemistry of Copper*, eds. K. D. Karlin and Z. Tyeklar, Chapman and Hall, New York, 1993.
7 M. K. Stern, J. K. Bashkin and E. D. Sall, *J. Am. Chem. Soc.*, 1990, **112**, 5357.
8 E. Uhlmann and A. Peyman, *Chem. Rev.*, 1990, **90**, 544.
9 A. De Mesmaeker, R. Haener, P. Martin and H. E. Moser, *Acc. Chem. Res.*, 1995, **28**, 366.
10 P. D. Cook, *Annu. Rep. Med. Chem.*, 1998.
11 S. Agrawal and R. P. Iyer, *Pharmacol. Ther.*, 1997, **76**, 151.
12 K.-H. Altmann, N. M. Dean, D. Fabbro, S. M. Freier, T. Geiger, R. Haener, D. Huesken, P. Martin, B. P. Monia, M. Muller, F. Natt, P. Nicklin, J. Phillips, U. Pieles, H. Sasmor and H. E. Moser, *Chimia*, 1996, **50**, 168.
13 L. A. Jenkins, J. K. Bashkin and M. E. Autry, *J. Am. Chem. Soc.*, 1996, **118**, 6822.
14 J. K. Bashkin and L. A. Jenkins, *J. Chem. Soc.*, *Dalton Trans.*, 1993, 3631.
15 J. K. Bashkin, J. K. Gard and A. S. Modak, *J. Org. Chem*, 1990, **55**, 5125.
16 J. K. Bashkin, R. J. McBeath, A. S. Modak, K. R. Sample and W. B. Wise, *J. Org. Chem.*, 1991, **56**, 3168.
17 J. K. Bashkin, S. M. Sondhi, U. Sampath, D. A. d′Avignon and A. S. Modak, *New J. Chem.*, 1994, **18**, 305.
18 A. S. Modak, J. K. Gard, M. C. Merriman, K. A. Winkeler, J. K. Bashkin and M. K. Stern, *J. Am. Chem. Soc.*, 1991, **113**, 283.
19 J. K. Bashkin, J. Xie, A. T. Daniher, L. J. Jenkins and G. Y. Yeh, in *DNA and RNA Cleavers and Chemotherapy of Cancer of Viral Diseases*, ed. B. Meunier, Kluwer, Dordrecht, 1996.
20 A. T. Daniher, J. Xie, S. Mathur and J. K. Bashkin, *Bioorg. Med. Chem.*, 1997, **5**, 1037.
21 H. Inoue, T. Furukawa and E. Ohtsuka, *Chem. Commun.*, 1999, 45.
22 G. Pickaert and R. Ziessel, *Tetrahedron Lett.*, 1998, **39**, 3497.
23 S. M. Zakeeruddin, M. K. Nazeeruddin, P. Pechy, F. P. Rotzinger, R. Humphry-Baker, K. Kalyanasundaram, M. Graetzel, V. Shklover and T. Haibach, *Inorg. Chem.*, 1997, **36**, 5937.
24 G. D. Storrier, S. B. Colbran and D. C. Craig, *J. Chem. Soc.*, *Dalton Trans.*, 1997, 3011.
25 T. Marquardt and U. Lüning, *Chem. Commun.*, 1997, 1681.
26 L. M. Vrana and K. J. Brewer, *J. Photochem. Photobiol., A*, 1997, **109**, 201.
27 A. M. W. C. Thompson, *Coord. Chem. Rev.*, 1997, **160**, 1.
28 D. J. Cardenas, P. Gavina and J.-P. Sauvage, *J. Am. Chem. Soc.*, 1997, **119**, 2656.
29 M. Maskus and H. D. Abruna, *Langmuir*, 1996, **12**, 4455.
30 A. Harriman and R. Ziessel, *Chem. Commun.*, 1996, 1707.
31 G. D. Storrier and S. B. Colbran, *J. Chem. Soc.*, *Dalton Trans.*, 1996, 2185.
32 E. C. Constable, A. M. W. Cargill Thompson, J. Cherryman and T. Liddiment, *Inorg. Chim. Acta*, 1995, **235**, 165.
33 J. C. Jeffery, J. P. Maher, C. A. Otter, P. Thornton and M. D. Ward, *J. Chem. Soc.*, *Dalton Trans.*, 1995, 819.
34 L. M. Vogler, C. Franco, S. W. Jones and K. J. Brewer, *Inorg. Chim. Acta*, 1994, **221**, 55.
35 E. C. Constable, A. M. W. Cargill Thompson and D. A. Tocher, *NATO ASI Ser. C*, 1992, **371**, 219.
36 S. Serroni and G. Denti, *Inorg. Chem.*, 1992, **31**, 4251.
37 G. R. Newkome, E. He and L. A. Godinez, *Macromolecules*, 1998, **31**, 4382.
38 G. R. Newkome and E. He, *J. Mater. Chem.*, 1997, **7**, 1237.
39 G. R. Newkome, J. Gross and A. K. Patri, *J. Org. Chem.*, 1997, **62**, 3013.
40 C. N. Moorefield and G. R. Newkome, *Adv. Dendritic Macromol.*, 1994, **1**, 1.
41 C. D. Eisenbach, U. S. Schubert, G. R. Baker and G. R. Newkome, *J. Chem. Soc.*, *Chem. Commun.*, 1995, 69.
42 G. R. Newkome, F. Cardullo, E. C. Constable, C. N. Moorefield and A. M. W. C. Thompson, *J. Chem. Soc.*, *Chem. Commun.*, 1993, 925.
43 G. R. Newkome, K. J. Theriot, V. K. Gupta, F. R. Fronczek and G. R. Baker, *J. Org. Chem.*, 1989, **54**, 1766.
44 G. R. Newkome, D. C. Hager and G. E. Kiefer, *J. Org. Chem.*, 1986, **51**, 850.
45 A. M. Verbruggen, *J. Nucl. Med.*, 1990, **17**, 346.
46 L. Yuanfang and W. Chuanchu, *Pure Appl. Chem.*, 1991, **63**, 147.
47 S. Jurisson, D. Berning, W. Jia and D. Ma, *Chem. Rev.*, 1993, **93**, 1137.
48 S. Jurisson, A. R. Ketering and W. A. Volkert, *Transition Met. Chem.*, 1997, **22**, 315.
49 J. K. Barton, *J. Biomol. Struct. Dyn.*, 1983, **1**, 621.
50 J. K. Barton, *Comments Inorg. Chem.*, 1985, **3**, 321.
51 C. S. Chow, L. S. Behlen, O. C. Uhlenbeck and J. K. Barton, *Biochemistry*, 1992, **31**, 972.
52 M. R. Kirshenbaum, R. Tribolet and J. K. Barton, *Nucleic Acids Res.*, 1988, **16**, 7943.
53 H.-Y. Mei and J. K. Barton, *Proc. Natl. Acad. Sci. U. S. A.*, 1988, **85**, 1339.
54 A. M. Pyle, E. C. Long and J. K. Barton, *J. Am. Chem. Soc.*, 1989, **111**, 4520.
55 P. B. Dervan, *Nature* (*London*), 1992, **359**, 87.
56 G. B. Dreyer and P. B. Dervan, *Proc. Natl. Acad. Sci. U. S. A.*, 1985, **82**, 968.
57 D. S. Sigman, *Acc. Chem. Res.*, 1986, **19**, 180.
58 V. M. Shelton and J. R. Morrow, *Inorg. Chem.*, 1991, **30**, 4295.
59 J. S. Taylor, P. G. Schultz and P. B. Dervan, *Tetrahedron*, 1984, **40**, 457.
60 J. K. Barton and S. R. Paranawithana, *Biochemistry*, 1986, **25**, 2205.
61 W. A. Volkert, W. F. Goeckler, G. J. Ehrhardt and A. R. Ketring, *J. Nucl. Med.*, 1991, **32**, 174.
62 D. E. Troutner, *Nucl. Med. Biol.*, 1987, **14**, 171.
63 S. C. Srivastava and R. C. Mease, *Nucl. Med. Biol.*, 1991, **18**, 589.
64 S. J. DeNardo, D. L. Kukis, L. A. Miers, M. D. Winthrop, L. A. Kroger, Q. Salako, S. Shen, K. R. Lamborn, P. H. Gumerlock, C. F. Meares and G. L. DeNardo, *J. Nucl. Med.*, 1998, **39**, 842.
65 X. Feng, R. H. Pak, L. A. Kroger, J. K. Moran, D. G. DeNardo, C. F. Meares, G. L. DeNardo and S. J. DeNardo, *Hybridoma*, 1998, **17**, 125.
66 D. P. Greiner, R. Miyake, J. K. Moran, A. D. Jones, T. Negishi, A. Ishihama and C. F. Meares, *Bioconjug. Chem.*, 1997, **8**, 44.
67 C. F. Meares, D. A. Goodwin, C. S. Leung, A. Y. Girgis, D. J. Silvester, A. D. Nunn and P. J. Lavender, *Proc. Natl. Acad. Sci. U.S.A.*, 1976, **73**, 3803.
68 C. F. Meares, M. J. McCall, D. T. Reardan, D. A. Goodwin, C. I. Diamanti and M. McTigue, *Anal. Biochem.*, 1984, **142**, 68.
69 C. F. Meares, M. J. McCall, S. V. Deshpande, S. J. DeNardo and D. A. Goodwin, *Int. J. Cancer Suppl.*, 1988, **2**, 99.
70 C. F. Meares, M. K. Moi, H. Diril, D. L. Kukis, M. J. McCall, S. V. Deshapnde, S. J. DeNardo, D. Snook and A. A. Epenetos, *Br. J. Cancer Suppl.*, 1990, **10**, 21.
71 G. W. Philpott, S. W. Schwarz, C. J. Anderson, F. Dehdashti, J. M. Connett, K. R. Zinn, C. F. Meares, P. D. Cutler, M. J. Welch and B. A. Siegel, *J Nucl Med*, 1995, **36**, 1818.
72 P. A. Shubiger, R. Alberto and A. Smith, *Bioconjug. Chem.*, 1996, **7**, 165.
73 L. S. Hollis and S. J. Lippard, *J. Am. Chem. Soc.*, 1983, **105**, 4293.
74 K. W. Jennette, J. T. Gill and J. A. Sadownick, *J. Am. Chem. Soc.*, 1976, **98**, 6159.
75 S. J. Lippard, *Acc. Chem. Res.*, 1978, **11**, 211.

76 G. M. Intille, C. E. Pfluger and W. A. Baker, *J. Cryst. Mol. Struct.*, 1973, **3**, 47.
77 B. E. Halcrow and W. O. Kermack, *J. Chem. Soc.*, 1946, 155.
78 E. C. Constable, A. C. Thompson, D. A. Tocher and M. A. Daniels, *New J. Chem.*, 1992, **16**, 855.
79 K. T. Potts, D. A. Usifer, A. Guadalupe and H. D. Abruna, *J. Am. Chem. Soc.*, 1987, **109**, 3961.
80 K. T. Potts and D. Konwar, *J. Org. Chem.*, 1991, **56**, 4815.
81 D. Armspatch, E. C. Constable, F. Diderich, C. E. Housecroft and J.-F. Nierengarten, *Chem. Commun.*, 1996, 2009.
82 P. Lincoln and B. Norden, *Chem. Commun.*, 1996, 2145.
83 R. Ziessel, J. Suffert and M.-T. Youinou, *J. Org. Chem.*, 1996, **61**, 6535.
84 J.-P. Sauvage, J.-P. Collin, J.-C. Chambron, S. Guillerez, C. Coudret, V. Balzani, F. Barigelletti, L. De Cola and L. Flamigni, *Chem. Rev.*, 1994, **94**, 933.
85 E. C. Constable, C. E. Housecroft, M. Neuburger, A. G. Schneider and M. Zehneder, *J. Chem. Soc.*, *Dalton. Trans.*, 1997, 2427.
86 J. A. Varela, L. Castedo and C. Saa, *J. Org. Chem.*, 1997, **62**, 4189.
87 K. T. Potts, D. A. Usifer, A. Guadalupe and H. D. Abruna, *J. Am. Chem. Soc.*, 1987, **116**, 5981.
88 E. J. Gabe, Y. Le Page, J.-P. Charland, F. L. Lee and P. S. White, *J. Appl. Crystallogr.*, 1989, **22**, 384.
89 H. Flack, *Acta Crystallogr.*, *Sect. A*, 1983, **39**, 876.
90 A. C. Larsen, *Crystallographic Computing*, Munksgaard, Copenhagen, 1970.
91 Y. Le Page and E. J. Gabe, *J. Appl. Crystallogr.*, 1988, **12**, 464.
92 Y. Le Page, *J. Appl. Crystallogr.*, 1988, **21**, 983.
93 *International Tables for Crystallography*, Kynoch Press, Birmingham, 1974.
94 L. N. Pridgen and L. B. Killmer, *J. Org. Chem.*, 1981, **46**, 5402.
95 L. Ciana, I. Hamachi and T. Meyer, *J. Org. Chem.*, 1989, **54**, 1731.
96 A. Schepartz and B. Cuenoud, *Tetrahedron Lett.*, 1991, **1991**, 3325.
97 C. Ward and E. C. Constable, *J. Chem. Soc.*, *Dalton Trans.*, 1990, 1405.
98 K. Fukui, K. Iwane, T. Shimidizu and K. Tanaka, *Tetrahedron Lett.*, 1996, **37**, 4983.
99 C. K. Johnson, ORTEP II, Report ORNL-S13F, Oak Ridge National Laboratory, Oak Ridge, TN, 1976.
100 G. Nardin, L. Randaccio, G. Annibale, G. Natile and B. J. Pitteri, *J. Chem. Soc.*, *Dalton Trans.*, 1980, 220.
101 M. Melnick and R. V. Parish, *Coord. Chem. Rev.*, 1986, **70**, 157.
102 P. G. Jones, H. Rumpel, E. Schwartzmann, G. M. Sheldrick and H. Paulus, *Acta Crystallogr.*, *Sect. B*, 1979, **35**, 1435.

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