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Synthesis and characterization of dithioethers, and their Ru^{II} and Ru^{III} complexes

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ABSTRACT

The syntheses of nine, new dithioethers of the type $RS(CH_2)_xSR$, where $x = 2$ or 3 and R is an alkyl chain, as well as the known $x = 2$, R = phenyl or cyclohexyl compounds, are reported. The known dithioethers react with $RuCl_3 \cdot 3H_2O$ to form *trans*-$RuCl_2$(dithioether)$_2$ complexes **1** (R = Ph) and **2 (**R = C_6H_{11}), whereas from the other dithioethers $RuCl_2[RS(CH_2)_xSR]_2(\mu\text{-}Cl)_2$ complexes have been isolated, where $x = 3$, and R = Et (complex **3)**, ^{n}Pr (complex **4**), ^{n}Bu (complex **5**), and R = ^{n}pentyl (complex **6**). The complexes are well characterized, including X-ray structures for complexes **1** to **4**. The interest in these compounds stems from oxidation of the dithioethers to the corresponding disulfoxides and their Ru complexes.

Keywords: dithioethers; Ru(II and III) complexes; X-ray structures

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1. Introduction

Our long-time interest in Ru-dithioether complexes stems from use of platinum metal thioethers as hydrogenation catalysts [1], and Chatt *et al*. noted this in a 1971 paper on syntheses of a wide range of Ru^{II}- and Ru^{III}-chloro/bromo complexes containing organic mono-, di- , or tri-sulfides (thioethers); however, no crystal structures were given [2]. Our current interest in Ru-dithioether species was based on the finding that some could be converted to the corresponding sulfoxide complexes by O_2-oxidation [3] or an oxidant such as dimethyldioxirane or *m*-CPBA [4]. A specific aim of synthesizing $RuCl_2$(dithioether)$_2$ complexes was to determine the *cis*- or *trans*-geometry, and then oxidize the coordinated dithioethers to the Ru-disulfoxides to investigate if this geometry was retained. Stereochemistry within the coordinated sulfoxides and disulfoxides is also of significant interest, particularly within ruthenium complexes considering: (a) the anti-cancer and other biological activities such as hypoxic agents, as found for $RuCl_2(DMSO)_4$, and other Ru-sulfoxide/disulfoxide complexes [5,6]; and (b) the radiosensitizing activity of such species when containing also a nitroimidazole co-ligand [6].

This current paper reports on the synthesis of 9 new and 2 known dithioethers, and their reactions with the commercially available $RuCl_3 \cdot 3H_2O$. Table 1 shows the commonly used names and abbreviations of the dithioethers.

Findings on the corresponding sulfoxides and related ones, and their interaction with $RuCl_3 \cdot 3H_2O$, will be reported later, together with their *in vitro* studies such as cell accumulation and toxicity, and DNA binding [7].

Table 1

Names and, when appropriate, abbreviations used for the $RS(CH_2)_xSR$ dithioethers; the alternative name refers to replacement of a CH_2 by a S-atom in linear CH_2-chain groups.

x	R	Name	Abbreviation	Alternative name
2	*n*-butyl	1,2-bis(butylthio)ethane	BBTE	5,8-dithiadodecane
2	*n*-hexyl	1,2-bis(hexylthio)ethane	BHTE	7,10-dithiahexadecane
2	phenyl	1,2-bis(phenylthiol)ethane	BPhTE	
2	cyclohexyl	1,2-bis(cyclohexylthio)ethane	BCyTE	
2	*n*-pentyl	1,2-bis(pentylthio)ethane	BPeTE	6,9-dithiatetradecane
3	ethyl	1,3-bis(ethylthio)propane	BETP	3,7-dithianonane
3	*n*-propyl	1,3-bis(propylthio)propane	BPTP	4,8-dithiaunadecane
3	*t*-butyl	2,8-dimethyl-3,7-dithianonane	B^{t}PTP	
3	*n*-butyl	1,3-bis(butylthio)propane	BBTP	5,9-dithiatridecane
3	*n*-pentyl	1,3-bis(pentylthio)propane	BPeTP	6,10-dithiapentadecane
3	phenyl	1,3-bis(phenylthio)propane	BPhTP	

2. Experimental section

2.1. General

1,2-Dibromoethane was a Fisher Scientific product, and 1,3-dibromopropane was obtained from MCB, while ethane-, propane-, butane-, pentane-, hexane- and cyclohexyl-thiols, were Aldrich products; benzenethiol was an Eastman product. Other common commercial chemicals were purchased from Fisher Scientific, and used as provided. Syntheses of the dithioethers are described in Section 2.2.

$RuCl_3 \cdot 3H_2O$ was donated by Colonial Metals Inc. All common solvents used were at least of reagent grade; $CDCl_3$ was purchased from MSD Isotopes. Alumina (neutral, Brockman activity I) was purchased from Fisher chemicals. All samples (products and solvents) were stored in air, and all syntheses and measurements were carried out in air unless otherwise noted. Syntheses of the Ru^{II} and Ru_2^{III} complexes are described in Sections 2.3 and 2.4, respectively. Elemental analyses (EA) were performed in the UBC chemistry department on a Carlo Erba 1106 instrument, with data having an accuracy of ±0.3%.

NMR spectra were obtained in $CDCl_3$ solutions of the compounds using a Bruker AC-200E (200 MHz) instrument. Proton shifts are given with reference to the residual $CHCl_3$ solvent peak (δ 7.24) as the internal standard, relative to TMS. The ^{1}H-NMR shifts are reported as indicated by s = singlet; t = triplet; q = quartet; quin = quintet; sext = sextet; m = multiplet, br = broad. UV-visible data were measured on a Hewlett-Packard 8452A diode array spectrophotometer, λ_{max} being given in nm, followed by an extinction coefficient given as log ε. Mass spectra were measured using +LSIMS on a KRATOS Concept IIHQ.

Determination of the μ_{eff} and number of unpaired electrons for selected paramagnetic Ru^{III} complexes was performed at r.t. using a Johnson-Matthey Mk1 Magnetic Susceptibility Balance. Conductivity measurements were attempted at room temperature (r.t. ~20 °C) at ~10^{-3} M concentrations using a Thomas Serfass conductivity bridge, and a cell from Yellow Springs Instrument Company, the cell constant being determined as 1.016.

2.2. Synthesis of Dithioethers

2.2.1. 3,7-Dithianonane (BETP)

Ethanethiol (30 mL, 400 mmol) was added dropwise to a saturated solution (50 mL) of NaOH in MeOH cooled in a dry-ice/acetone bath; the mixture was then stirred at 70 ºC for 1 h, and then cooled again prior to dropwise addition of 1,3-dibromopropane (20.6 mL, 200 mmol) with stirring. After being warmed at 70 ºC for 1 h, the solution was poured into H_2O (100 mL), and the oily, immiscible dithioether layer was collected. The aqueous layer was extracted three times with Et_2O (40 mL) portions, the organic residues being combined; the Et_2O was removed by rotary evaporation, and the oily product was dried over $MgSO_4$. Yield 21 g (64 %). Anal. Calc.(found) for $C_7H_{16}S_2$: C, 51.17 (51.0); H, 9.81 (9.8). ^{1}H-NMR: δ2.60 (m, 8H, CH_2SCH_2), 1.85 (quin, 2H, $CH_2CH_2CH_2$), 1.25 (t, 6H, CH_3). Mass spectrum: 164 $[M]^+$, 135 $[M\text{-}C_2H_5]^+$.

2.2.2. 4,8-Dithiaunadecane (BPTP)

As above, but using 1-propanethiol (30 mL, 330 mmol) and 1,3-dibromopropane (16.8 mL, 165 mmol). Yield 28 g (88 %). Anal. Calc. (found) for $C_9H_{20}S_2$: C, 56.19 (57.7); H, 10.48 (10.8). ^{1}H-NMR: δ 2.60 (t, 4H, CH_2CH$_2$CH_2), 2.50 (t, 4H, CH_2CH$_2$CH$_3$), 1.85 (quin, 2H, $CH_2CH_2CH_2$), 1.60 (sext, 4H, $CH_2CH_2CH_3$), 1.02 (t, 6H, CH_3). Mass spectrum:192 $[M]^+$, 149 $[M\text{-}C_3H_7]^+$.

2.2.3. 2,8-Dimethyl-3,7-dithianonane (B^{i}PTP)

As above, but using 2-propanethiol (40 mL, 430 mmol) and 1,3-dibromopropane (21.9 mL, 210 mmol). Yield 32 g (80 %). Anal. Calc. (found) for $C_9H_{20}S_2$: C, 56.19 (55.32); H, 10.48 (10.39). ^{1}H-NMR: δ 2.90 (m, 2H, $(CH_3)_2CHS$), 2.60 (t, 4H, $CH_2CH_2CH_2$), 1.85 (quin), 2H, $CH_2CH_2CH_2$), 1.30 (d, 12H, $SCH(CH_3)_2$). Mass spectrum: 193 $[M]^+$.

2.2.4. 5,9-Dithiatridecane (BBTP)

As above, but using butanethiol (40 mL, 370 mmol) and 1,3-dibromopropane (18.9 mL, 187 mmol). Yield 36 g (87 %). Anal. Calc. (found) for $C_{11}H_{24}S_2$: C, 59.94 (59.6); H, 10.97 (11.1). ^{1}H-NMR: δ 2.60 (m, 8H, CH_2SCH_2), 1.85 (quin, 2H, $CH_2CH_2CH_2$), 1.56 (quin, 4H, $CH_2CH_2CH_3$), 1.42 (st, 4H, CH_2CH_3), 0.92 (t, 6H, CH_3). Mass spectrum: 220 $[M]^+$, 163 $[M\text{-}C_4H_9]^+$.

2.2.5. 6,10-Dithiapentadecane (BPeTP)

As above, but using pentanethiol (23.8 mL, 192 mmol) and 1,3-dibromopropane (9.7 mL, 96 mmol). Yield 21 g (88 %). Anal. Calc. (found) for $C_{13}H_{28}S_2$: C, 62.84 (60.6); H, 11.36 (11.1). ^{1}H-NMR: δ 2.56 (m, 8H, CH_2SCH_2), 1.85 (quin, 2H, $CH_2CH_2CH_2$), 1.56 (quin, 4H, $CH_2CH_2CH_2CH_3$), 1.35 (m, 8H, $CH_2CH_2CH_3$), 0.92 (t, 6H, CH_3). Mass spectrum: 248 $[M]^+$, 177 $[M\text{-}C_5H_{11}]^+$.

2.2.6. 1,3-Bis(phenylthio)propane (BPhTP)

As above, but using benzenethiol (50 mL, 487 mmol) and 1,3-dibromopropane (24.7 mL, 244 mmol). Yield 47 g (74 %). Anal. Calc. (found) for $C_{15}H_{16}S_2$: C, 69.18 (68.3); H, 6.19 (6.3). ^{1}H-NMR: δ 7.55 (m, 10H, C_6H_5), 2.93 (m, 4H, $CH_2CH_2CH_2$), 2.10 (m, 2H, $CH_2CH_2CH_2$). Mass spectrum: 260 $[M]^+$. The ^{1}H NMR data compare well with literature data [9].

2.2.7. 5,8-Dithiadodecane (BBTE)

As above, but using butanethiol (13 mL, 120 mmol) and 1,2-dibromoethane (5.3 mL, 61 mmol). Yield 14.5 g (58 %). Anal. Calc. (found) for $C_{10}H_{22}S_2$: C, 58.19 (58.4); H, 10.74 (10.8). ^{1}H-NMR: δ 2.73 (t, 4H, SCH_2CH_2S), 2.55 (t, 4H, CH_2S), 1.45 (m, 8H, $CH_2CH_2CH_3$), 0.90 (t, 6H, CH_3). Mass spectrum: 206 $[M]^+$, 149 $[M\text{-}C_4H_9]^+$.

2.2.8. 6,9-Dithiatetradecane (BPeTE)

As above, but using pentanethiol (9.8 mL, 80 mmol) and 1,2-dibromoethane (3.4 mL, 40 mmol). Yield 6.1 g (65 %). Anal. Calc. (found) for $C_{12}H_{26}S_2$: C, 61.48 (61.1); H, 11.18 (11.0). ^{1}H-NMR: δ 2.75 (t, 4H, SCH_2CH_2S), 2.55 (t, 4H, CH_2S), 1.60 (quin, 4H, CH_2CH$_2$CH$_2$CH$_3$), 1.35 (m, 8H, CH_2CH_2CH$_3$), 0.92 (t, 6H, CH_3). Mass spectrum: 234 $[M]^+$.

2.2.9. 7,10-Dithiahexadecane (BHTE)

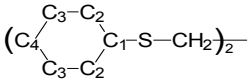
As above, but using hexanethiol (40 mL, 280 mmol) and 1,2-dibromoethane (12.2 mL, 142 mmol). Yield 25 g (67 %). Anal. Calc. (found) for $C_{14}H_{30}S_2$: C, 64.06 (63.9); H, 11.52 (11.4). ^{1}H-NMR: δ2.75 (t, 4H, SCH_2CH_2S), 2.55 (t, 4H, CH_2S), 1.55 (quin, 4H, CH_2CH$_2$CH$_2$CH$_2$CH$_3$), 1.30 (m, 12H, CH_2CH_2CH_2CH$_3$), 0.95 (t, 6H, CH_3). Mass spectrum: 262 $[M]^+$.

2.2.10. 1,2-Bis(phenylthio)ethane (BPhTE)

As above, but using benzenethiol (50 mL, 487 mmol) and 1,2-dibromoethane (21 mL, 240 mmol). However, the aqueous layer was this time extracted three times with $CHCl_3$ (40 mL) portions and, after the organic residues were combined, the $CHCl_3$ was removed by evaporation. The white solid obtained was then recrystallized using CH_2Cl_2 (7 mL) and Et_2O (100 mL). Yield 39 g (65 %). Anal. Calc. (found) for $C_{14}H_{14}S_2$: C, 68.25 (68.2); H, 5.73 (5.7). ^{1}H-NMR: δ 7.15 (m, 10H, C_6H_5), 3.10 (t, 4H, CH_2CH_2). The ^{1}H NMR data agree well with literature values [8,9].

2.2.11. 1,2-Bis(cyclohexylthio)ethane (BCyTE)

As above, but using cyclohexylthiol (50 mL, 400 mmol) and 1,2-dibromoethane (17.6 mL, 204 mmol). Yield 23.7 g (45 %). Anal. Calc. (found) for $C_{14}H_{26}S_2$: C, 65.06 (64.9); H, 10.14 (10.0).^{1}H-NMR: δ 2.70 (t, 4H, CH_2CH_2), 1.95, 1.75 (m 4H each, H_2), 1.58 (m, 2H, H_1), 1.29 (m, 12H, $H_{3,4}$) [$H_{1\text{-}4}$ define the bonded C-atom number as shown]. Mass spectrum: 258 $[M]^+$.



2.3. Synthesis of Mononuclear Ru(II) Dithioether Complexes

*2.3.1. Trans-$RuCl_2(BCyTE)_2 \cdot 2H_2O$ (**1**)*

Conc. HCl (100 μL) was added to a solution of $RuCl_3 \cdot 3H_2O$ (100 mg, 0.4 mmol) in EtOH (30 mL), and the mixture was refluxed for 5 h. 1,2-Bis(cyclohexylthio)ethane (BCyTE, 198 mg, 0.8 mmol) was added and the mixture was refluxed for a further 6 h. The resulting red precipitate was collected by filtration and dried *in vacuo*. Elemental analysis was performed on the isolated precipitate. Yield 223 mg (81 %). Anal. Calc. (found) for $C_{28}H_{52}Cl_2S_4Ru \cdot 2H_2O$: C, 46.39 (46.82); H, 7.78 (7.43). X-ray quality crystals were grown by recrystallization of the complex from DMF/CH_2Cl_2 (500 μL/2 mL) and were found to contain 2 CH_2Cl_2 solvates per molecule. The ^{1}H-NMR spectrum is a complex pattern of peaks at δ 1.20-3.35; attempts to assign the spectrum using ^{13}C, 2D-COSY and ^{1}H decoupling experiments were unsuccessful. UV-Vis (CH_2Cl_2) 438 (3.55), 400 (3.53), 280 (3.74), 236 (4.31).

*2.3.2. Trans-$RuCl_2(BPhTE)_2$ (**2**)*

The synthesis of the red complex was as described above, but using 1,2-bis(phenylthio)ethane (BPhTE, 188 mg, 0.8 mmol). The product was then dissolved in minimum CH_2Cl_2 and purified by column chromatography using neutral alumina with CH_2Cl_2 as eluant, this being removed by rotary evaporation. Yield 184 mg (73 %). Anal. Calc. (found) for $C_{28}H_{28}Cl_2RuS_4$: C, 50.59 (50.82); H, 4.24 (4.11). X-ray quality crystals were formed by evaporation of a DMF solution of the complex. ^{1}H-NMR: δ 7.65 (br s, 8H, *o*-C_6H_5), 7.28 (br s, 4H, *p*-C_6H_5), 7.12 (br s, 8H, *m*-C_6H_5), 3.07 (br s, 8H, CH_2CH_2). UV-Vis (CH_2Cl_2) 410 (3.50), 298 (4.55), 268 (4.54).

2.4. Synthesis of Dinuclear Ru_2^{III} Dithioether Complexes

*2.4.1. $[RuCl_2(BETP)]_2(\mu\text{-}Cl)_2$ (**3**)*

Conc. HCl (500 μL) was added to a solution of $RuCl_3 \cdot 3H_2O$ (500 mg, 2 mmol) in EtOH (30 mL), and the mixture was refluxed for 5 h. BETP 600 mg, 4 mmol) was then added and the mixture was refluxed for a further 6 h. The resulting dark-brown solution was then reduced in volume to an oil, to which added acetone (25 mL) gave a purple-brown precipitate. X-ray quality crystals were formed by slow evaporation of a solution of the precipitate in CH_2Cl_2. Yield 178 mg (24 %).

Anal. Calc. (found) for $C_7H_{16}Cl_3RuS_2$: C, 22.62 (22.4); H, 4.34 (4.3). UV-Vis (CH_2Cl_2) 454 (3.42), 376 (3.49), 268 (4.53). μ_{eff} = 3.8 ± 0.1 B. M.

*2.4.2. [RuCl$_2$(BPTP)]$_2$(μ-Cl)$_2$ (**4**)*

The procedure used was as described above in Section 2.4.1. but using $RuCl_3 \cdot 3H_2O$ (100 mg, 0.4 mmol) and BPTP (147 mg, 0.8 mmol); only 15 mL of acetone were added. X-ray crystals were again obtained from a CH_2Cl_2 solution of the precipitate. Yield 83 mg (52 %). Anal. Calc. (found) for $C_9H_{20}Cl_3RuS_2$: C, 27.04 (27.5); H, 5.04 (5.1). UV-Vis (CH_2Cl_2) 448 (2.62), 374 (2.61), 252 (3.44). μ_{eff} = 3.0 ± 0.1 B. M.

*2.4.3.[RuCl$_2$(BBTP)]$_2$(μ-Cl)$_2$ (**5**)*

Again the same procedure was used, but with $RuCl_3 \cdot 3H_2O$ (100 mg, 0.4 mmol), 5,9-BBTP (160 mg, 0.8 mmol), and 15 mL of acetone. Yield 43 mg (25 %). Anal. Calc. (found) for $C_{11}H_{24}Cl_3RuS_2$: C, 30.88 (30.7); H, 5.65 (5.5). UV-Vis (CH_2Cl_2) 454 (3.51), 376 (3.57), 268 (4.68). μ_{eff} = 3.2 ± 0.1 B. M.

*2.4.4. [RuCl$_2$(BPeTP)]$_2$(μ-Cl)$_2$ (**6**)*

The above method was used with $RuCl_3 \cdot 3H_2O$ (100 mg, 0.4 mmol), BPeTP (190 mg, 0.8 mmol) and a 15 mL addition of acetone. Yield 100 mg (55 %). Anal. Calc. (found) for $C_{13}H_{28}Cl_3RuS_2$: C, 34.25 (34.3); H, 6.19 (6.3). UV-Vis (CH_2Cl_2) 434 (3.41), 396 (3.45), 266 (4.86), 216 (4.83). μ_{eff} = 3.4 ± 0.1 B. M.

2.5. X-ray crystallography

The data for the four structures were collected on a Rigaku AFC7/ADSC CCD diffractometer with graphite-monochromated Mo-Kα radiation. All crystals were mounted on glass fibers with oil and data were collected at -93 °C. Data for complexes **1**, **2**, and **4** were each collected to a maximum 2θ of 60.1°, while data for complex **3** were collected to 63.6°. The structures were each solved using Intrinsic Phasing [10], and refined using Shelxl-2018 [11]. Complexes **1**, **3,** and **4** each crystallize with one half-molecule in the asymmetric unit, related to the other by inversion symmetry; complex **2** crystallizes with one complete molecule in the asymmetric unit. Complexes **1** and **4** each crystallize with one molecule of solvent CH_2Cl_2 in the asymmetric unit. All non-

hydrogen atoms were refined anisotropically; H-atom positions were calculated geometrically and refined using a riding model. The ORTEP plots for complexes **1-4** are shown in Figs. 1, 2, 4 and 5, respectively, and selected bond lengths and angles are given in Tables 2 and 3. Full experimental parameters and details of the structures are given in CIF format in the Supplementary Information.

3. Results and discussion

3.1. Dithioethers

The $RS(CH_2)_nSR$ dithioethers, where n =2 or 3, and R = alkyl, cyclohexyl or phenyl, were prepared by the reported methodology [2,8,9] of reacting an appropriate thiol with 1,2-dibromoethane or 1,3-dibromopropane in MeOH containing NaOH, the basic solution neutralising the HBr co-product. Different solvents and bases, including use of elemental sodium, have been used by others [8]. All the thioethers are new, except 1,2 bis(phenylthiol)ethane) (BPhTE) and 1,3-bis(phenylthiol)propane) (BPhTP) and, except for the latter, are all hygroscopic oils, whose elemental analyses were not always satisfactory. The oxidations of all the above dithioethers to the corresponding disulfoxide will be reported later, together with their reactions with various Ru precursors [7].

3.2. Dithioether complexes of Ru

Syntheses of $RuX_3(thioether)_3$ complexes (thioether = DMS or TMS; X = Cl or Br) by reactions of $RuCl_3{\cdot}3H_2O$ with DMSO or TMSO in the presence of HCl were reported in 1990 by our group [12], in which thioether formation was attributed to redox processes involving Ru^{III} and the sulfoxide, as shown in equations 1 and 2. A related procedure, but using higher temperatures (130-140 *vs.* 70-80 °C), produces the ionic *trans*-complexes, $[(DMSO)_2H]^+[RuCl_4(DM\underline{S}O)_2]^-$ and $[(TMSO)H]^+[RuCl_4(TM\underline{S}O)_2]^-$, where TMSO = tetramethylenesulfoxide [12,13].

$$2Ru^{III} + DMSO + H_2O \rightarrow 2Ru^{II} + DMS(O)_2 + 2H^+ \quad (1)$$

$$2Ru^{II} + R_2SO + 2H^+ \rightleftharpoons 2Ru^{III} + R_2S + H_2O \quad (2)$$

The Ru^{III} reduction, and oxidation of DMSO to the sulfone (eqn.1), were established in 1991 by the reaction of *mer*-$RuCl_3(DMSO)_3$ (in DMSO under Ar) to *trans*-$RuCl_2(DMSO)_4$ [13a]; evidence for equilibrium reaction (eqn.2) has also been presented for a system with R = Bu [14].

Complications are possible if the sulfoxides are not purified: e.g. DMS impurity in DMSO can reduce Ru^{III} to Ru^{II} [12b], and also of significance is that commercial $RuCl_3 \cdot 3H_2O$ is a mixture of Ru^{III} and Ru^{IV} species, the latter likely being a hydroxo species [15**]**. It is not surprising that the redox aspects of syntheses involving the trichloride and thiol or dithiols (or the corresponding sulfoxides) are not well understood.

Reported in 1971 is that $RuCl_3 \cdot 3H_2O$ reacts with mono-(S), di-(SS), or tri-organic sulfides (SSS) to give, respectively, the complexes *mer*-$[RuCl_3S_3]$, $[\{RuCl_3(SS)_{1.5}\}_n]$, *trans*-$[RuCl_2(SS)_2]$, or $[RuCl_3(SSS)]$ [2]. The $[\{RuCl_3(RSCH_2CH_2SR)_{1.5}\}_n]$ complexes (R = Me, Et, Pr or Ph) were too insoluble for molecular weight determination, but were thought to be at least dinuclear with one chelated and one bridging disulphide ligand; unfortunately there were no crystal structures reported in this publication [2]. The isolation of the by-product *trans*-$RuCl_2(BPhTE)_2$ in this 1971 paper was rationalized by suggesting that this diphenyldithioether was a stronger reducing agent than the R = Me, Et or Pr analogues [2]; however, our studies show that reactions of the dicyclohexyl- or diphenyl-dithioether with $RuCl_3 \cdot 3H_2O$ result in isolation of both *trans*-$RuCl_2(BCyTE)_2$ (**1**) and *trans*-$RuCl_2(BPhTE)_2$ (**2**), implying that such a conclusion is not valid in a general sense. Nevertheless, the isolation of the dinuclear Ru^{III} complexes **3** to **6**, all with dialkyl groups, tends to support the suggestion; presumably the bulky cyclohexyl group could be a factor. Related to this apparently complicated redox chemistry is that the dialkyl-dithioethers listed in Section 2.2. are converted to the corresponding sulfoxides by acid-catalyzed oxidation using DMSO [7], whereas the diarylsulfoxides were synthesized by H_2O_2 oxidation of the corresponding diarylsulfides by a reported method [16]. Redox studies on these Ru systems are needed to help clarify the synthetic data. Our studies on the Ru complexes of diaryl- and dialkyl-sulfoxides [7] will be reported elsewhere.

Worth mentioning is that there are complexes of the type *cis*-$MX_2(BBTE)$, where M = Pd and Pt, X = halide, and BBTE = 1,2-bis(benzylthio)ethane) [17]; $[RhCl_3(PhSCH_2SPh)_3]$, $[IrCl_3(PhSCH_2SPh)_3]$ and $RuCl_3(PhSCH_2SPh)_2 \cdot EtOH$ have also been reported [18]. None of these complexes was characterized crystallographically [17,18], but there is a structure of $Rh_2Cl_2(CO)_2$[bis(ethylthio)methane]$_2$ [19].

In summary, our studies reveal that reactions of BPhTE and BCyTE with $RuCl_3 \cdot 3H_2O$ give mononuclear *trans*-$RuCl_2(SS)_2$ complexes (**1** and **2**, Section 2.3), whereas the longer chain

dithioethers BETP, BPTP, BBTP, and BPeTP (Table 1) give the dinuclear Ru_2^{III} complexes $[RuCl_2(SS)]_2(\mu\text{-}Cl)_2$, (**3**-**6**, Section 2.4). Again, the details of the redox chemistry remain unclear.

*3.2.1. Mononuclear Ru(II) dithioether complexes: trans-$RuCl_2(BCyTE)_2$ (**1**) and trans-$RuCl_2(BPhTE)_2$(**2**)*

The BCyTE complex (**1**) was first isolated as a dihydrate, but recrystallization from a DMF/CH_2Cl_2 solution gave crystals containing 2 CH_2Cl_2 solvates per molecule. The ORTEP diagram of the centrosymmetric structure is shown in Fig. 1; Fig. S1 shows the unit cell with the solvates. Selected bond lengths and angles are given in Table 2; there are no significant H-bonding interactions with the CH_2Cl_2 molecules. The Ru-Cl bond lengths of 2.43 Å are essentially the same as those found in the corresponding disulfoxide complex *cis*-$RuCl_2(BCySE)_2$, where BCySE = 1,2-bis(cyclohexylsulfinyl)ethane [7], implying that the *trans* influence of this sulfoxide moiety and Cl^- are similar; the Ru-S bond lengths (2.36 Å) for the dithioether complex are about 0.03 Å longer than those of the sulfoxide complex [7]. The ^1H NMR spectrum of **1** in $CDCl_3$ is a broad complex pattern that could not be assigned by using ^{13}C, 2D-COSY, or ^1H decoupling experiments. No conductivity was observed for the *trans*-bis(dithioether) complexes in CH_2Cl_2 solution, indicating no loss of chloride, and the broad signals likely result from the rotation of the cyclohexyl rings.

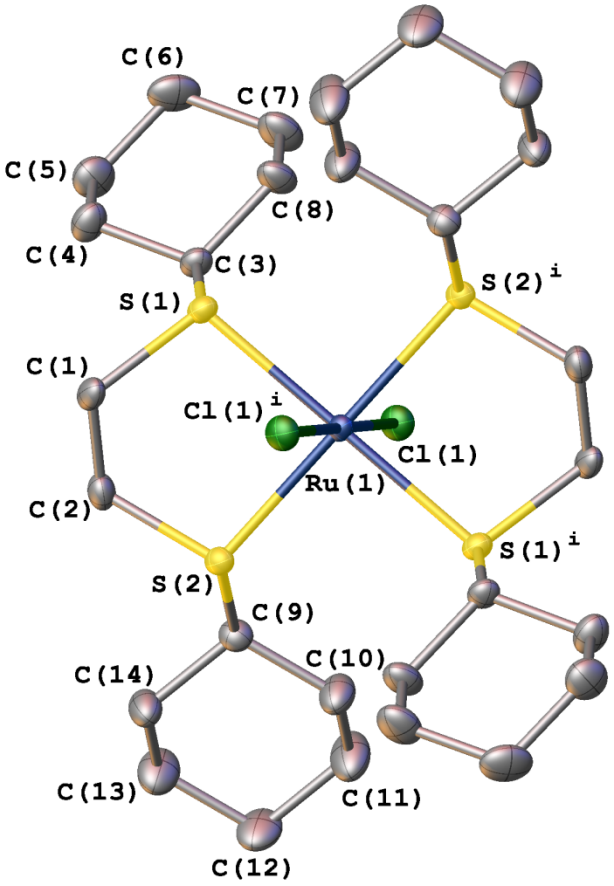


Fig. 1. An ORTEP drawing of *trans*-$RuCl_2(BCyTE)_2$ (**1**) with 50 % probability shown; H-atoms are omitted for clarity. The none-interacting CH_2Cl_2 molecules are not shown, but are included in the unit cell structure (Fig. S1).

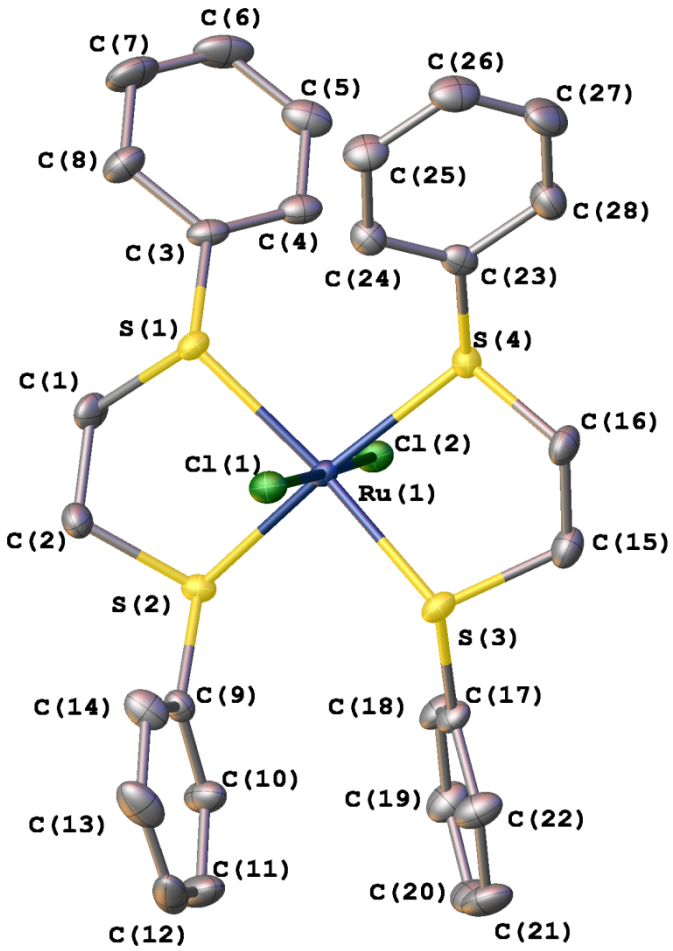


Fig. 2. An ORTEP drawing of *trans*-$RuCl_2(BPhTE)_2$ (**2**) with 50 % probability thermal ellipsoids shown; H-atoms are omitted for clarity.

Table 2. Selected bond lengths (Å) and angles (º) for *trans*-$RuCl_2(BCyTE)_2 \cdot 2CH_2Cl_2$ (**1**) and *trans*-$RuCl_2(BPhTE)_2$ (**2**).

Bond or angle	*trans*-$RuCl_2(BCyTE)_2 \cdot 2CH_2Cl_2$ [**1**]	*trans*-$RuCl_2(BPhTE)_2$ [**2**]
Ru-Cl	2.4268(9)	2.4232(11), 2.4251(11)
Ru-S	2.3627(10), 2.3643(9)	2.3424(10), 2.3591(10)
C-S	1.814(3)-1.838(3)	1.810(4)-1.830(4),[a] 1.782(4)-1.797(4)[b]
cis angles	84.12(3)-95.88(3)	83.72(4)-98.07(4)
trans angles	180.0	167.61(3)-178.11(3)
C-S-C	97.76(12), 104.23(12)	98.28(17)-102.37(17)
S-C-C[a]	110.38(16), 112.78(18)	107.0(3)-108.6(3)
S-C-C[b]	105.76(17)-112.83(18)	115.9(3)-123.6(3)
Ru-S-C[a]	101.47(9), 104.04(9)	102.62(13)-104.21(13)
Ru-S-C[b]	110.98(9), 117.55(9)	116.97(12)-121.58(13)
S-Ru-S[c]	87.22(4); 180.0	85.99(4), 85.30(4) ; 167.61(3), 167.67(3)

[a] Backbone $(CH_2)_2$ atoms. [b] C of Cy or Ph substituents. [c] Data given as cis ; trans.

The X-ray structure of *trans*-$RuCl_2(BPhTE)_2$ (**2**) (Fig. 2, Table 2) confirms the geometry previously suggested from IR data [2]. All the bond lengths are within 0.02 Å of those of complex **1**, except for the C(Ph)-S bond that is ~0.06 Å shorter than the C(Et-S) bond; the major difference in the corresponding bond angles of complexes **1** and **2** is in the S-C-C angles, where the carbon atoms are those of the phenyl- or cyclohexyl-groups: the angle in **1** is ~11° larger. The cis S-Ru-S angles in **1** and **2** are all in the 85.30 - 87.22 degree range; the trans S-Ru-S angles in **1** are 180.0°, and those in **2** are both ~167.6°.

To the best of our knowledge, no structurally characterized Ru (chloro)dithioether complexes (either of Ru^{II} or Ru^{III}) have been reported previously. There are cationic Ru^{II} complexes with BPhTE, where the S-atoms are trans to phenanthroline N-atoms, and the Ru-S bond lengths are 2.30-2.40 Å [20], in the same range as those of complexes **1** and **2**. Similar values are seen in many Ru-monosulfide complexes with various co-ligands [21].

The ^1H NMR spectrum in $CDCl_3$ of the free ligand BPhTE shows a singlet at δ 3.10 for the CH_2CH_2 protons and a δ 7.15 multiplet for the phenyl protons. In complex **2**, shifts at δ 7.65, 7.28

and 7.12, are assigned to the *o*-, *p*- and *m*-protons, respectively, and are based on the resonance structures shown in Fig. 3; these show that the S-atom removes electron density from the *o*- and *p*-positions and results in downfield shifts of these signals, while the *m*-protons are not directly affected. Of interest, the synthesis of **2** used $RuCl_3 \cdot 3H_2O$ and BPhTE, with EtOH as solvent in the presence of HCl (yield 73%), whereas that 'same' method reported by Chatt *et al*. used a solution in non-acidified 2-methoxyethanol (yield 65%) [2]. The difference in the synthetic methods could even result from a different source of the ruthenium precursor; this was not given in ref. 2.

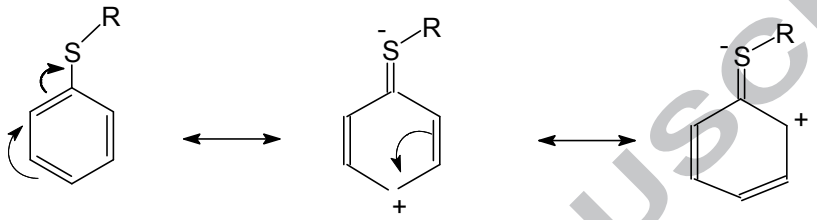


Fig. 3. Resonance structures of a phenyl thioether.

Mentioned in the Introduction is the report that Ru^{II} thioether complexes can be converted with dimethyldioxirane to the corresponding sulfoxide complexes; an example given was $[RuCp(chiraphos)(SR/R')]PF_6$, where R/R' = Me/Ph, Me/^{i}Pr, Me/Bz, Et/Bz or Me/Cy **[**4a]. This suggested a possible oxidation route of **1** and **2** to the corresponding Ru disulfoxide complexes; an attempt to oxidize **2** by this method, however, was unsuccessful: no ν_{SO} was detected in an isolated crude product, and no colour change of the reaction solution was observed.

3.2.2. Dinuclear Ru_2^{III}-dithioether complexes

Reactions of 3,7-dithianonane, 4,8-dithiaunadecane, 5,9-dithiatridecane, and 6,10-dithiapentadecane with $RuCl_3 \cdot 3H_2O$ gave, respectively, the dark purple-brown, dinuclear Ru_2^{III} complexes $[RuCl_2(SS)]_2(\mu\text{-}Cl)_2$, where SS = BETP (**3**), BPTP (**4**), BBTP (**5**), and BPeTP (**6**). Crystal structures of **3** and **4** (Figs. 4, 5, and Table 3) are very similar, not surprisingly since the only difference is the S-alkyl (Et *vs*. Pr). Somewhat surprisingly, since the crystals were made via the same method (from a CH_2Cl_2 solution), the X-ray structure of **4** shows 2 CH_2Cl_2 solvates whereas **3** has no solvate molecules; however, crystals of the butyl and pentyl analogues **5** and **6** could not be isolated.

Differences in the corresponding bond lengths and angles in **3** and **4** (Table 2) are again small. The terminal Ru-Cl bond lengths (trans to S) are essentially the same, and are only about 0.03 Å longer than those trans to the μ-Cl, implying a small trans influence of S compared to the μ-Cl. Similar relative data and implication are seen for the Ru-μ-Cl bond lengths that are trans to the S or a terminal-Cl, where a relative difference of ~0.07 Å is seen. There are only minor differences in: the Ru-S bond lengths (~0.01 Å), the Ru-Cl-Ru angles (< 2 degrees), the Ru-S-C(propyl) *vs*. the Ru-S-C(ethyl) angles. (< 2 degrees); the cis-S-Ru-S angles are 94.44 or 95.61° and there are no Ru-Ru bonds. The Ru-μ-Cl bond lengths in **3** and **4** are up to 0.1 Å longer than the trans Ru-Cl bonds; these Ru^{III} bonds are up to 0.1 Å shorter than the Ru^{II}-Cl bonds in complexes **1** and **2**. The structural data for **3** and **4** may be compared with those of another $Ru_2^{III}(\mu\text{-Cl})_2$ species $Ru_2Cl_2(PPh_3)_2(\mu\text{-Cl})_2(\mu\text{-salhn})$, H_2salhn being a tetradentate N_2O_2 donor Schiff base with two dissociable phenolic protons [22]; here, the terminal Ru-Cl bonds are 2.320 and 2.341 Å, and the longer Ru-μ-Cl bonds are in the range 2.369 to 2.428 Å, similar values and trends to those found in **3** and **4.**

X-ray quality crystals of complexes **5** and **6** were not obtained, but their elemental values analyses and UV-Vis data (similar to those of **3** and **4**) support their analogous formulations.

The solid-state magnetic susceptibilities of all four complexes were 3.0 to 3.8 (± 0.1) B. M. per Ru, consistent with a single, unpaired electron, at none-interacting Ru^{III} centres. No conductivity was observed for these complexes in CH_2Cl_2 solution, and the complexes were insoluble in water. Of note, some of the sulfoxides, synthesized by oxidation of the dithioethers (see Section 3.1), form analogous bis(disulfoxide), chloro-bridged, dinuclear Ru^{III} complexes that are water-soluble and lead to a relatively high degree of DNA bonding [7]; this thesis work is currently being arranged for publication.

Also, of note, the suggested formulation of $[RuCl_3(EtSCH_2CH_2SEt)_{1.5}]_n$ suggested by Chatt *et al*. was described as 'probably at least binuclear' with one chelating and one bridging disulphide [2]; this contrasts with our quite different structure for the 1,3-bis(ethylthio)propane analogue $[RuCl_2(BETP)]_2(\mu\text{-Cl})_2$ (Fig. 4); both elemental analyses for the formulations are correct. The different products could result from steric effects, just $(CH_2)_2$ *vs*. $(CH_2)_3$ groups, but a more likely possibility is the difference in the solvent systems used in the syntheses: again, acidified EtOH by our group, whereas Chatt's group used just EtOH [2].

Table 3. Selected bond lengths (Å) and bond angles (º) for $[RuCl_2(BETP)]_2(\mu\text{-}Cl)_2$ and $[RuCl_2(BPTP)]_2(\mu\text{-}Cl)_2$.

Bond or Angle	$[RuCl_2(BETP)]_2(\mu\text{-}Cl)_2$ **3**	$[RuCl_2(BPTP)]_2(\mu\text{-}Cl)_2$ **4**
Ru-Cl[a]	2.3249(9),[b] 2.3496(9)[c]	2.3200(12),[b] 2.3566(13)[c]
Ru-Cl[d]	2.3911(9), 2.4628(9)	2.3842(12), 2.4591(12)
Ru-S	2.3196(9), 2.3675(9)	2.3306(13), 2.3561(13)
C-S	1.812(3)-1.820(3)	1.810(5)-1.851(5)
cis angles	84.14(3)-96.73(3)	82.94(4)-97.50(4)
trans angles	172.07(3)-175.84(3)	173.35(4)-175.94(4)
C-S-C	99.98(16), 100.46(11)	98.9(3), 101.0(3)
S-C-C[e]	113.1(2), 117.0(2)	112.1(4), 117.2(4)
S-C-C[f]	110.1(2), 112.74(19)	111.3(4), 112.2(4)
Ru-S-C[e]	110.16(12), 111.81(11)	110.17(12), 112.74(19)
Ru-S-C[f]	107.79(12), 110.60(11)	109.81(18), 110.79(18)
Ru-Cl-Ru	95.86(3)	97.05(4)
S-Ru-S	94.44(4)	95.61(5)

[a] Terminal Cl. [b] *Trans* to Cl. [c] *Trans* to S. [d] Bridging Cl. [e] Backbone C-atoms. [f] End substituents.

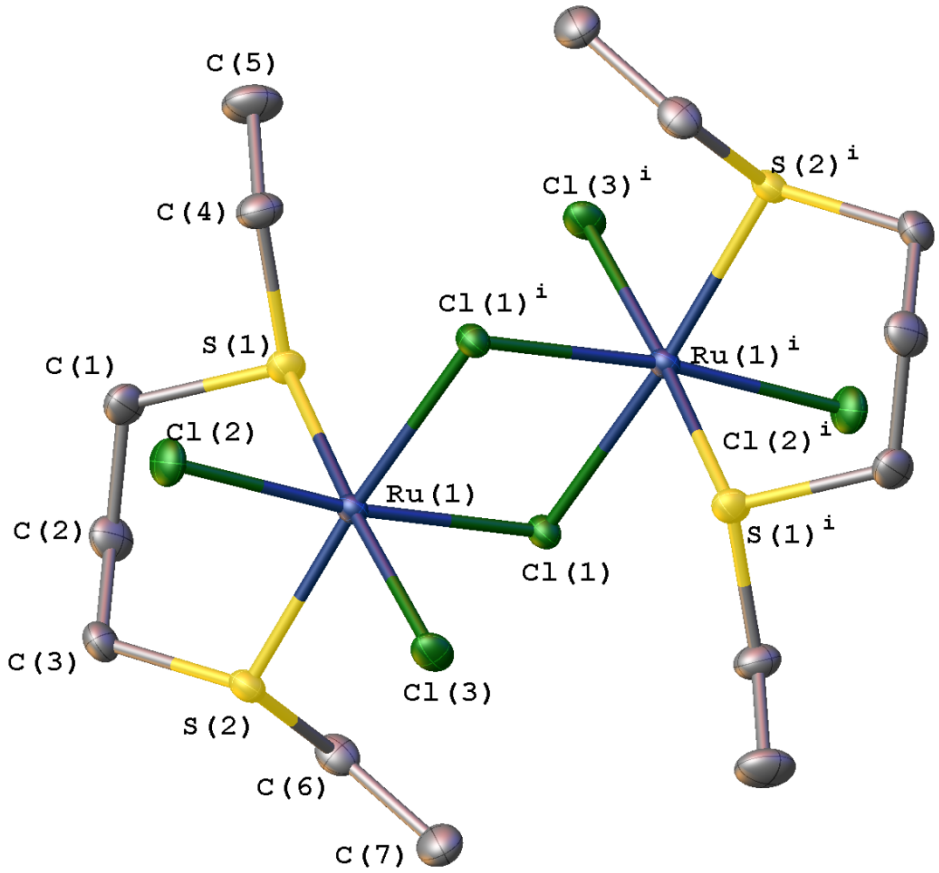


Fig. 4. An ORTEP drawing of $[RuCl_2(BETP)]_2(\mu\text{-}Cl)_2$ (**3**) with 50 % probability thermal ellipsoids shown; H-atoms are omitted for clarity.

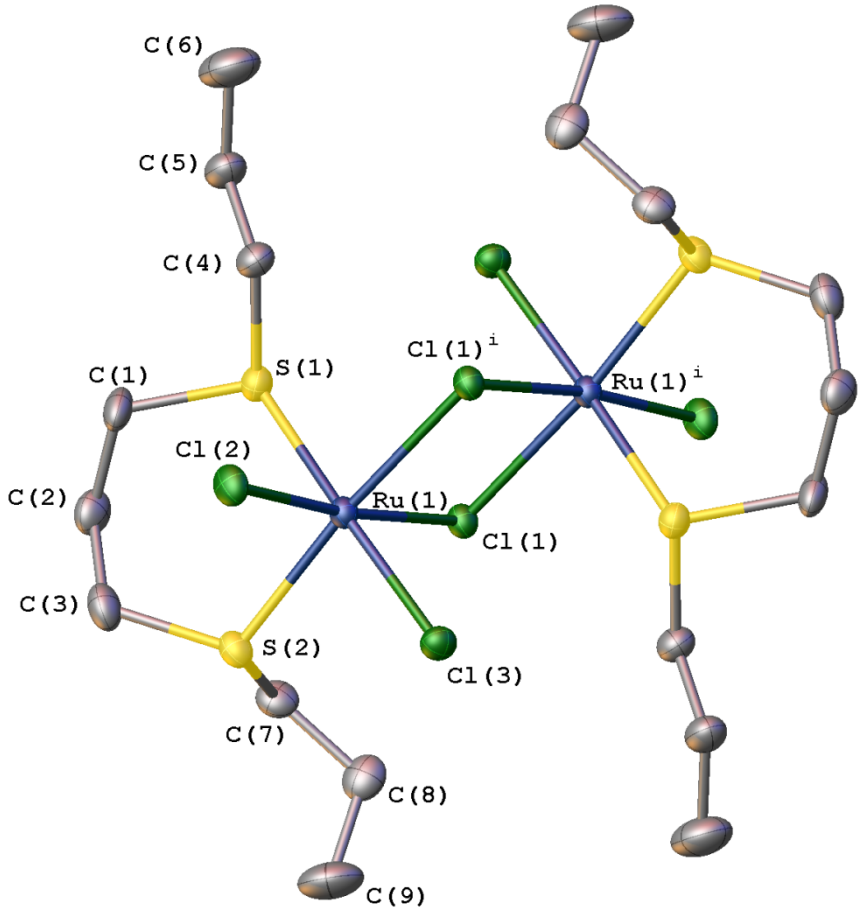


Fig. 5. An ORTEP drawing of $[RuCl_2(BPTP)]_2(\mu\text{-}Cl)_2$ (**4**) with 50 % probability thermal ellipsoids shown. The H-atoms are omitted for clarity.

4. Conclusions

Nine new, and two known, dithioethers of the type $RS(CH_2)_xSR$, where x = 2 or 3, and R is an alkyl or aryl chain, are reported. Their reactions with $RuCl_3 \cdot 3H_2O$ generate either *trans*-$RuCl_2(dithioether)_2$ or $[RuCl_2(RS(CH_2)_xSR)]_2(\mu\text{-}Cl)_2$ complexes, with both types being characterized crystallographically. This current paper clarifies uncertainties in structures of Ru-thioether complexes, and forms the basis of studies on the related sulfoxide systems. Further studies (to be published) show that the dithioethers can be oxidized to the corresponding disulfoxides that also form ruthenium complexes; such complexes are of the type known for their biological properties, such as cell accumulation and toxicity, and DNA binding.

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Appendix A. Supplementary data

Supplementary material is Fig. S1. CCDC numbers 1895702-1895705 contain the supplementary crystallographic data for complexes **3**, **4**, **1** and **2**, respectively; these data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online at https……..

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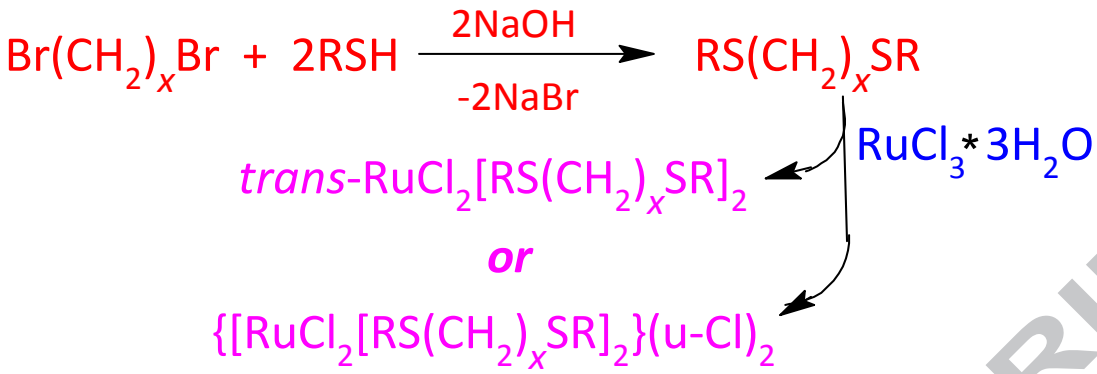

x = 2 or 3 ; R = alkyl, or Ph, or cyclohexyl

Highlights:

Syntheses of dithioethers, and their chloro -Ru(II and III) complexes
X-ray structures