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Synthesis and characterisation of macromolecules containing multiple tetrazole functionalities

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ABSTRACT

The synthesis of tetra-tetrazole macromolecules, containing various aromatic cores including benzene, pyridine and pyrazine directly attached to the tetrazole moieties, is described. This variation allowed for the generation of ligands with greater potential for metal ion complexation. Metal ion complexation reactions of the tetra-tetrazole macromolecules with the chelating pyridyl-tetrazole arms result in the formation of metal complexes where the metal ion was bound at the pendant arms rather than at the central core.

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1. Introduction

The development of 'click' chemistry, as described by Sharpless and co-workers,[1,2] has resulted in an increase in the number of publications involving tetrazoles.[3–7] There are also several reviews on tetrazoles in the literature, including their use as carboxylic acid bioisosteres in drug discovery and as functional ligands in co-ordination chemistry.[8–10] Our interest in tetrazoles stems from their use as precursors for the formation of new functionalised polytetrazole macrocycles, which could find application, for example, as sensors or in molecular recognition. We have previously reported the synthesis and structural characterisation of several tetra-tetrazole macrocycles from 1,2-, 1,3- and 1,4-dicyanobenzene and 2,6-pyridinedicarbonitrile derivatives, as well as the first example of a host–guest interaction between a tetra-tetrazole macrocycle and a solvent molecule.[10–14] In order to increase the flexibility of tetra-tetrazole ligands, we have removed some of the rigidity of the system by synthesising macromolecules to include flexible pendant arms, thus allowing the pendant arms to adapt their conformation for complexation to a metal ion more easily than analogous macrocycles. Macromolecules containing several tetrazole groups have been previously reported.[15–17] This paper focuses on the synthesis and characterisation of tetra-tetrazole macromolecules using the bis-tetrazoles 1,3-bis(tetrazol-5-yl) benzene[14] (**1**), 2,6-bis(2*H*-tetrazol-5-yl)pyridine[13] (**2**) and 2,3-bis(1*H*-tetrazol-5-yl)pyrazine (**3**) as the starting building blocks (see Schemes 1 and 2). Preliminary studies on the complexation reactions of these macromolecules with several metal salts have also been conducted.

2. Results and discussion

The bis-tetrazole compounds (**1**, **2** and **3**) were synthesised following reported procedures from 1,3-dicyanobenzene, 2,6-pyridinedicarbonitrile and 2,3-pyrazinedicarbonitrile, respectively.[13,14,18] The ^{13}C NMR spectra of the three compounds showed a signal at ~158 ppm for **1**, at ~155 ppm for **2** and at ~150 ppm, confirming the formation of the tetrazole systems.[11–16] The synthesis of 2-(6′-bromohexyl)-5-phenyl-2*H*-tetrazole (**4**) and 2-(6″-bromohexyl)-(2-tetrazol-5-yl)pyrazine (**6**) was carried out using a similar procedure to that previously reported for the synthesis of 2-(6″-bromohexyl)-(2-tetrazol-5-yl)pyridine (**5**).[19] In the ^{1}H NMR spectra of **4** and **6**, two triplet signals, at ~4.9 ppm and at ~3.4 ppm, corresponding to the expected shift for the side-chain $N-CH_2$ and CH_2-Br signals were observed. The ^{13}C NMR spectra of **4** and **6** showed that the tetrazole carbon signal resonated at ~162 ppm indicative of N2 alkylation.

The phenyl macromolecules **7** and **8** were synthesised by reacting 2-(6′-bromohexyl)-5-phenyl-2*H*-tetrazole (**4**) with 1,3-bis(tetrazol-5-yl)benzene (**1**) in acetonitrile with triethylamine as base to afford the tetra-tetrazole macromolecules, as in Scheme 1.

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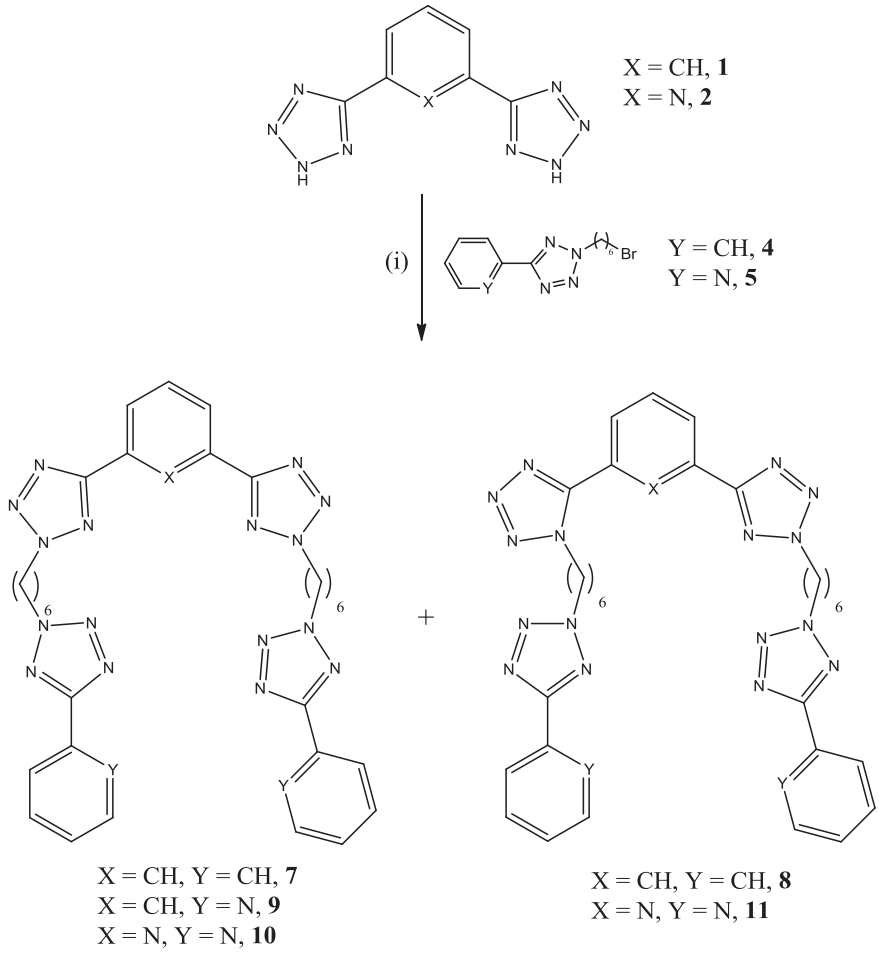
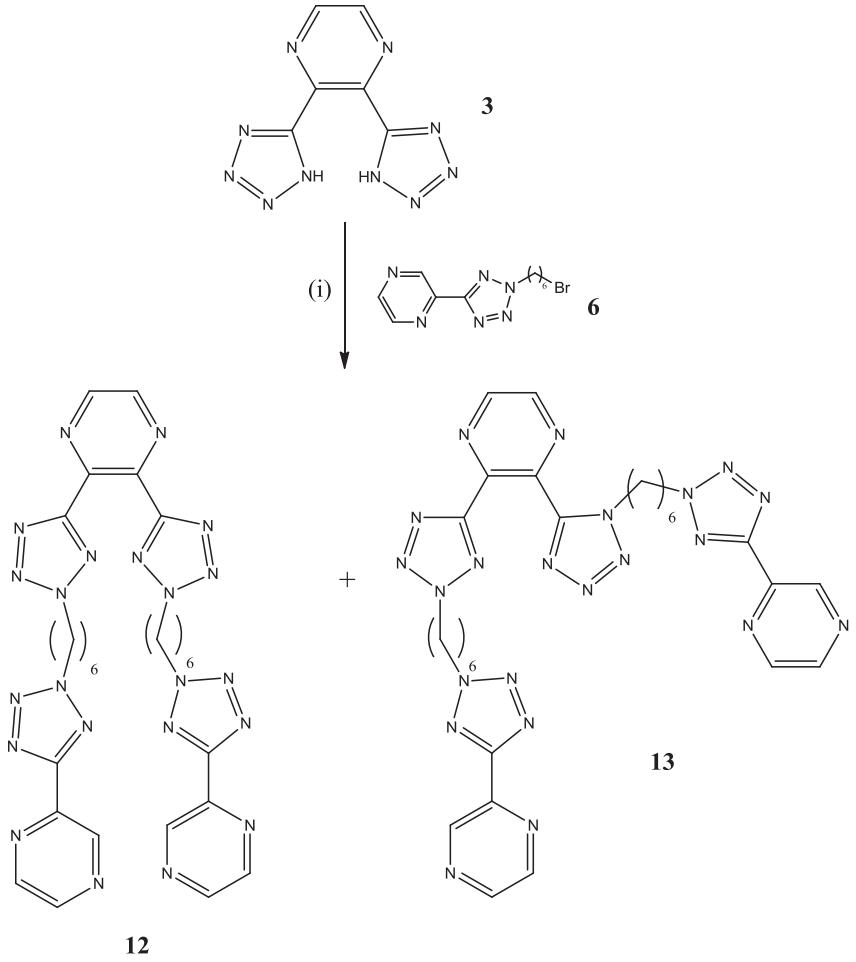


Scheme 1. Reagents and conditions: (i) Et_3N, MeCN, Δ, 24 h.

Both the symmetric **7** and asymmetric **8** tetra-tetrazole macromolecules were isolated from the crude reaction mixture. The symmetric compound **7** was the major product of the reaction and was isolated, as a white solid, in 41% yield with a melting point of 107—109 °C. The ^{1}H NMR spectrum of **7** had a small number of signals due to the plane of symmetry within the molecule. The signals associated with bis(tetrazol-5-yl)benzene region were as expected with a singlet, doublet and triplet signal being observed at 8.93, 8.26 and 7.64 ppm, respectively. The signals of the phenyl moiety attached to the *mono*-tetrazole appeared as a multiplet at 7.47 ppm, similar to that observed in the starting material **4**. The symmetry of the molecule was confirmed by a single triplet signal observed for the eight protons of the *N*2 substituted methylene carbons at 4.66 ppm. The other methylene signals were observed at 2.09 and 1.46 ppm. The ^{13}C NMR spectrum confirmed one signal for the four *N*2 substituted tetrazoles at 165.1 ppm. The alkyl region was uncomplicated with three signals observed at 25.7, 29.1 and 52.9 ppm, respectively.

The asymmetric macromolecule **8** was also isolated as a white solid, in 23% yield, with a melting point of 111—114 °C. The ^{1}H NMR spectrum confirmed the asymmetric nature of the compound as most signals were doubled due to the asymmetry. The four signals at 8.83, 8.36, 8.13 and 7.69 ppm for the central phenyl ring were indicative of asymmetric alkylation. A triplet was observed for the methylene attached to the *N*2 substituted tetrazoles at 4.65 ppm and a second triplet was observed at 4.48 ppm for the *N*1 substituted tetrazole. The remaining methylene signals were observed as multiplets. The ^{13}C NMR spectrum confirmed the substitution pattern with the appearance of three peaks for the tetrazoles at 165.5 and 163.6 ppm for the *N*2 substituted tetrazoles and at 153.9 ppm for the *N*1 substituted tetrazole. The signals for the methylene carbons adjacent to the tetrazole moieties were seen at 53.1 and 52.8 ppm for the carbons adjacent to the *N*2 substituted tetrazoles and at 47.9 ppm for the *N*1 substituted tetrazole.

The pyridyl-substituted phenyl macromolecule **9** was synthesised by reacting 2-(6″-bromohexyl)-(2-tetrazol-5-yl)pyridine (**5**) with 1,3-bis(tetrazol-5-yl)benzene (**1**) in acetonitrile with triethylamine as base, as in Scheme 1. The tetra-tetrazole macromolecule **9** was isolated as a white solid in 28% yield. The mass balance of the reaction was unreacted starting materials and intractable side products, which could not be fully separated or characterised. The product **9** was readily identified by ^{1}H NMR and ^{13}C NMR spectroscopy, which showed a simple splitting pattern as a result of the plane of symmetry in the molecule. If asymmetry had been observed, there would have been a doubling of signals in the NMR spectra, as were observed in the case of compound **8**. In the ^{1}H NMR spectrum, the signals associated with bis(tetrazol-5-yl)benzene region were again observed at 8.92, 8.23 and 7.62 ppm, respectively, as a singlet, doublet and triplet signal, as had been previously observed in compound **7**. The formation of the tetra-tetrazole macromolecule **9** was confirmed by the disappearance of the CH_2—Br signal at ca. 3.40 ppm and the retention and doubling of the integration of the *N*2—CH_2 signal. This signal was observed as a double-triplet at 4.69 ppm. The ^{13}C NMR spectrum showed two peaks at 164.8 ppm and at 164.6 ppm, identifying that the compound was *N*2 substituted, with the difference in the



Scheme 2. Reagents and conditions: (i) Et_3N, MeCN, Δ, 24 h.

signals being due to the attachment to either a pyridyl system or a phenyl system. Further peaks, which identified the formation of the macromolecule, were the appearance of the two methylene signals adjacent to the tetrazole nitrogens at 53.2 and 52.9 ppm, respectively.

The next tetra-tetrazole macromolecules involved the replacement of 1,3-bis(tetrazol-5-yl)benzene **1** with 2,6-bis(2*H*-tetrazol-5-yl)pyridine **2** (see Scheme 2). This change offered a further point where metal ion complexation may occur. The isolated yields of both the symmetric (**10**) and asymmetric (**11**) compounds were 11% and 8%, respectively. The IR spectra of both products were very similar due to their near identical chemical structure, and contained stretches at 2953 and 2857 cm^{-1} for the pyridyl aromatic C–H stretches and the typical tetrazole stretches at 1651 cm^{-1} (>C=N–), 1593 cm^{-1} (–N=N–) and 1260 cm^{-1} (C–N). The molecular formula of both the symmetric and asymmetric compounds was confirmed by mass spectrometry and elemental analysis. The ^{1}H NMR spectrum of **10** confirmed its symmetric nature as the protons on the central pyridine ring appeared as a single doublet and a triplet at 8.35 ppm and at 8.05 ppm, respectively. The signals associated with the 2-(1*H*-tetrazol-5-yl)pyridine part of the molecule were observed as two doublets at 8.47 and 8.32 ppm and a triplet at 8.07 ppm, respectively. The appearance of a single multiplet at 4.72 ppm for the methylene protons adjacent to the tetrazole carbons confirmed the plane of symmetry in **10**. The ^{13}C NMR analysis confirmed the tetrazole carbon signals at 165.0 and 164.4 ppm for the *N*2 substituted tetrazoles. A single carbon signal was observed for the methylene carbons adjacent to the tetrazole nitrogens at 53.4 ppm, which again confirmed the structure of **10**. The ^{1}H NMR analysis of **11** confirmed the asymmetric nature as nearly all the signals were split due to the lack of a plane of symmetry. All the proton signals of the central pyridine ring were observed. The splitting of the 2,6-di(2*H*-tetrazol-5-yl)pyridine moiety was as observed in the symmetric analogue **10**. As seen in the previous asymmetric phenyl macromolecules, two triplet signals were observed at 5.39 ppm for the *N*1–CH_2 substituted tetrazoles and at 4.70 ppm for the *N*2–CH_2 substituted tetrazoles. The ^{13}C NMR spectrum confirmed the tetrazole carbon signals at 164.8 and 163.9 ppm for the *N*2 substituted tetrazoles and the *N*1 substituted tetrazole carbon was seen at 154.4 ppm. The signals at 53.2 ppm (N1) and 49.9 ppm (N2) of the carbons adjacent to the tetrazoles were as expected.

2,3-Bis(1*H*-tetrazol-5-yl)pyrazine **3** was reacted with 2-(2-(6-bromohexyl)-2*H*-tetrazol-5-yl)pyrazine **6** to yield the symmetric (**12**) and asymmetric (**13**) regioisomers, as shown in Scheme 2. The asymmetric product was expected to be the minor product due to the steric effect of the bulky aromatics at the end of the alkyl chain, but both products were obtained as slightly yellow oils in 8% yields. The IR spectra of both products **12** and **13** were nearly identical due to their similar chemical structure. Both the asymmetric and symmetric compounds were confirmed by mass spectrometry and elemental analysis. The ^{1}H NMR spectrum of **12** confirmed the symmetric nature of the compound as the signal for the pyrazine hydrogens of the central ring was observed as a single singlet at 8.88 ppm. The symmetric nature was further identified by the appearance of a single signal for the methylene group adjacent to the

tetrazoles, which was observed as a multiplet at 4.74 ppm. The ^{13}C NMR analysis confirmed the tetrazole carbon signals at 162.7 and 162.4 ppm for the *N*2 substituted tetrazoles. A single carbon signal was also observed for the methylene carbons adjacent to the tetrazole nitrogens at 53.4 ppm. In the case of compound **13**, the ^{1}H NMR spectrum confirmed the asymmetric nature of the compound as nearly all the signals were doubled due to this asymmetry. Two signals were observed for the pyrazine hydrogens of the central ring of the macromolecule at 8.97 and 8.88 ppm. Two triplet signals were observed for the methylene carbons adjacent to the tetrazole nitrogens, one at 4.74 ppm for the *N*1 substituted tetrazoles and the second for *N*2 substituted tetrazoles at 4.63 ppm, similar to what was observed for the asymmetric macromolecules previously discussed (**8** and **10**). The ^{13}C NMR analysis confirmed the tetrazole carbon signals at 162. and 162.4 ppm for the *N*2 substituted tetrazoles, while the *N*1 substituted tetrazole was seen at 151.4 ppm. The asymmetry of the central pyrazine ring was also observed with four signals at 145.7, 144.7, 143.0 and 142.9 ppm. Two signals at 53.4 (N1) and 48.2 ppm (N2) for the methylene carbons adjacent to the tetrazoles were also observed.

As the yields of several of the macromolecules were very low, metal ion complexation studies were only undertaken in earnest with **9**. The tetra-tetrazole macromolecule **9** was designed with the chelating site between the pendant pyridine and tetrazole rings, as this has the ability to form five-membered rings.[19] It was found that when metal ion complexation reactions were attempted with the tetra-tetrazole macromolecules containing the phenyl moieties (**7** and **8**) in solution, no shifts in either ^{1}H NMR spectra or UV–vis spectra resulted. When complexation reactions were attempted with the pyridyl tetra-tetrazole macromolecule **9**, it suggested that complexation had resulted as examined by ^{1}H NMR and UV–vis titrations.

The aromatic region of the ^{1}H NMR spectrum of compound **9** (bottom) and the shifts induced by the addition of varying numbers of molar equivalents of $Zn(ClO_4)_2$ are shown in Fig. 1. All spectra were run in CD_3OD, as $Zn(ClO_4)_2$ has considerable solubility in this solvent. Fig. 1 also shows a labelled structure of the tetra-tetrazole macromolecule **9**. The perchlorate salt was chosen as it was hoped that crystals of any metal complex formed might crystallise more easily from solution using this anion. However, no crystals were observed.

An immediate shift was observed on addition of 0.5 mol equiv of $Zn(ClO_4)_2$ and shifts were observed up to 10 mol equiv of $Zn(ClO_4)_2$. The phenyl signals *a*, *d* and *f* did not shift significantly over the course of the titration experiment. The main shifts, however, were observed for the pyridyl-tetrazole moiety. The clearest indication of complexation was observed for the proton beside the pyridyl nitrogen *b*, which had shifted downfield by 0.18 ppm. The remaining pyridyl signals all showed large shifts downfield and the signals for protons *c* and *e* were observed to gradually merge into one signal after the addition of 15 equiv of Zn^{2+} ion. No further significant shift was observed on addition of five more equivalents, which may signify that one species now predominated in solution or that all the complexation sites had now been occupied by the metal ion. Another clear sign that complexation involved the pyridyl nitrogen and tetrazole nitrogen was the shift of the methylene proton signal attached to the tetrazole ring. A multiplet, consisting of overlapping triplets, was observed in the free ligand due to all the tetrazoles being N2 substituted. On addition of the Zn^{2+} ion, these two signals began to differentiate from one another with the signal for the *N*2 substituted tetrazoles attached to the pyridine rings shifting downfield from 4.76 to 4.83 ppm. Although a small shift was observed, the multiplicity was clearly shown. The fact this was a clear triplet might indicate that a symmetric species predominated in solution. If complexation had occurred on only one of the pendant arms, then the triplet signal would have been further split, but as this was not the case it was assumed the predominant species in solution was symmetric in nature.

Based on this ^{1}H NMR complexation study, two transition metal complexes of the ligand **9** were synthesised and characterised. The tetra-tetrazole macromolecule **9** was reacted with $CuCl_2 \cdot 2H_2O$ and $Co(SCN)_2$ metal salts. The macromolecule was dissolved in $CHCl_3$. To this was added a MeOH solution of the metal salt. The resulting highly coloured solution was then stirred for one hour and after several days a highly coloured solid was obtained (Fig. 2).

The IR spectra of both **14** and **15** showed several clear differences in peak position when compared to that of **9**. In **15**, there was a thiocyanate peak at 2073 cm^{-1}, which was not present in **9**. Furthermore, this band has shifted from 2152 cm^{-1} in the metal salt $Co(SCN)_2$ to 2073 cm^{-1}. The spectra of both **14** and **15** showed that the stretches of the pyridine and tetrazole rings of the pendant arms had shifted to higher wavenumber upon complexation to both the Cu^{2+} and Co^{2+} ion, respectively. The shifts in wavenumber were similar to those observed for the complexation of **5** with $CuCl_2 \cdot 2H_2O$ and $Co(SCN)_2$ as previously reported.[19] In the UV–vis spectra of **14** and **15**, a d–d* transition was observed at 760 nm and 751 nm, respectively, which tailed into the visible region similar to that described by Gallardo.[17] We have shown the pyridine-tetrazole

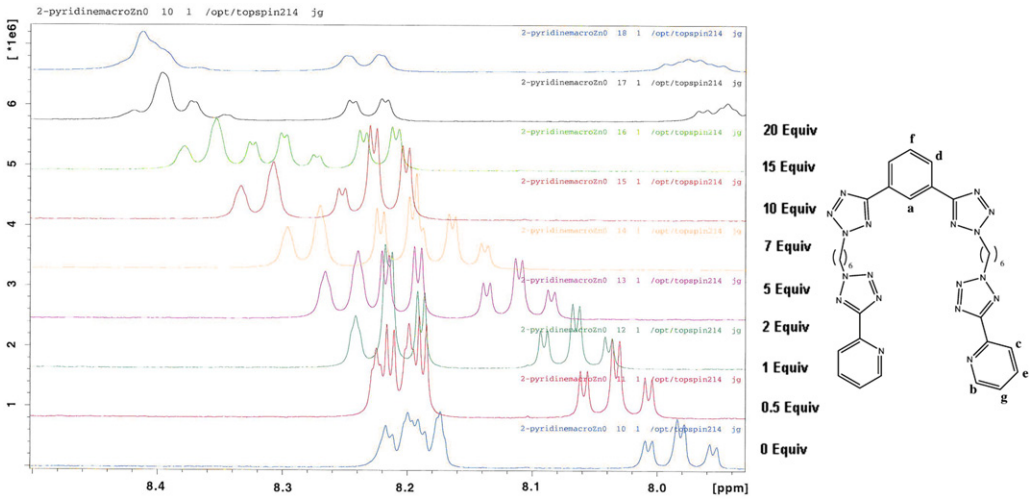


Fig. 1. Aromatic region in ^{1}H NMR spectra of **9** and those obtained upon addition of Zn^{2+} ion equivalents (CD_3OD as solvent), with molecule showing labelled protons for partial spectra.

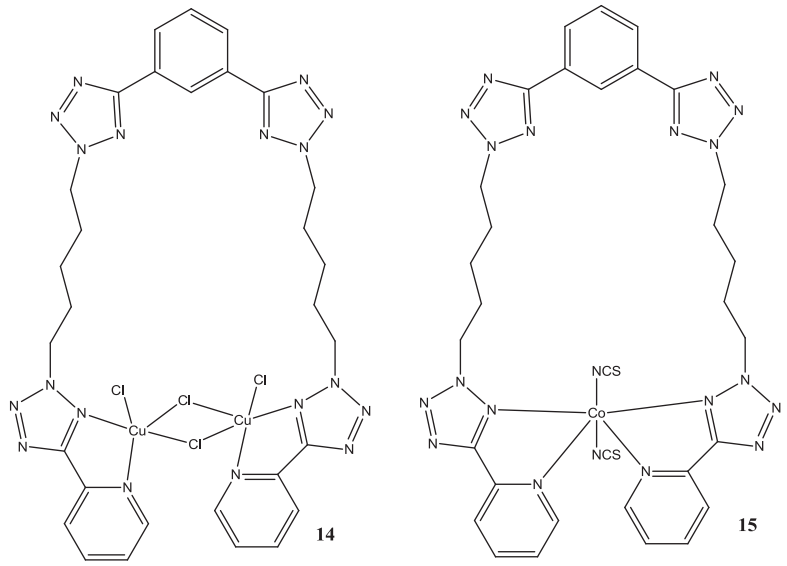


Fig. 2. Suggested structures for the copper (**14**) and cobalt (**15**) complexes of macromolecule **9**.

moiety can form a five-membered ring when being complexed to metal ions, and in particular the use of $CuCl_2$ has led to dimeric copper species.[19] The spectroscopic results along with the elemental analysis, in combination with the crystallographic data previously reported for metal complexes of **5**,[19] suggest the structures of complexes **14** and **15**, as shown in Fig. 2.

There is also the possibility that both the metal ions in complexes **14** and **15** could bind intermolecularly, rather than intramolecularly as shown in Fig. 2, which would result in an oligomeric structure. This type of structure would also be consistent with the analytical data. Without an X-ray crystal structure, it is impossible to prove, which structure is correct. However, based on the crystallographic data previously reported for metal complexes of **5**,[19] it is impossible to favour intramolecular binding over intermolecular binding, as the position of the pendant alkyl chain has no influence on the binding of the metal ion as previously discussed.

3. Conclusions

The synthesis of tetra-tetrazole macromolecules, containing benzene, pyridine and pyrazine as the central ring in the macromolecule, are described. This variation has allowed for the generation of ligands with greater potential for metal ion complexation. The tetra-tetrazole macromolecules with the benzene core, containing a chelating pyridine-tetrazole pendant arm, lead to the formation of several metal complexes. In all cases, complexation is only observed at the pendant arm and not at the central core. This would suggest that the central core is redundant. We are currently undertaking further metal ion complexation reactions with the macromolecules containing the pyridine and pyrazine central core, as these compounds now contain several potential binding sites. The results of these studies will be reported in due course.

4. Experimental

4.1. General

^1H and ^{13}C NMR (δ ppm; J Hz) spectra were recorded on a JEOL JNM-LA300 FT-NMR spectrometer using saturated $CDCl_3$ solutions with Me_4Si reference, unless indicated otherwise, with resolutions of 0.18 Hz and 0.01 ppm, respectively. Infrared spectra (cm^{-1}) were recorded as KBr discs or liquid films between KBr plates using either a Nicolet Impact 410 FT-IR spectrometer. Melting point analyses were carried out using a Stewart Scientific SMP 1 melting point apparatus and are uncorrected. Mass spectrometry was carried out at the Centre for Synthesis and Chemical Biology (CSCB), University College, Dublin using Quattro micro™ LC–MS/MS and LCT mass spectrometers. Microanalyses were carried out at the Microanalytical Laboratory of University College, Dublin. Magnetic susceptibility measurements were carried out at room temperature using a Johnson Matthey Magnetic Susceptibility Balance with $[HgCo(SCN)_4]$ as reference. UV–vis spectra were recorded using a T80 UV–vis spectrophotometer in MeOH (spectrophotometric grade) unless stated. Spectra were recorded from 210 to 900 nm. Standard Schlenk techniques were used throughout. Starting materials were commercially obtained and used without further purification. The synthesis of compounds **1**, **2**, **3** and **5** has been described previously.[13,14,18,19] *Caution! Nitrogen-rich compounds such as tetrazole derivatives are used as components for explosive mixtures.*[8] *In our laboratory, the reactions described were run on several gram scales, and no problems were encountered. However, great caution should be exercised when heating or handling compounds of this type. Caution! Although not encountered in our experiments, perchlorate salts of metal ions are potentially explosive and should be manipulated with care and used only in small quantities.*

4.2. 2,3-Bis(1*H*-tetrazol-5-yl)pyrazine (3)

A suspension of 2,3-pyrazinedicarbonitrile (2.60 g, 0.02 mol), sodium azide (2.90 g, 0.043 mol), ammonium chloride (2.30 g, 0.043 mol) and lithium chloride (0.60 g, 0.014 mol) in anhydrous dimethylformamide (60 mL) was stirred for 10 h at 110 °C. After this time, the solution was cooled and the insoluble salts were removed by filtration. The solvent was then evaporated under reduced pressure and the residue was dissolved in deionised water (200 mL) and acidified with concentrated HCl (3 mL), to initiate precipitation. The product was filtered, washed with water (3×40 mL) and dried to afford a brown solid, which was recrystallised from hot ethanol to afford a yellow crystalline solid (3.27 g, 76%), mp 268–270 °C (lit. 265 °C).[18] Found: C, 33.38; H, 1.98; N, 64.80. $C_6H_4N_{10}$ requires C, 33.34; H, 1.87; N, 64.79%; ν_{max} (KBr) 3415 (N–H), 2928, 2855, 1651, 1601, 1452, 1278 cm^{-1}; δ_H (300 MHz,

DMSO-d_6) 9.16 (2H, s, pyz-H), 3.56 (2H, br s, NH); δ_C (75 MHz, DMSO-d_6) 150.3 (CN_4), 146.1, 139.8.

4.3. 2-(6′-Bromohexyl)-5-phenyl-2*H*-tetrazole (4)

To 5-phenyl-1*H*-tetrazole (1.00 g, 6.80 mmol) dissolved in acetonitrile (30 mL) was added potassium carbonate (9.40 g, 68.0 mmol). The resulting suspension was stirred at reflux for 30 min and to the hot solution was added 1,6-dibromohexane (6.10 g, 25.0 mmol). The reaction mixture was then stirred at reflux temperature for a further 24 h. After cooling and removal of inorganic solids, the solvent was removed under reduced pressure to afford an oil, which was purified by column chromatography on silica gel (initially at a ratio of petroleum ether/ethyl acetate 4:1, followed by the ratio of 3:2) to give a waxy white solid (3.2 g, 50%), mp 42–44 °C. Found: C, 50.46; H, 5.51; N, 18.09. $C_{13}H_{17}BrN_4$ requires C, 50.50; H, 5.54; N, 18.12%; R_f (3:2 petroleum ether/ethyl acetate) 0.74; ν_{max} (KBr) 2957, 2855, 1663, 1514, 1458, 1255 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.15 (2H, br d, Ar–H), 7.48–7.45 (3H, m, Ar–H), 4.66 (2H, t, J=7.0 Hz, CH_2N), 3.37 (2H, t, J=6.2 Hz, CH_2Br), 2.08–2.06 (2H, m, CH_2), 1.85–1.83 (2H, m, CH_2), 1.41–1.39 (4H, m, CH_2); δ_C (75 MHz, $CDCl_3$) 164.9 (CN_4), 130.2, 128.9, 127.4, 126.7, 52.9 (CH_2N), 33.5 (CH_2Br), 32.3, 29.1, 27.4, 25.5.

4.4. 2-(6″-Bromohexyl-(2-tetrazol-5-yl))pyrazine (6)

To 2-(1*H*-tetrazol-5-yl)pyrazine (1.00 g, 6.80 mmol) dissolved in acetonitrile (30 mL) was added potassium carbonate (9.40 g, 68.0 mmol). The resulting suspension was stirred at reflux for 30 min and to the hot solution was added 1,6-dibromohexane (6.10 g, 25.0 mmol). The reaction mixture was then stirred at reflux temperature for a further 24 h. After cooling and removal of inorganic solids, the solvent was removed under reduced pressure to afford an oil, which was purified by column chromatography on silica gel (initially at a ratio of petroleum ether/ethyl acetate 4:1, followed by the ratio of 3:2). This gave the product **6** as a clear oil (0.55 g, 26%). Found: C, 42.53; H, 4.91; N, 26.95. $C_{11}H_{15}BrN_6$ requires C, 42.46; H, 4.86; N, 27.01%; R_f (3:2 petroleum ether/ethyl acetate) 0.29; ν_{max} (KBr) 2956, 1663, 1514, 1458, 1255 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 9.62 (1H, s, pyz-H), 8.73 (2H, br d, pyz-H), 4.94 (2H, t, J=6.9 Hz, CH_2N), 3.37 (2H, t, J=6.2 Hz, CH_2Br), 2.02–2.00 (2H, m, CH_2), 1.70–1.68 (2H, m, CH_2), 1.42–1.40 (4H, m, CH_2); δ_C (75 MHz, $CDCl_3$) 162.6 (CN_4), 146.2, 145.7, 143.7, 141.8, 49.6 (CH_2N), 33.7 (CH_2Br), 32.4, 29.7, 27.5, 25.5.

4.5. Preparation of phenyl macromolecules (7 and 8)

Compound **1** (0.50 g, 2.30 mmol) was dissolved in acetonitrile (50 mL). To this was added triethylamine (1.50 mL, 11.0 mmol). The resulting solution was stirred at reflux for 30 min and to the hot solution **4** (2.10 g, 7.00 mmol) was added and heating was continued for a further 24 h. After cooling, the solvent was removed under reduced pressure to afford a yellow oil, which was then purified by column chromatography on silica gel (initially at the ratio of chloroform/methanol 99:1, followed by the ratio 95:5).

*4.5.1. 5-Phenyl-2-(6-(5-(3-(2-(6-(5-phenyl-2H-tetrazol-2-yl)hexyl)-2H-tetrazol-5-yl)phenyl)-2H-tetrazol-2-yl)hexyl)-2H-tetrazole (**7**).* White solid (0.63 g, 41%), mp 107–109 °C. Found: C, 60.75; H, 5.73; N, 33.44. $C_{34}H_{38}N_{16}$ requires C, 60.88; H, 5.71; N, 33.41%; R_f (99:1 chloroform/methanol) 0.30; ν_{max} (KBr) 2920, 2851, 1648, 1527, 1465, 1263 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.93 (1H, s, Ph–H), 8.26 (2H, d, J=7.7 Hz, Ph–H), 8.13 (4H, d, J=7.7 Hz, Ph–H), 7.64 (1H, t, J=7.7 Hz, Ph–H), 7.47–7.46 (6H, m, Ph–H), 4.66 (8H, t, J=7.0 Hz, CH_2N), 2.09–2.08 (8H, m, CH_2), 1.46–1.45 (8H, m, CH_2); δ_C (75 MHz, $CDCl_3$) 165.1 (CN_4), 130.3, 129.6, 128.9, 128.5, 128.2, 127.4, 126.8, 125.2, 52.9 (CH_2N), 29.1, 25.7; HRMS (ES): $[M+1]^+$, found 671.3543. $C_{34}H_{39}N_{16}$ requires 671.3544.

*4.5.2. 5-Phenyl-2-(6-(5-(3-(1-(6-(5-phenyl-2H-tetrazol-2-yl)hexyl)-1H-tetrazol-5-yl)phenyl)-2H-tetrazol-2-yl)hexyl)-2H-tetrazole (**8**).* White solid (0.35 g, 23%), mp 111–114 °C. Found: C, 60.84; H, 5.68; N, 33.42. $C_{34}H_{38}N_{16}$ requires C, 60.88; H, 5.71; N, 33.41%; R_f (99:1 chloroform/methanol) 0.48; ν_{max} (KBr) 2927, 2855, 1618, 1528, 1465, 1261 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.44 (1H, s, Ph–H), 8.36 (1H, d, J=7.7 Hz, Ph–H), 8.13 (4H, d, J=7.7 Hz, Ph–H), 7.80 (1H, d, J=7.8 Hz, Ph–H), 7.69 (1H, t, J=7.8 Hz, Ph–H), 7.48–7.46 (6H, m, Ph–H), 4.65 (6H, t, J=7.1 Hz, CH_2N^2), 4.48 (2H, t, J=7.2 Hz, CH_2N^1), 2.06–2.05 (8H, m, CH_2), 1.41–1.40 (8H, m, CH_2); δ_C (75 MHz, $CDCl_3$) 165.5 (CN_4), 163.6 (CN_4), 153.9 (CN_4), 130.5, 130.3, 129.4, 128.9, 128.7, 127.4, 126.8, 126.7, 53.1 (CH_2N^2), 52.8 (CH_2N^2), 47.9 (CH_2N^1), 29.0, 25.7; HRMS (ES): $[M+1]^+$, 671.3545. $C_{34}H_{39}N_{16}$ requires 671.3544.

4.6. 2-(2-(6-(5-(3-(2-(6-(5-(Pyridin-2-yl)-2*H*-tetrazol-2-yl)hexyl)-2*H*-tetrazol-5-yl)phenyl)-2*H*-tetrazol-2-yl)-2*H*-tetrazol-5-yl))pyridine (9)

Compound **1** (0.10 g, 0.06 mmol) was dissolved in acetonitrile (50 mL). To this was added triethylamine (0.30 mL, 0.16 mmol). The resulting solution was stirred at reflux for 30 min and to the hot solution **5** (0.40 g, 0.18 mmol) was added and heating was continued for a further 24 h. After cooling and removal of inorganic solids, the solvent was removed under reduced pressure to afford a yellow oil, which was then purified by column chromatography on silica gel (initially at a ratio of chloroform/methanol 99:1, followed by the ratio 19:1). This gave the product **9** as a white solid (0.12 g, 28%), mp 88–90 °C. Found: C, 57.23; H, 5.41; N, 37.23. $C_{32}H_{36}N_{18}$ requires C, 57.13; H, 5.39; N, 37.48%; R_f (19:1 chloroform/methanol) 0.54; ν_{max} (KBr) 2965, 2851, 1629, 1515, 1452, 1249 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.92 (1H, s, Ph–H), 8.78 (2H, d, J=7.7 Hz, pyr-H), 8.26 (2H, d, J=7.7 Hz, pyr-H), 8.23 (2H, d, J=7.7 Hz, Ph–H), 7.89 (2H, t, J=7.7 Hz, pyr-H), 7.62 (1H, t, J=7.8 Hz, Ph–H), 7.41 (2H, t, J=7.7 Hz, pyr-H), 4.69 (8H, t, J=6.9 Hz, CH_2N), 2.11–2.10 (8H, m, CH_2), 1.46–1.45 (8H, m, CH_2); δ_C (75 MHz, $CDCl_3$) 164.8 (CN_4), 164.6 (CN_4), 150.3, 146.8, 137.1, 129.5, 128.5, 128.2, 125.2, 124.8, 122.0, 53.2 (CH_2N), 52.9 (CH_2N), 29.0, 25.7; HRMS (ES): $[M+1]^+$, found 673.3444. $C_{32}H_{37}N_{18}$ requires 673.3448.

4.7. Preparation of pyridyl macromolecules (10 and 11)

Compound **2** (1.40 g, 1.78 mmol) was dissolved in acetonitrile (50 mL) and to this was added triethylamine (1.20 mL, 8.90 mmol). The resulting solution was stirred at reflux for 30 min and to this was added **5** (1.70 g, 5.35 mmol). The solution was then refluxed for 24 h. After cooling, the solvent was removed under reduced pressure to afford a yellow oil, which was then purified by column chromatography on silica gel using the ratio of chloroform/methanol (99:1).

*4.7.1. 2-(2-(6-(5-(6-(2-(6-(5-(Pyridine-2-yl)-2H-tetrazol-2-yl)hexyl)-2H-tetrazol-5-yl)pyridin-2-yl)-2H-tetrazol-1-yl)hexyl)-2H-tetrazol-5-yl)pyridine (**10**).* White solid (0.10 g, 8%); mp 132–135 °C. Found: C, 55.22; H, 5.28; N, 39.48. $C_{31}H_{35}N_{19}$ requires C, 55.26; H, 5.24; N, 39.50%; R_f (99:1 chloroform/methanol) 0.70; ν_{max} (KBr) 2952, 1651, 1593, 1466, 1418, 1263 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.78 (2H, d, J=7.7 Hz, pyr-H), 8.35 (2H, d, J=7.6 Hz, pyr-H), 8.26 (2H, d, J=7.7 Hz, pyr-H), 8.05 (1H, t, J=7.7 Hz, pyr-H), 7.87 (2H, t, J=7.7 Hz, pyr-H), 7.40 (2H, br t, pyr-H), 4.72 (8H, t, J=6.9 Hz, CH_2N), 2.10–2.09 (8H, m, CH_2), 1.44–1.43 (8H, m, CH_2); δ_C (75 MHz, $CDCl_3$) 165.0 (CN_4), 164.4 (CN_4), 150.3, 147.5, 146.8, 138.3, 137.1,

124.8, 123.5, 122.4, 53.4 (CH_2N), 29.9, 29.2, 25.9; HRMS (ES): $[M]^+$, found 673.3379. $C_{31}H_{35}N_{19}$ requires 673.3323.

*4.7.2. 2-(2-(6-(5-(6-(2-(6-(5-(Pyridine-2-yl)-2H-tetrazol-2-yl) hexyl)-2H-tetrazol-5-yl)pyridin-2-yl)-1H-tetrazol-1-yl)hexyl)-2H-tetrazol-5-yl)pyridine (**11**).* White solid (0.12 g, 11%); mp 129–132 °C. Found: C, 55.20; H, 5.21; N, 39.53. $C_{31}H_{35}N_{19}$ requires C, 55.26; H, 5.24; N, 39.50%; R_f (99:1 chloroform/methanol) 0.74; ν_{max} (KBr) 2953, 2857, 1651, 1593, 1465, 1418, 1260 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.77 (2H, br d, pyr-H), 8.47 (1H, d, J=7.7 Hz, pyr-H), 8.32 (1H, d, J=7.7 Hz, pyr-H), 8.23 (2H, d, J=7.7 Hz, pyr-H), 8.07 (1H, t, J=7.8 Hz, pyr-H), 7.86 (2H, br t, pyr-H), 7.42 (2H, br t, pyr-H), 5.39 (2H, t, J=7.3 Hz, CH_2N^1), 4.70 (6H, t, J=7.4 Hz, CH_2N^2), 2.12–2.11 (8H, m, CH_2), 1.45–1.44 (8H, m, CH_2); δ_C (75 MHz, $CDCl_3$) 164.8 (CN_4), 164.7 (CN_4), 155.4 (CN_4), 150.3, 147.5, 146.8, 138.7, 137.1, 124.8, 124.2, 123.8, 122.3, 53.2 (CH_2N^2), 49.9 (CH_2N^1), 29.7, 29.0, 25.8, 25.6; HRMS (ES): $[M+1]^+$, found 674.3394. $C_{31}H_{36}N_{19}$ requires 674.3401.

4.8. Preparation of pyrazyl macromolecules (12 and 13)

Compound **3** (0.10 g, 0.64 mmol) was dissolved in acetonitrile (50 mL) and to this was added triethylamine (0.20 mL, 1.60 mmol). The resulting solution was stirred at reflux for 30 min and to this was added **6** (0.60 g, 1.90 mmol). The solution was then refluxed for 24 h. After cooling, the solvent was removed under reduced pressure to afford a yellow oil, which was then purified by column chromatography on silica gel using the ratio of chloroform/methanol (99:1).

*4.8.1. 2,3-Bis(2-(6-(5-(pyrazin-2-yl)-2H-tetrazol-2-yl)hexyl)-2H-tetrazol-5-yl)pyrazine (**12**).* Yellow oil (0.09 g, 8%). Found: C, 49.76; H, 4.71; N, 45.48. $C_{28}H_{32}N_{22}$ requires C, 49.70; H, 4.77; N, 45.54%; R_f (99:1 chloroform/methanol) 0.35; ν_{max} (KBr) 2923, 2852, 1653, 1534, 1455, 1260 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 9.48 (2H, s, pyz-H), 8.88 (2H, s, pyz-H), 8.74 (2H, br d, pyz-H), 8.71 (2H, br d, pyz-H), 4.74 (4H, t, J=7.1 Hz, CH_2N), 4.69 (4H, t, J=7.1 Hz, CH_2N), 2.11–2.10 (8H, m, CH_2), 1.45–1.44 (8H, m, CH_2); δ_C (75 MHz, $CDCl_3$) 162.7 (CN_4), 162.4 (CN_4), 145.7, 144.9, 144.8, 143.8, 142.8, 142.6, 53.4 (CH_2N), 53.2 (CH_2N), 29.0, 25.7; HRMS (ES): $[M+1]^+$, found 677.3261. $C_{28}H_{33}N_{22}$ requires 677.3259.

*4.8.2. 2-(1-(6-(5(-(Pyrazine-2-yl)-2H-tetrazol-2-yl)hexyl)-1H-tetrazol-5-yl)-3-(2-(6-5-(pyrazin-2-yl)-2H-tetrazol-2-yl)hexyl)-2H-tetrazol-5-yl)pyrazine (**13**).* Yellow oil (0.09 g, 8%). Found: C, 49.74; H, 4.83; N, 45.60. $C_{28}H_{32}N_{22}$ requires C, 49.70; H, 4.77; N, 45.54%; R_f (99:1 chloroform/methanol) 0.40; ν_{max} (KBr) 2926, 2854, 1653, 1536, 1465, 1261 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 9.48 (2H, s, pyr-H), 8.97 (1H, d, J=7.7 Hz, pyz-H), 8.88 (1H, d, J=7.7 Hz, pyz-H), 8.74 (2H, br d, pyz-H), 8.70 (2H, br d, pyz-H), 4.74 (4H, t, J=6.9 Hz, CH_2N^2), 4.63 (2H, t, J=6.8 Hz, CH_2N^2), 4.53 (2H, t, J=7.1 Hz, CH_2N^1), 2.08–2.07 (8H, m, CH_2), 1.41–1.40 (8H, m, CH_2); δ_C (75 MHz, $CDCl_3$) 162.8 (CN_4), 162.4 (CN_4), 151.4 (CN_4), 145.9, 145.8, 145.7, 144.7, 144.5, 143.8, 143.0, 142.9, 53.4 (CH_2N^2), 48.2(CH_2N^1), 29.2, 29.0, 28.9, 25.5; HRMS (ES): $[M+1]^+$, found 677.3258. $C_{28}H_{33}N_{22}$ requires 677.3259.

4.9. Metal complexes of 9

To a chloroform solution (10 mL) of **9** (0.02 g, 0.03 mmol) was added a solution of the appropriate metal salt (0.03 mmol) in methanol (5 mL). The resulting highly coloured solution was stirred at room temperature for 1 h. It was then allowed to stand for several days, which resulted in highly coloured solids, which were removed by filtration.

*4.9.1. [Cu_2(**9**)Cl_4].* Dark green solid (0.02 g, 65%); mp >300 °C. Found: C, 41.12; H, 3.76; N, 26.92. $C_{32}H_{36}Cl_4Cu_2N_{18}$ requires C, 40.82; H, 3.85; N, 26.77%; ν_{max} (KBr) 2957, 2854, 1669, 1522, 1460, 1363, 1262 cm^{-1}; μ_{eff} 2.8 B.M.; UV–vis (MeOH): 760 nm, ε=70 M^{-1} cm^{-1}.

*4.9.2. [Co(**9**)$(SCN)_2$].* Dark blue solid (0.02 g, 65%); mp >300 °C. Found: C, 45.12; H, 4.35; N, 31.12. $C_{34}H_{36}CoN_{20}S_2$ requires C, 45.03; H, 4.00; N, 30.89%; ν_{max} (KBr) 2957, 2854, 2073, 1606, 1502, 1459, 1380, 1248 cm^{-1}; μ_{eff} 4.4 B.M.; UV–vis (MeOH): 751 nm, ε=32 M^{-1} cm^{-1}; 508 nm, ε=65 M^{-1} cm^{-1}.

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