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Oligoethyl ether derivatives of ester functionalised nickel(II) macrocycles

Michaele J. Hardie,[a] Nino Malic,[b] Peter J. Nichols[b] and Colin L. Raston[a,*]

[a]*School of Chemistry, University of Leeds, Leeds LS2 9JT, UK*
[b]*School of Chemistry, Monash University, Clayton 3800, Melbourne, Australia*

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Abstract—γ,γ′-Ester functionalisation of the macrocycle 5,7,12,14-tetramethyldibenzo[*b*,*i*]-1,4,8,11-tetraazacyclotetradecinenickel-(II) (Ni(TMTAA)), using two alternative methods, either based on oxalyl chloride or 'triphosgene', has been effective in the synthesis of novel cyclic crown ether-type molecules containing a rigid, saddle shaped nickel(II) macrocycle and an oligoethyl ether chain. Mono-ester derivatisation using triphosgene allows access to compounds with two Ni(TMTAA) units bridged by oligoethyl ethers of various chain length.

The macrocycle (5,7,12,14-tetramethyldibenzo[*b*,*i*]-1,4,8,11-tetraazacyclotetradecine-nickel(II) (Ni(TMTAA)) **1** is a versatile supramolecular tecton, which can act as a divergent receptor.[1–5] Host–guest complexes with neutral globular molecules such as C_{60}, *o*-carborane, and P_4(S or Se)$_3$ are well known,[1,2] and it has recently been shown to form complexes with globular superions such as alkali metal cryptate salts of cobalt(III) bis(dicarbollide)[4] and carborane.[5]

The synthesis of modified Ni(TMTAA) through substitution at the γ,γ′ positions has been extensively researched,[6–8] and involves reaction with acid chlorides.[7,8] In view of the above rich supramolecular chemistry of Ni(TMTAA), addition of pendant functional groups through such substitution reactions offers an attractive method for the synthesis of novel receptors of higher complexity. Our attention has been directed towards the synthesis of ester derivatives of Ni(TMTAA) as a versatile method for the addition of extended functionality. We note that a similar procedure has recently been reported in which pendant alkoxycarbonyl and aryloxycarbonyl substituents have been attached to dibenzotetraaza[14]annulenes.[8] Herein, we report the synthesis of Ni(TMTAA) di-ester derivatives bearing oligoethyl ether groups as novel crown ether-type molecules along with mono-ester derivatives where two Ni(TMTAA) units are bridged by oligoethyl ether units.

Functionalisation of **1** involves multi-step in situ procedures with an implied acid chloride intermediate, **3** (Scheme 1). Two equivalents of oxalyl chloride react with **1** forming what is believed to be a glyoxyl chloride derivative **2**, which undergoes a thermally induced decarbonylation, losing two molecules of carbon monoxide, en route to **3**. Analogous reactions utilising oxalyl chloride to introduce chlorocarbonyl groups onto aromatic systems are usually carried out in the presence of a Friedel–Crafts catalyst.[9] However, examples of chlorocarbonylation of both aromatic and non-aromatic systems where this catalyst is not necessary are also known.[10] An alternative synthesis of **3** using 'triphosgene' (bis(trichloromethyl) carbonate)[11] (Scheme 1) avoids heating the reaction mixture. Triphosgene in the presence of a nucleophile breaks down to form phosgene in situ.[11] It is thus a convenient and safer[12] alternative to the use of oxalyl chloride and indeed phosgene itself.

Addition of tetraethylene glycol, pentaethylene glycol or hexaethylene glycol to **3**, in situ, under high dilution conditions, affords, after chromatography, the corresponding cyclic oligoethyl ether derivatives **4a**,**b**,**c** in 9, 26 and 39% yields, respectively.[13] ^{1}H NMR show a characteristic spectra indicative of the symmetry of the molecules. This is also evident in the ^{13}C NMR spectra which show the carbonyl carbons as a single downfield peak at about 171.5 ppm. The ESI mass spectra show the singly charged, protonated molecular ions [(M+H$^+$)] with the expected isotopic patterns.

* Corresponding author. Tel.: +44 0113 233 6555; fax: +44 0113 233 6401; e-mail: c.l.raston@chem.leeds.ac.uk

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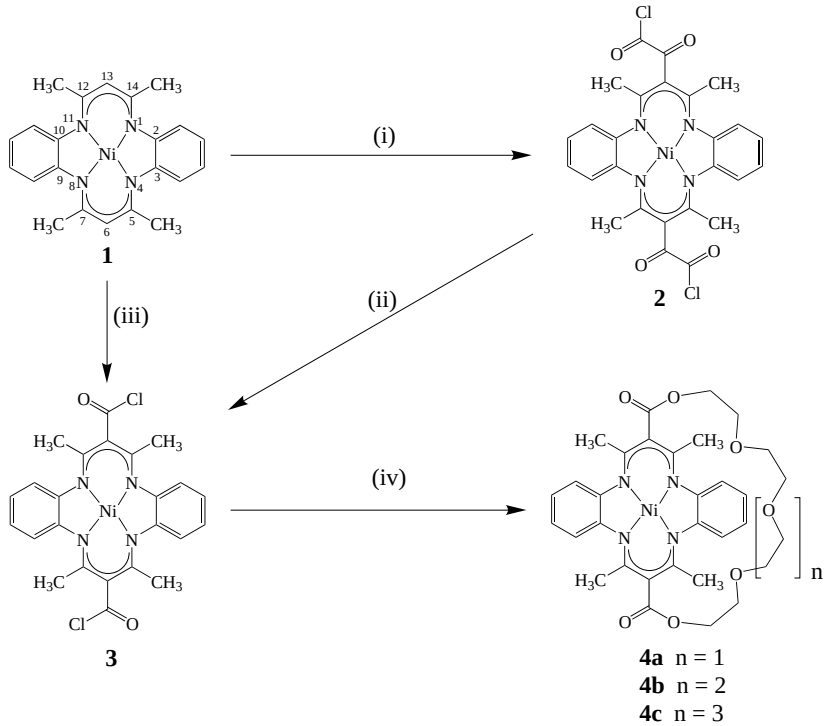
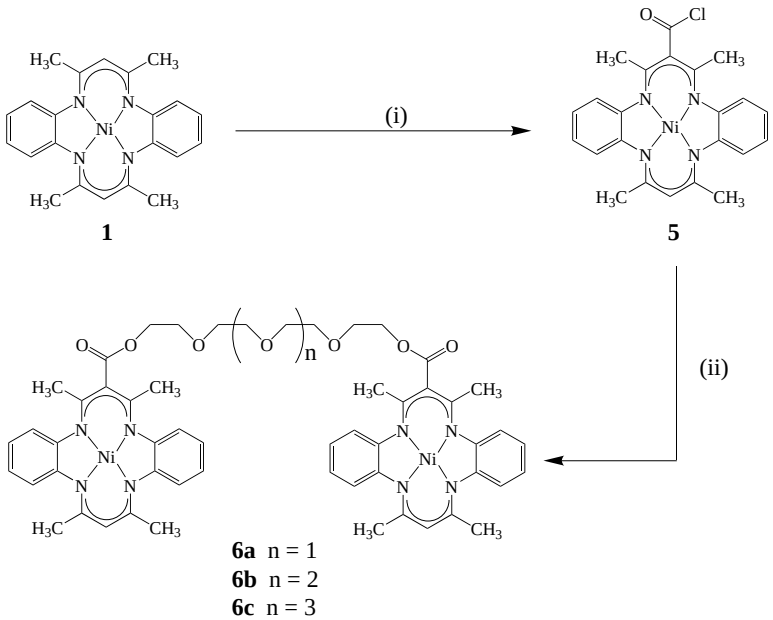


Scheme 1. *Reagents and conditions*: (i) Oxalyl chloride, anhydrous THF, pyridine, rt, 15 min; (ii) 50°C, 30 min; (iii) triphosgene (2/3 equiv.), anhydrous THF, pyridine, 0°C, 30 min; (iv) (tetra, penta, and hexa)-ethylene glycol, rt.

Modification of the above triphosgene procedure enables the synthesis of mono-ester derivatives of Ni(TMTAA), notably **6a**,**b**,**c**[14] in 26, 31 and 24% yields, respectively (Scheme 2). However, attempts to synthesise **6a**–**c** using oxalyl chloride did not succeed. Presumably the high reactivity of oxalyl chloride with Ni(TMTAA) does not allow for a homogeneous mixture of reactants prior to reaction, thus affecting the formation of the desired mono-substituted intermediate **5**. The use of triphosgene, on the other hand, would allow for greater homogeneity of reactants since it must interact with a nucleophile prior to its decomposition to phosgene.[11]

^{1}H NMR spectra for the dimers **6a**–**c** are more complex, and are consistent with mono-substituted Ni(TMTAA) derivatives. The ESI mass spectra shows protonated molecular ions [(M+H$^+$)] for all three dimers.



Scheme 2. *Reagents and conditions*: (i) THF, triphosgene (1/3 equiv.), pyridine, 0°C, 30 min; (ii) (tetra, penta, and hexa)-ethylene glycol, rt.

Crystals suitable for X-ray structure elucidation were obtained for **4a** and **4c**.[15] Those of **4a** were grown from CH_2Cl_2/hexane. Its structure shows the 'saddle' shape of the Ni(TMTAA) moiety with the tetraethyl ether spanning the methyl-faced concave surface. Two CH_2Cl_2 molecules occupy the cavity with their hydrogens facing inwards and within hydrogen bonding distance (between 2.242 and 2.640 Å) to the tetraethyl ether oxygens (Fig. 1). CH_2Cl_2 molecules also occupy space between individual molecules within the crystal lattice. Overall, the asymmetric unit is comprised of two unlike molecules of **4a** and seven molecules of CH_2Cl_2. The two individual units of **4a** are different due to the way the CH_2Cl_2 molecules are hydrogen bonded to the tetraethyl ether oxygens. One unit adopts a more symmetrical conformation with a bifurcated H-bond to the central tetraethyl ether oxygen, whilst the other unit is more distorted with single hydrogen bonds to alternating oxygens (Fig. 1). Complementarity of curvature plays a role in the way the individual molecules pack together, interplay being between the curved surfaces of the tetraethyl ether unit of one molecule and the benzo-faced concave domain of another.

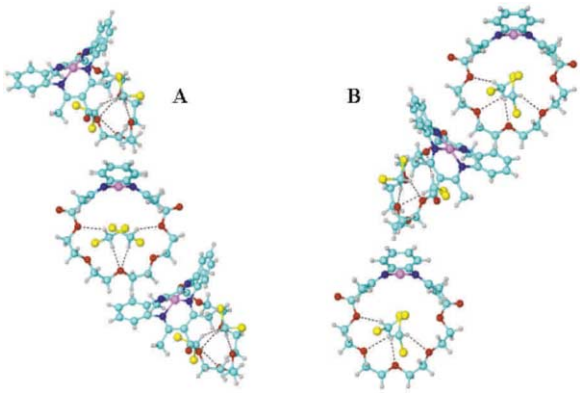


Figure 1. Structure of **4a** showing molecules with the symmetrical H-bonding of CH_2Cl_2 (**A**) and unsymmetrical H-bonding (**B**).

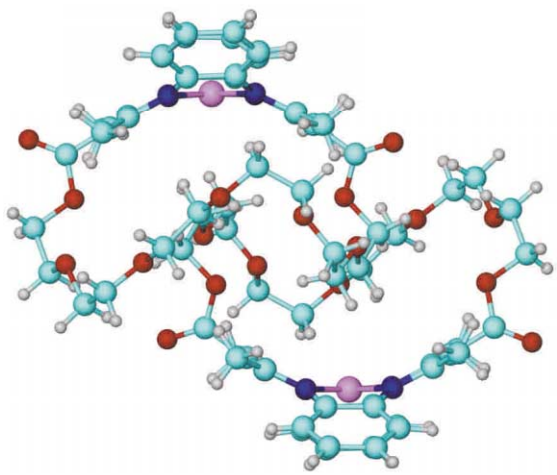


Figure 2. Two symmetrically interlocking units of **4c**.

Crystals of **4c** were grown from acetonitrile/water. Its structure displays a folded conformation of the bridging hexaethyl ether component, which interacts and symmetrically interlocks with the hexaethyl ether component of a second molecule of **4c** (Fig. 2). There are no solvent molecules found within the cyclic ether or in the lattice. The folded conformation of the bridging hexaethyl ether chain suggests that it possesses significant flexibility, but this is not the case for **4a** in which there is some strain associated with the C(carbonyl)–C(macrocycle) bonds (torsion angle:[†] unsymmetrical **4a**, 170.24 and 176.32°; symmetrical **4a**, 173.61 and 173.12°). This is also a possible contributing factor to the overall low yield obtained for **4a**.

Application of these molecules as receptors for metal cations, particularly those of the group one elements such as sodium and potassium is currently being investigated. They may be regarded as new crown ether-type molecules of varying cavity size. The use of the synthetic procedures outlined herein have potential for the synthesis of other novel Ni(TMTAA) based receptors of higher complexity.

Acknowledgements

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[†] Plane generated from five-membered rings (N^1–C^{11}–C^{12}–C^{13}–N^{14}–N^1) and (N^4–C^5–C^6–C^7–N^8–N^4) within macrocycle; angles calculated from (plane centroids)-$C^{6(13)}$–C(carbonyl).

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13. *Synthesis* of **4a**: (Caution! Oxalyl chloride is very toxic and corrosive. Wear appropriate protective clothing and carry out all procedures in a well ventilated hood.) **1** (500 mg, 1.25 mmol) was dissolved in anhydrous THF (ca. 150 ml) together with anhydrous pyridine (1 ml). Oxalyl chloride (1.25 ml of a 2 M solution in CH_2Cl_2, 2.50 mmol) was added dropwise with stirring at rt, under argon. The resulting deep red/brown solution was heated at 50°C for 1 h, after which time it had turned deep purple, and was then allowed to cool to rt. A solution of tetraethylene glycol (0.22 ml, 1.25 mmol) in anhydrous THF (ca. 3 ml) was added dropwise with gentle stirring over 15–20 min. The mixture was allowed to stir for an additional 2 h, then filtered and the solvent was evaporated. The residue was purified by column chromatography (silica, ethyl acetate, loaded onto column with a minimum amount of CH_2Cl_2). The purple fraction was collected and the solvent was evaporated to give **4a** as a deep purple/green solid. Yield: 0.070 g (9%). Mp 297°C. $2(C_{32}H_{36}N_4NiO_7)\cdot 3CH_2Cl_2$ (loss of solvent CH_2Cl_2) requires: C, 51.93; H, 5.07; N, 7.23. Found: C, 51.91; H, 4.93; N, 7.28%. ^{1}H NMR (300 MHz, C_6D_6, 298 K) δ 1.85 (s, 12H; CH_3), 3.25 (m, 4H; $CO_2CH_2CH_2$), 3.37 (t, ^3J= 5.6 Hz, 4H; CH_2O), 3.58 (t, ^3J=5.6 Hz, 4H; CH_2O), 4.14 (m, 4H; $CO_2CH_2CH_2$), 6.38 (m, 8H; ArH). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 298 K) δ 19.2, 64.9, 69.7, 70.3, 70.9, 118.0, 121.5, 123.0, 146.8, 154.9, 171.0 (C=O). IR (KBr): ν 2868, 1714 (C=O), 1543, 1386, 1204, 1081, 751 cm^{-1}. ESI-MS (ES$^+$, 30 v) m/z 647.2 [(M+H)$^+$]. (Compounds **4b** and **4c** were prepared as described for **4a**.) **4b** was isolated as a dark green microcrystalline solid in 26% yield. Mp 316°C. $C_{34}H_{40}N_4NiO_8$ requires: C, 59.06; H, 5.83; N, 8.10. Found: C, 58.98; H, 5.58; N, 7.81%. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K) δ 2.06 (s, 12H; CH_3), 3.64–3.70 (m, 4H; $CO_2CH_2CH_2$), 3.74–3.78 (m, 12H; CH_2O), 4.29 (m, 4H; CO_2CH_2), 6.62 (m, 8H; ArH). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 298 K) δ 19.4, 65.0, 69.1, 70.3, 71.0, 71.1, 117.7, 121.6, 122.8, 147.0, 154.0, 171.3 (C=O). IR (KBr): ν 2872, 1713 (C=O), 1541, 1384, 1208, 1078, 756 cm^{-1}. ESI-MS (ES$^+$, 25 v) m/z 691.3 [(M+H)$^+$]. **4c** was isolated as a dark green microcrystalline solid in 39% yield. Mp 299.5°C. $C_{36}H_{44}N_4NiO_9$ requires: C, 58.79; H, 6.03; N, 7.62. Found: C, 58.79; H, 5.99; N, 7.48%. ^{1}H NMR (300 MHz, $CDCl_3$, 298 K) δ 2.08 (s, 12H; CH_3), 3.52–3.55 (m, 4H; CH_2O), 3.64–3.67 (m, 12H; CH_2O), 3.75 (m, 4H; $CO_2CH_2CH_2$), 4.33 (m, 4H; $CO_2CH_2CH_2$), 6.62 (m, 8H; ArH). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 298 K) δ 19.5, 64.5, 68.8, 70.3, 70.6, 70.7, 70.9, 117.5, 121.6, 122.6, 147.1, 154.1, 171.3 (C=O). IR (KBr): ν 2868, 1711 (C=O), 1540, 1383, 1208, 1077, 756 cm^{-1}. ESI-MS (ES$^+$, 25 v) m/z 735.4 [(M+H)$^+$].
14. *Synthesis* of **6a**: **1** (300 mg, 0.75 mmol) was dissolved in anhydrous THF (30 ml) containing anhydrous pyridine (0.25 ml, 3.10 mmol) and the solution was cooled to 0°C. A solution of triphosgene (74 mg, 25.0 mmol) in anhydrous THF (5 ml) was added dropwise with stirring. Stirring was then continued for 2 h at 0°C under nitrogen before allowing the solution to reach rt. Anhydrous tetraethylene glycol (0.073 g, 0.065 ml, 0.38 mmol) was added dropwise with vigorous stirring and the mixture was allowed to stir for an additional 2 h before being filtered and the solvent evaporated. The residue was purified by column chromatography (silica, ethyl acetate) to yield a dark green microcrystalline solid (105 mg, 26%). Mp 169–172°C. $C_{54}H_{58}N_8Ni_2O_7\cdot CH_2Cl_2$ requires: C, 58.28; H, 5.34; N, 9.89. Found: C, 58.94; H, 5.53; N, 9.53%. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ 2.03 (s, 12H; CH_3), 2.08 (s, 12H; CH_3), 3.63 (s, 8H; OCH_2), 3.73 (t, ^3J=4.8 Hz, 4H; $CO_2CH_2CH_2$), 4.31 (t, ^3J=4.8 Hz, 4H; CO_2CH_2), 4.78 (s, 2H; CH), 6.51–6.68 (m, 16H; ArH). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, 298 K) δ 19.86, 21.85, 63.96, 69.00, 70.47, 70.63, 111.10, 117.00, 120.71, 121.57, 121.77, 122.83, 147.12, 147.18, 154.25, 155.22, 171.49 (C=O). IR (KBr) ν 1706 (C=O) 1637, 1617, 1539, 1456, 1434, 1389, 1218, 1064, 748 cm^{-1}. ESI-MS (ES$^+$, 50 v) m/z 1047.4 [(M+H)$^+$]. (Compounds **6b** and **6c** were prepared as described for **6a**.) **6b** was isolated as a dark green microcrystalline solid in 31% yield. Mp 148°C. $C_{56}H_{62}N_8Ni_2O_8$ requires: C, 61.56; H, 5.72; N, 10.26. Found: C, 60.25; H, 5.44; N, 10.79%. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ 2.03 (s, 12H; CH_3), 2.09 (s, 12H; CH_3), 3.59–3.65 (overlapping peaks, 12H; OCH_2), 3.75 (t, ^3J=4.8 Hz, 4H; $CO_2CH_2CH_2$), 4.32 (t, ^3J=4.8 Hz, 4H; CO_2CH_2), 4.79 (s, 2H; CH), 6.54–6.69 (m, 16H; ArH). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, 298 K) δ 19.85, 21.84, 63.96, 68.98, 70.45, 70.56, 70.59, 111.10, 116.99, 120.71, 121.56, 121.76, 122.82, 147.12, 147.17, 154.24, 155.22, 171.49 (C=O). IR (KBr) ν 1705 (C=O), 1638, 1618, 1540, 1457, 1389, 1219, 1065, 747, 618, 473 cm^{-1}. ESI-MS (ES$^+$, 70 v) m/z 1091.4 [(M+H)$^+$]. **6c** was isolated as a dark green microcrystalline solid in 24% yield. Mp 125°C. $C_{58}H_{66}N_8Ni_2O_9$ requires: C, 61.29; H, 5.85; N, 9.86. Found: C, 61.38; H, 5.72; N, 9.89%. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ 2.01 (s, 12H; CH_3), 2.08 (s, 12H; CH_3), 3.58–3.63 (overlapping peaks, 16H; OCH_2), 3.74 (t, ^3J=4.8 Hz, 4H; $CO_2CH_2CH_2$), 4.31 (t, ^3J=4.8 Hz, 4H; CO_2CH_2), 4.76 (s, 2H; CH), 6.52–6.66 (m, 16H; ArH). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz, 298 K) δ 19.90, 21.87, 64.00, 69.03, 70.51, 70.57, 70.61, 70.62, 111.13, 117.03, 120.75, 121.60, 121.81, 122.86, 147.17, 147.22, 154.31, 155.26, 171.53 (C=O). IR (KBr) ν 1705 (C=O), 1540, 1457, 1435, 1389, 1218, 1065, 746 cm^{-1}. ESI-MS (ES$^+$, 70 v) m/z 1134.3 [(M+H)$^+$].
15. *Crystal data* for compounds **4a** and **4c** (in parentheses): $C_{71}H_{86}Cl_{14}N_8Ni_2O_{14}$ [$C_{36}H_{44}N_4NiO_9$], M_r=1889.20 [735.46], monoclinic, $P2_1$ ($P2_1/n$), a=11.833(2) [11.5443(1)], b=20.358(4) [16.5026(2)], c=17.240(3) [18.8129(3)] Å, β=91.67(3) [97.080(1)]°, V=4151.3(14)

[3556.74(8)] Å^3, $D_{calcd} = 1.511$ [1.373] g cm^{-3}, $\mu = 0.969$ (0.605) cm^{-1} (no correction), $Z = 2$ (4), $T = 123(2)$ K, 57297 (47103) reflections collected, 23648 (8810) unique reflections, $R_{int} = 0.0780$ (0.051), $\theta_{max} = 30.02$ (28.29)°, [14792 (6855) observed, $I > 2\sigma(I)$, 991 (627) parameters, one restraint (no restraints), $R_1 = 0.0735$ (0.0402), $wR_2 = 0.1904$ (0.0769)], $S = 1.045$ (1.014). X-Ray data were collected on an Enraf–Nonius Kappa CCD single-crystal diffractometer with Mo-Kα radiation ($\lambda = 0.71073$ Å). The structures were solved by direct methods with SHELXS-97 and refined by full-matrix least-squares on F^2 using SHELXL-97. All non-hydrogen atoms were refined anisotropically, and hydrogens were included at geometrically estimated positions for **4a** and fully refined for **4c**.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 166422 and 166423. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0) 1223-336033 or email: deposit@ccdc.cam.ac.uk].