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Synthesis of Chiral Atropoisomeric Square-planar Nickel(II) and Copper(II) Complexes formed by Macrocyclic Ligands containing Pendant Polyether Groups and a Quaternary Ammonium Group†

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Novel copper(II) and nickel(II) complexes of macrocyclic Schiff bases formed from derivatives of *N,N'*-bis(2-benzoylphenyl)oxamide and 1,2-diaminoethane have been prepared. In one case, separation of atropoisomeric chiral complexes has been achieved by preparative chromatography on SiO_2. Quaternization of some of the complexes with an excess of MeI affords chiral complexes possessing a positively charged quaternary ammonium group and polyether podands in addition to a weakly electrophilic metal site.

The use of classical transition-metal complexes of N- and/or O-donor ligands as effective and sometimes stereospecific catalysts of oxidation,[1] reduction,[2] hydrolysis,[3] and other transformations of organic compounds[4] is a challenging area of both organic and inorganic chemistry. One of many possible avenues of exploration in this field could be the design and synthesis of transition-metal complexes bearing additional functional side groups incapable of interaction with the central metal ion but capable of non-covalent interactions with an organic substrate.[5] The formation of such a metal complex–substrate supramolecular architecture follows the same principles that underlie biological substrate–receptor interactions. By varying the structure of the side groups one can create a receptor system 'tailored' for a particular type of substrate and even be able to bring the substrate into a catalytically effective position relative to the central metal ion. Another area of application of these systems could be in various classes of inclusion chemistry, the obvious examples being various transport and separation processes.

The present work describes the syntheses and properties of some novel neutral complexes of Ni^{II} and Cu^{II} (**1a**)—(**1e**), with macrocyclic Schiff bases, formed from the corresponding derivatives of *N,N'*-bis(2-benzoylphenyl)oxamide (**2a**) and (**2b**) and 1,2-diaminoethane (**3a**)—(**3c**), as well as the synthesis of novel charged complexes (**1f**)—(**1h**). The following paper will be concerned with the ability of complexes bearing polyether podands and a quaternary ammonium group to serve as effective carriers for amino acid anions from water into an organic phase in a biphasic system.

Results and Discussion

Synthesis of Macrocyclic Ligands.—Compound (**2a**) was prepared according to Scheme 1 by Friedel–Crafts acylation of *p*-(2-methoxyethoxy)toluene (**5**) with *N*-tosylanthraniloyl chloride (**6**) as the key stage, followed by the removal of the tosyl group in (**7**) and successive acylation of (**8**) with oxalyl chloride.

Compound (**2b**) was obtained from 2-amino-2'-methoxybenzophenone (**9**) (Scheme 2) by demethylation with HBr and subsequent successive treatment of 2-amino-2'-hydroxybenzophenone (**10**) with 10-(toluene-*p*-sulphonyloxy)-2,5,8-trioxadecane (**11**) and oxalyl chloride. An attempt to obtain (**2b**) according to Scheme 1 by Friedel–Crafts acylation of the corresponding *p*-tolylpolyether with (**6**) was unsuccessful.

(*R*)-1,2-Diamino-1-(*p*-nitrophenyl)ethane dihydrochloride (**3b**) and (*R*)-1,2-diamino-1-(*p*-aminophenyl)ethane trihydrochloride (**3c**) were obtained according to Scheme 3, starting from (*R*)-phenylglycine with an optical purity greater than 99%. Nitration of (*R*)-1,2-di(acetylamino)-1-phenylethane (**16**) with 90% HNO_3 gave a mixture of *o*- and *p*-nitro derivatives. The *para* isomer (**17**) was separated by crystallization, and its hydrogenation over Pd–Al_2O_3 in MeOH furnished (*R*)-1,2-di-(acetylamino)-1-(*p*-aminophenyl)ethane (**18**). Hydrolysis of (**17**) and (**18**) afforded (**3b**) and (**3c**).

Syntheses of Macrocyclic Complexes (**1**).—Complexes (**1a**)—(**1e**) were obtained by the condensation of appropriate compounds (**2a**) or (**2b**), (**3a**)—(**3c**), and a metal salt in MeOH solution in the presence of NaOMe. The charged complexes (**1f**)—(**1h**) were prepared by quaternizing the aniline nitrogen atom of (**1c**)—(**1e**) with an excess of methyl iodide. An attempt to prepare (**1c**) by direct catalytic hydrogenation of (**1b**) over Pd–Al_2O_3 at ambient temperature and pressure failed.

Atropoisomerism in Nickel(II) Complexes of Schiff Bases derived from Oxamide (**2a**) *and the Ethylenediamine Derivatives* (**3a**)—(**3c**).—Examination of molecular models of target Schiff-base complexes showed that these might exist as a mixture of atropoisomers. Atropoisomerism in organic chemistry is a well studied phenomenon.[6a,b] Atropoisomeric porphyrins and their metal complexes have recently been prepared and studied.[6b] The similarity between the metal porphyrin complexes and complexes (**1**) is obvious. Complex (**1a**), which was earlier prepared[7] from (**2a**), ethylenediamine (**3a**), and a nickel(II) salt, provides unequivocal evidence for the existence of isomerism. Two atropoisomers of (**1a**), stable at ambient temperature, were separated, and the *X*-ray crystal structure analysis of *cis*-(**1a**) was carried out[7] (see Figure 1). Two rotational barriers about the pivotal C–C bond for complex (**1i**), a simplified model of the target complexes, were found using the molecular mechanics approach.[8] The rotation transition-state enthalpies were calculated to be 10 and 20 kcal mol^{-1}, the first barrier reflecting steric interaction of the methoxy-substituent with the hydrogen substituents on the ethylenediamine moiety in one planar transition state of the atropoisomerization, and another derived from the interaction of the methoxy-substituent with the hydrogen substituent on the phenyl ring which is much more rigidly fixed than ethylenediamine in the macrocyclic framework of the complex. The barrier in (**1a**) might be greater,

† *Non-S.I. units employed:* cal = 4.184 J, mmHg ≈ 133 Pa.

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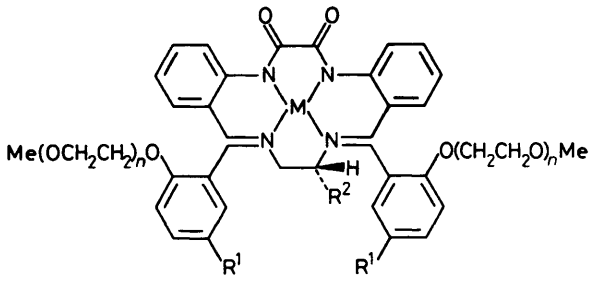
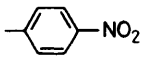
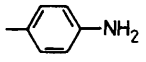
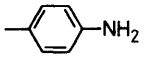
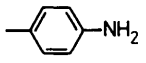
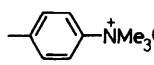
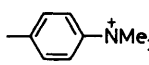
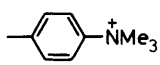
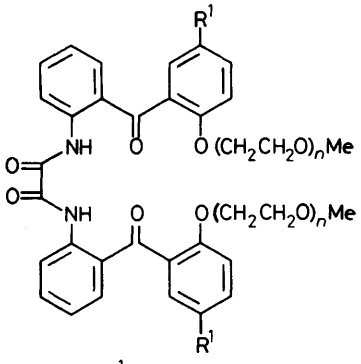
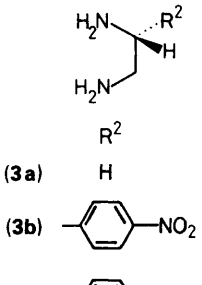
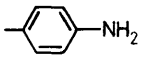


	R^1	R^2	n	M
(1a)	Me	H	1	Ni
(1b)	Me		1	Ni
(1c)	Me		1	Ni
(1d)	Me		1	Cu
(1e)	H		3	Ni
(1f)	Me		1	Ni
(1g)	Me		1	Cu
(1h)	H		3	Ni
(1i)	Me	H	0	Ni



	R^1	n
(2a)	Me	1
(2b)	H	3

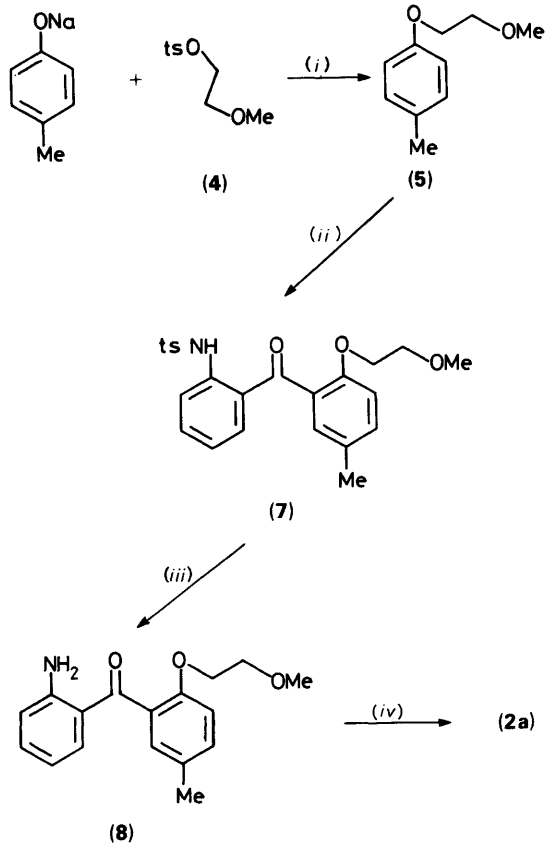


	R^2
(3a)	H
(3b)	
(3c)	

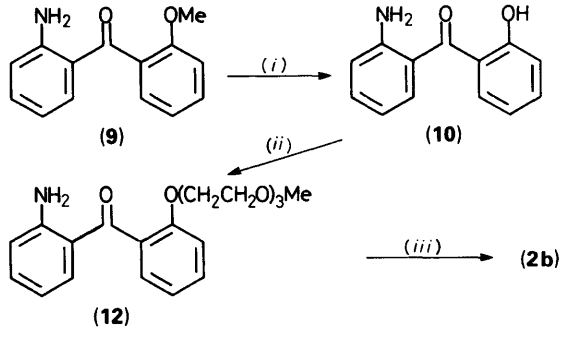
taking into account the larger size of the pendant group. This is supported by the fact that conversion of *cis*- or *trans*-(**1a**) to the equilibrium mixture of isomers proceeds slowly only in boiling toluene (110 °C) but not in boiling MeOH (64 °C) or MeCN (82 °C).

Complexes (**1b**)—(**1h**), in addition to the type of atropo-isomerism discussed above, have an asymmetric carbon atom, bringing the number of theoretically possible isomers to four (Figure 2). This prediction was supported by the ^{1}H n.m.r. spectra of the complexes in solution. Preparative t.l.c. on SiO_2 was employed to separate three of the four possible isomers of complex (**1b**); (**I**)—(**III**) (see Experimental section) in a ratio of 4 : 1 : 4. The fourth isomer was detected on the chromatogram only in trace amounts. Probably, this ratio reflects the kinetic selectivity of isomer formation.

The diastereoisomers of complex (**1b**) are red substances



Scheme 1. ts = Tosyl. (*i*) $MeOCH_2CH_2OH$; (*ii*) compound (**6**), $AlCl_3$; (*iii*) H_2SO_4; (*iv*) $(COCl)_2$



Scheme 2. (*i*) HBr, $MeCO_2H$; (*ii*) $tsO(CH_2CH_2O)_3Me$ (**11**), K_2CO_3; (*iii*) $(COCl)_2$

having almost identical electronic spectra and similar optical rotatory dispersion (o.r.d.) curves (Figure 3). Significant differences were observed in the ^{1}H n.m.r. spectra of the isomers, which were used to assign their configuration.

The diamagnetic ring current of the *p*-nitrophenyl ring in complex (**1b**) causes upfield shifts of those signals of the aryl methyl and MeO groups which occur on the same side of the co-ordination plane and are influenced by the shielding zone of the *p*-nitrophenyl substituent (Figure 2). Chemical shifts of the corresponding groups in (**1a**) serve as a reference point. The magnitude of the shift is inversely proportional to the distance from the substituents to the *p*-nitrophenyl ring. On this basis an α-*trans*, β-*trans* configuration was assigned to isomer (**III**) of (**1b**), α-*trans*, β-*cis* to (**II**), and α-*cis*, β-*trans* to (**I**).

According to their ^{1}H n.m.r. spectra, the charged nickel(II) complexes (**1f**) and (**1h**) constitute a mixture of isomers, and there is no doubt that (**1g**) is also a mixture. Unfortunately, we

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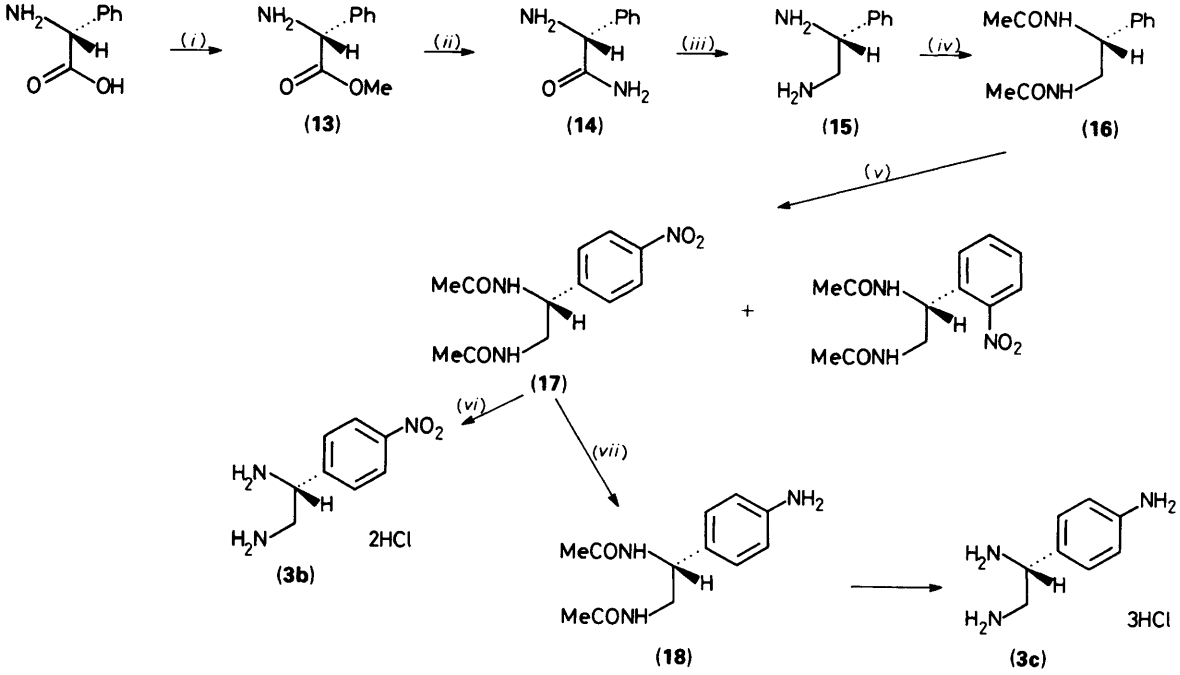

Scheme 3. (*i*) $SOCl_2$, MeOH; (*ii*) concentrated NH_3; (*iii*) $LiAlH_4$; (*iv*) $(MeCO)_2O$; (*v*) HNO_3; (*vi*) HCl, water; (*vii*) H_2, $Pd–Al_2O_3$

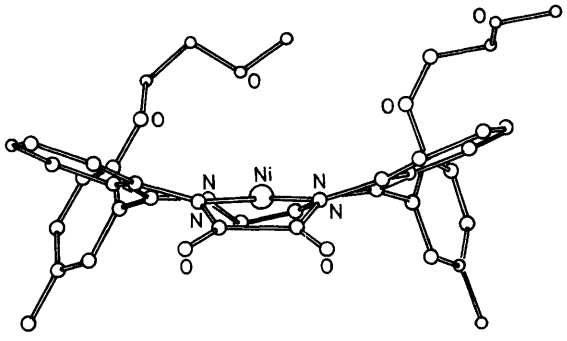

Figure 1. Perspective drawing of complex *cis*-(**1a**), derived from *X*-ray analysis data taken from ref. 7

were unable to achieve a satisfactory separation of the isomeric complexes (**1f**)—(**1h**), and further work with the compounds (see the following paper) was carried out using their isomeric mixtures.

Conclusion

The synthesis of a new type of chiral atropoisomeric macrocyclic complex possessing a rigidly fixed weak electrophilic metal site, a positively charged quaternary ammonium group, and polyether podands has been reported. The stereochemical assortment of the groups may provide the necessary architecture for selective binding of a negatively charged substrate possessing both electrophilic and nucleophilic sites. Biologically important anions, such as those of α-hydroxycarbonic and α-amino acids, seem to be the most likely candidates for molecular recognition by this type of complex.

Experimental

Instrumental Techniques.—Proton n.m.r. spectra were recorded on Tesla-NMR-BS-467A (60 MHz) and Brucker WP-200 (200 MHz) instruments; hmds was used throughout as an internal reference for $CDCl_3$ solutions, and hmds sealed in a glass capillary was used for D_2O solutions. U.v.–visible spectra were obtained with a Specord M-40 spectrophotometer and o.r.d. curves with a JASCO ORD/UV-5 instrument. Optical rotations were measured on a Perkin-Elmer 241 polarimeter.

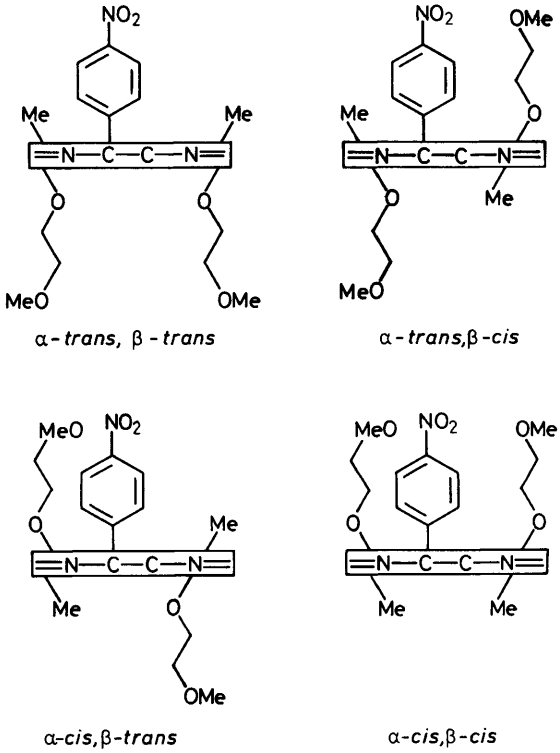

Figure 2. Schematic representation of the four isomers of complex (**1b**); *cis* and *trans* isomers are designated according to the relative orientation of the podands and the 4-nitrophenyl substituent

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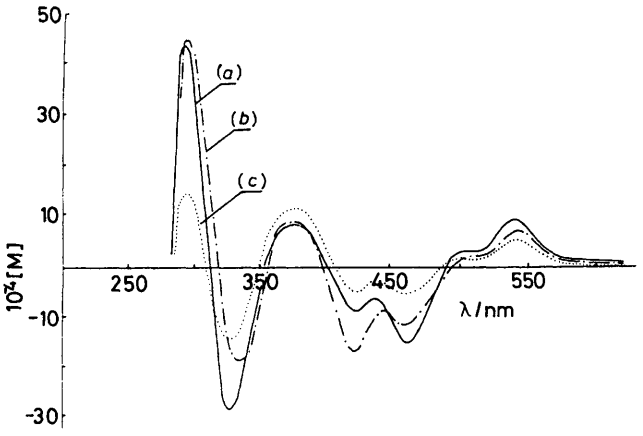

Figure 3. O.r.d. curves for individual isomers of complex (**1b**) in ethanol solution at 25 °C: (*a*) (**I**); (*b*) (**II**); and (*c*) (**III**)

The molecular mechanics calculations for complex (**1i**) were performed using program MOLBD-3[9] on a Soviet-made ES-1061 minicomputer. The minimization of the calculated energy was carried out for several conformations of one of the two 2-methoxy-5-methylphenyl substituents relative to the main co-ordination plane of the complex; 20° steps of rotation about the pivotal C–C bond were taken.

Materials.—All the reagents were supplied by Reakhim (U.S.S.R), except for $HO(CH_2)_2O(CH_2)_2O(CH_2)_2OMe$ (Fluka), 2-aminobenzophenone (Merck), and (*R*)-phenylglycine (Reanal, Budapest), which had an optical purity of 99%, as confirmed by enantiomeric g.l.c. analysis (for a description of the method see ref. 10). DC-Plastifikfolien Kieselgel 60 F_{254} and Kieselgel 60 F_{254} (Merck) were used for t.l.c. and preparative t.l.c., respectively, and silica gel L40/100 (Chemapol, Prague) for column chromatography. Sephadex LH-20 was from Pharmacia (Sweden), and anionite Dowex MSA-1 (Serva) was employed for anion exchange of the charged complexes.

Methanolic solutions of NaOMe were prepared by dissolving metallic sodium in MeOH under Ar. Concentrated HNO_3 was prepared according to ref. 11.

N-Tosylanthranilic acid was prepared by condensation of anthranilic acid and toluene-*p*-sulphonyl chloride, according to ref. 12, and had m.p. 223—225 °C (from EtOH–water) (lit.,[12] 229—230 °C). Oxalyl chloride was prepared from oxalic acid and PCl_5,[13] b.p. 62 °C (lit.,[13] 64 °C). *N*-Tosylanthraniloyl chloride (**6**) was prepared from *N*-tosylanthranilic acid and PCl_5,[14] m.p. 126—129 °C (lit.,[14] 128—129 °C). 2-Amino-2′-methoxybenzophenone (**9**) was obtained according to a procedure described previously[15] and had m.p. 108—110 °C (from EtOH–water) (lit.,[15] 109—111 °C).

4-(Toluene-*p*-sulphonyloxy)-2-oxabutane (**4**) and 10-(toluene-*p*-sulphonyloxy)-2,5,8-trioxadecane (**11**) were prepared according to the general method.[16] Compound (**4**): b.p. 142—144 °C (1 mmHg) (lit.,[17] 168 °C, 3 mmHg); n_{589}^{25} 1.5090 (lit.,[18] 1.5085); $\delta_H(CDCl_3)$ 2.27 (3 H, s, aryl CH_3), 3.10 (3 H, s OCH_3), 3.43 (2 H, t, CH_2), 4.03 (2 H, t, CH_2), 7.13 and 7.60 (4 H, AA′XX′, J = 20 Hz, aryl). Compound (**11**) was obtained as a viscous oil and used further without purification; $\delta_H(CCl_4)$ 2.23 (3 H, s, aryl CH_3), 3.1 (3 H, s, OCH_3), 3.16—3.96 (12 H, m, CH_2), 7.0 and 7.46 (4 H, AA′XX′, J = 7.8 Hz, aryl H).

p-(2-*Methoxyethoxy*)*toluene* (**5**). To a solution of *p*-cresol (7 g, 65 mmol) in methylcelozolve (50 cm^3), metallic sodium (1.5 g, 65 mmol) was added with cooling under Ar. When the dissolution of sodium was complete, compound (**4**) (10 g, 46 mmol) was added and the mixture refluxed for 10—11 h, then cooled and poured into an aqueous NaOH solution. The mixture was extracted several times with diethyl ether. The extracts were combined, washed with a 7% aqueous NaOH solution, dried over Na_2CO_3, and evaporated. The residue was distilled to yield compound (**5**) (5 g, 67%), b.p. 235—237 °C (lit.,[19] 230 °C); n_{589}^{20} 1.5070; $\delta_H(CDCl_3)$ 2.1 (3 H, s, aryl CH_3), 3.2 (3 H, s, OCH_3), 3.4 (2 H, t, CH_2), 3.7 (2 H, t, CH_2), 6.47 and 6.77 (4 H, AA′XX′, J = 20 Hz, aryl H).

2-(2-*Methoxyethoxy*)-5-*methyl*-2′-*tosylaminobenzophenone* (**7**). To a stirred and cooled solution of compounds (**5**) (5.6 g, 33.6 mmol) and (**6**) (10.8 g, 33.5 mmol) in anhydrous dichloroethane (12 cm^3) was added in portions $AlCl_3$ (14.5 g, 109 mmol). The mixture was stirred at ambient temperature until all of (**5**) had disappeared (10—12 h as monitored by t.l.c. on SiO_2, $CHCl_3$). The reaction mixture was poured on a mixture of ice (50 g), and 2 mol dm^3 HCl (10 cm^3) and extracted with $CHCl_3$. The extracts were washed successively with diluted HCl solution, water, 5% NaOH solution, and water, then dried over $MgSO_4$ and evaporated *in vacuo*. The residue was triturated with ether, the precipitate was filtered off, washed with ether, and dried in air to give compound (**7**) (5.7 g, 35%), m.p. 153—155 °C (from EtOH–ether) (Found: C, 65.60; H, 5.80; N, 3.00. $C_{24}H_{25}NO_5S$ requires C, 65.60; H, 5.75; N, 3.20%); $\delta_H(CDCl_3)$ 2.23 (3 H, s, aryl CH_3), 2.32 (3 H, s, aryl CH_3), 3.06 (3 H, s, OCH_3), 3.26 (2 H, t, CH_2), 3.88 (2 H, t, CH_2), and 6.76—7.80 (11 H, m, aryl H).

2-*Amino*-2′-(2-*methoxyethoxy*)-5′-*methylbenzophenone* (**8**). The tosyl group of compound (**7**) was removed as described in the literature.[20] Crude (**8**) was obtained as a thick yellow oil which was used without further purification; $\delta_H(CCl_4)$ 2.23 (3 H, s, aryl CH_3), 3.05 (3 H, s, OCH_3), 3.33 (2 H, t, CH_2), 3.90 (2 H, t, CH_2), and 6.30—7.30 (7 H, m, aryl H).

N,N′-*Bis*{o-[2-(2′-*methoxyethoxy*)-5-*methylbenzoyl*]*phenyl*}-*oxamide* (**2a**). To a solution of compound (**8**) (1.55 g, 54 mmol) in a mixture of anhydrous CH_2Cl_2 (10 cm^3) and pyridine (1 cm^3) was added $(COCl)_2$ (0.23 cm^3, 27 mmol) dropwise with stirring. The temperature of the reaction mixture was maintained at 10 °C. The precipitate of compound (**2a**) was filtered off, washed with ethanol, followed by ether, and dried in air. Yield 0.9 g (54%), m.p. 222—223 °C [from dimethylformamide(dmf)–EtOH] (Found: C, 69.40; H, 7.00; N, 4.25. $C_{36}H_{36}N_2O_8$ requires C, 69.20; H, 5.80; N, 4.50%).

2-*Amino*-2′-*hydroxybenzophenone* (**10**). 2-Amino-2′-methoxybenzophenone (**9**) (5 g, 22 mmol) was refluxed for 24 h in a mixture of concentrated HBr (25 cm^3) and glacial acetic acid (25 cm^3). After the disappearance of (**9**), monitored by t.l.c. (SiO_2, $CHCl_3$), the reaction mixture was poured into water; the pH of the solution was brought to 3—4 with Na_2CO_3, and the mixture was extracted with $CHCl_3$. The organic layer was washed with water, dried over Na_2SO_4, and evaporated *in vacuo*. Crude compound (**10**) was obtained in a yield of 85% (4 g) as a red oil and was used further without purification.

2-*Amino*-2′-(3,6,9-*trioxadecyloxy*)*benzophenone* (**12**). A mixture of compound (**10**) (1 g, 4.69 mmol), K_2CO_3 (0.8 g, 5.8 mmol), (**11**) (1.75 g, 5.5 mmol), and dmf (6 cm^3) was stirred at 130 °C for 2 h until the disappearance of (**10**) (t.l.c., SiO_2, $CHCl_3$). The reaction mixture was diluted with water and extracted with ether. The organic layer was dried over $MgSO_4$, concentrated *in vacuo*, and the residue was chromatographed on a column of SiO_2 (300 × 20 mm, ether) to give compound (**12**) (1.3 g, 77%) as a thick yellow oil: $\delta_H(CDCl_3)$ 3.24 (3 H, s, OCH_3), 3.32—3.55 (10 H, m, CH_2), 3.94 (2 H, t, aryl CH_2O), and 6.30—7.30 (8 H, m, aryl H).

N,N′-*Bis*{o-[2-(3′,6′,9′-*trioxadecyloxy*)*benzoyl*]*phenyl*}-*oxamide* (**2b**). To a solution of compound (**12**) (0.9 g, 2.5 mmol) in a mixture of anhydrous CH_2Cl_2 (3 cm^3) and pyridine (1 cm^3) was added oxalyl chloride (0.13 cm^3, 1.51 mmol) with stirring at room temperature, and the stirring was continued for 1 h. The reaction mixture was diluted with $CHCl_3$. The organic

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layer was washed with water, dried over $MgSO_4$, and concentrated *in vacuo*. Compound (**2b**) was obtained in a yield of 50% (1.2 g), m.p. 85—87 °C (from EtOH); $\delta_H(CDCl_3)$ 3.27 (6 H, s, OCH_3), 3.33—3.53 (20 H, m, CH_2), 4.00 (4 H, t, aryl CH_2O), 6.88—7.57 (14 H, m, aryl H), 8.78 and 8.84 (2 H, d, aryl H).

Methyl (R)-*phenylglycinate* (**13**). The hydrochloride of compound (**13**) was obtained according to the literature[21] and had m.p. 214—215 °C (lit.,[21] 202 °C); α (589 nm, *c* 1, water −121° [lit.,[21] −121° (*c* 0.09, water)]. Ammonia was bubbled into a suspension of this hydrochloride (36.5 g, 0.18 mol) in $CHCl_3$ (150 cm^3). Precipitated ammonium chloride was filtered off and washed with $CHCl_3$. The organic washings were combined and evaporated *in vacuo*. The residue was distilled *in vacuo* and the fraction boiling at 96—97 °C (5 mmHg) was collected to give compound (**13**) (29 g, 97%).

(R)-*Phenylglycinamide* (**14**). A solution of compound (**13**) (30 g) in concentrated aqueous NH_3 (30 cm^3) was kept at room temperature for 2 d and then evaporated to dryness. The residue was recrystallized from benzene–EtOH to yield compound (**14**) (30 g, 85%, m.p. 130—136 °C [lit.,[22] 130—131 °C (for the racemic compound)]; α (589 nm, 23 °C, *c* 0.8, water) −96.7°, $[M]^{23}_{546}$ −175° (*c* 0.8, in water) {lit.,[21] $[M]^{20}_{546}$ −221° (*c* 0.8, water) (for the hydrochloride)}.

(R)-1,2-*Diamino*-1-*phenylethane* (**15**). To a suspension of $LiAlH_4$ (3.7 g, 97.6 mmol) in anhydrous thf (50 cm^3) was added compound (**14**) (4.9 g, 32.6 mmol) in small portions with stirring and cooling at 5 °C. After the addition was complete the reaction mixture was refluxed for 8 h and then decomposed by slowly adding a 1% aqueous solution of KOH (25 cm^3). The residue was filtered off and washed with benzene (3—20 cm^3). The organic solvent was dried with Na_2CO_3, evaporated, and the residue was distilled *in vacuo* to give compound (**15**) (2.3 g, 55%), b.p. 105—108 °C (4 mmHg) (lit.,[23] 104 °C, 1—2 mmHg); α (589 nm, 23 °C, −29.7°) (lit.,[23] −35.2°); n^{23}_{589} = 1.5390; $\delta_H(CDCl_3)$ 3.64 and 3.76 (2 H, AB part of ABX, J_{AX} = 9, J_{BX} = 6, J_{AB} = 24 Hz, CH_2), 4.77 (1 H, X part of ABX, CH), and 7.49—7.69 (5 H, m, aryl H).

(*R*)-1,2-Di(acetylamino)-1-phenylethane (**16**) was prepared as described in the literature[23] and had m.p. 174—174.5 °C (lit.,[23] 174 °C); α (589 nm, 20 °C, *c* 0.12, anhydrous EtOH) −83.3°; $[M]^{20}_D$ −183.5° (*c* 0.12, anhydrous EtOH) [lit.,[23] −178 °C (*c* 0.12—0.07, anhydrous EtOH)]; $\delta_H(CD_3OD)$ 1.86 (3 H, s, CH_3), 1.99 (3 H, s, CH_3), 3.39 (2 H, AB part of ABX, J_{AX} = 8, J_{BX} = 6, J_{AB} = 29 Hz, CH_2), 5.09 (1 H, X part of ABX, CH), and 7.17—7.34 (5 H, m, aryl H).

(*R*)-1,2-Di(acetylamino)-1-(*p*-nitrophenyl)ethane (**17**) was prepared as described in the literature[24] and had m.p. 199—200 °C (lit.,[24] 172—174 °C for a racemic compound) (Found: C, 54.65; H, 5.60; N, 15.70. $C_{12}H_{15}N_3O_4$ requires C, 54.35; H, 5.70; N, 15.85%); α (589 nm, 23 °C, *c* 0.12, anhydrous EtOH); −59.6°; $\delta_H(CD_3OD)$ 1.86 (3 H, s, CH_3), 1.97 (3 H, s, CH_3), 3.57 and 3.43 (2 H, AB part of ABX, J_{AX} = 8, J_{BX} = 6, J_{AB} = 27, CH_2), 5.12 (1 H, X part of ABX, CH), 7.57 and 8.21 (4 H, AB, J_{AB} = 8 Hz, aryl H).

(*R*)-1,2-Di(acetylamino)-1-(*p*-aminophenyl)ethane (**18**) was obtained by hydrogenation of (**17**) (0.3 g, 1.13 mmol) over Pd–Al_2O_3 (0.1 g) in MeOH and purified by chromatography on SiO_2 ($CHCl_3$–EtOH, 4:1). Yield 91% (0.21 g), m.p. 77—79 °C; $\delta_H(CD_3OD)$ 1.89 (3 H, s, CH_3), 1.94 (3 H, s, CH_3), 3.41 and 3.48 (2 H, AB part of ABX, J_{AX} = 5, J_{BX} = 4, J_{AB} = 14 Hz, CH_2), 4.94 (1 H, X part of ABX, CH), 6.71 and 7.09 (4 H, AA′XX′, *J* = 8 Hz, aryl H).

(*R*)-1,2-Diamino-1-(*p*-nitrophenyl)ethane dihydrochloride (**3b**) and (*R*)-1,2-diamino-1-(*p*-aminophenyl)ethane trihydrochloride (**3c**) were obtained by hydrolysis of (**17**) and (**18**) under the conditions described in ref. 24. Yield of (**3b**) 86%, m.p. 240—250 °C (decomp.) [lit.,[24] 235—245 °C (decomp.) for a racemic compound]; α(589 nm, 23 °C, *c* 0.5, water) +36.0°; $\delta_H(D_2O)$ 3.15 and 3.24 (2 H, AB part of ABX, J_{AX} = 7, J_{BX} = 5, J_{AB} = 19 Hz, CH_2), 4.37 (1 H, X part of ABX, CH), 7.25 and 7.80 (4 H, AB, J_{AB} = 8 Hz, aryl H). Yield of (**3c**) 90%, m.p. 180—185 °C (decomp.); α(589 nm, 20 °C, *c* 0.03, EtOH) +20.0°, (365 nm, 20 °C, *c* 0.03, EtOH) +53.3°; $\delta_H(D_2O)$ 3.68 and 3.75 (2 H, AB part of ABX, J_{AX} = 5, J_{BX} = 4, J_{AB} = 17, CH_2), 5.09 (1 H, X part of ABX, CH), 7.57 and 7.80 (4 H, AA′XX′, *J* = 8 Hz, aryl H).

Mixture of diastereoisomeric complexes of {(R)-7,8,15,18-*Tetrahydro*-5,10-bis(2′-*methoxyethoxy*-5′-*methylphenyl*)-7-(p-*nitrophenyl*)*dibenzo*[e,m][1,4,8,11]*tetra-azacyclotetradecine*-16,17-*dionato*-(2−)-$N^6N^9N^{15}N^{18}$}*nickel*(II) (**1b**). To a suspension of compound (**2a**) (0.17 g, 0.272 mmol) in anhydrous MeOH (3 cm^3) was added $Ni(NO_3)_2 \cdot 6H_2O$ (0.08 g, 0.277 mmol) and a solution of (**3b**) (0.07 g, 0.275 mmol) in 1.75 mol dm^{-3} NaOMe (0.85 cm^3). The mixture was stirred for 1 h under Ar at 55 °C, neutralized with 5% aqueous $MeCO_2H$ solution, and extracted with $CHCl_3$. The extracts were evaporated *in vacuo* and a mixture of four red isomers of (**1b**) was purified by SiO_2 ($CHCl_3$–acetone) and LH-20 (benzene–ethanol, 3:1) chromatography. The total yield of (**1b**) was 0.17 g (78%), m.p. 170—175 °C (Found: C, 63.85; H, 5.05; N, 7.95. $C_{44}H_{41}N_5NiO_8$ requires C, 63.95; H, 5.00; N, 8.45%); $\delta_H(CD_3OD)$ 1.88—2.30 (6 H, m, aryl CH_3), 2.90—3.33 (6 H, m, OCH_3), 3.45—4.76 (11 H, m, aliphatic H), and 5.80—9.30 (18 H, m, aryl H).

Separation of the diastereoisomers of compound (**1b**) was accomplished by preparative t.l.c. on SiO_2 ($CHCl_3$–acetone, 9:1). Four red bands were separated in the order of their R_f values [(**I**) < (**II**) < (**III**) < (**IV**)] in a ratio of (**I**)/(**II**)/(**III**) equal to 4:1:4, whereas isomer (**IV**) was present in trace amount. The isomers were additionally purified on a Sephadex LH-20 column.

(**I**): $\lambda_{max.}$(EtOH) 410 (log ε 3.86), 390 (3.83), 325 (4.36), and 280 nm (4.51); α (589 nm, 25 °C, *c* 0.091, EtOH) +109.9°; $\delta_H(CDCl_3)$ 1.93 (3 H, s, aryl CH_3), 2.10 (3 H, s, aryl CH_3), 3.28 (3 H, s, OCH_3), 3.32 (3 H, s, OCH_3), 3.00—4.45 (11 H, m, aliphatic H), 5.88—8.68 (18 H, m, aryl H), 7.85 and 8.20 (4 H, AA′XX′, *J* = 8 Hz, aryl H).

(**II**): $\lambda_{max.}$(EtOH) 410 (log ε 3.78), 3.90 (3.75), 325 (4.30), and 280 nm (4.46); α (589 nm, 25 °C, *c* 0.1, EtOH) +120°; $\delta_H(CDCl_3)$ 2.04 (3 H, s, aryl CH_3), 2.30 (3 H, s, aryl CH_3), 3.00—4.70 (11 H, m, aliphatic H), 3.08 (3 H, s, OCH_3), 3.36 (3 H, s, OCH_3), 5.85—8.80 (16 H, m, aryl H), 7.93 and 8.20 (4 H, AA′XX′, *J* = 8 Hz, aryl H).

(**III**): $\lambda_{max.}$(EtOH) 410 (log ε 3.55), 390 (3.53), 325 (4.23), and 280 nm (4.41); α (589 nm, 25 °C, *c* 0.23, EtOH) +171°; $\delta_H(CDCl_3)$ 2.10 (3 H, s, aryl CH_3), 2.33 (3 H, s, aryl CH_3), 3.00—4.70 (11 H, m, aliphatic H), 3.08 (3 H, s, OCH_3), 3.38 (3 H, s, OCH_3), 5.90—8.75 (18 H, m, aryl H), 7.88 and 8.20 (4 H, AA′XX′, *J* = 8 Hz, aryl H). The o.r.d. curves of the individual diastereoisomers are shown in Figure 3.

Diastereoisomeric Mixtures of Complexes (**1c**)—(**1e**).—To a stirred mixture of equimolar amounts of compound (**2a**) or (**2b**) and the appropriate metal(II) nitrate (hydrate) in absolute MeOH at 50—55 °C under Ar was added a solution of an equimolar quantity of (**3c**) and a 10-fold excess of NaOMe in absolute MeOH. The reaction mixture was stirred at 50—55 °C until (**2a**) or (**2b**) disappeared (monitoring by t.l.c. on SiO_2; $CHCl_3$–acetone, 5:1). After cooling, the reaction was quenched with aqueous acetic acid, and the complexes were extracted with $CHCl_3$. The complexes were purified by column chromatography on SiO_2, the eluants being $CHCl_3$–acetone (9:1) for (**1c**) and (**1d**) and benzene–EtOH (3:1) for (**1e**). Complex (**1c**) was collected as two red fractions, (**1d**) as a single brown fraction, and (**1e**) as a single red fraction. These complexes were purified additionally on a Sephadex LH-20 column (benzene–EtOH, 3:1).

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(**1c**): Yield 82%, m.p. 185—190 °C (Found: C, 66.20; H, 5.70; N, 8.60. $C_{44}H_{43}N_5NiO_6$ requires C, 66.35; H, 5.45; N, 8.80%); $\delta_H(CDCl_3)$ 1.90—2.20 (6 H, m, aryl CH_3), 2.70—3.25 (6 H, m, OCH_3), 3.30—4.62 (11 H, m, aliphatic H), 5.9—7.6 and 8.41—8.73 (18 H, m, aryl H).

(**1d**): Yield 60%, m.p. 185—190 °C.

(**1e**): Yield 72%, m.p. 79—82 °C (Found: C, 63.85; H, 5.65; N, 7.20. $C_{50}H_{55}N_5NiO_{10}$ requires C, 63.55; H, 5.85; N, 7.40%); $\delta_H(CDCl_3)$ 3.18—3.31 (6 H, m, OCH_3), 3.37—4.22 (29 H, m, aliphatic H), and 5.78—8.72 (20 H, m, aryl H).

Diasteroisomeric Mixtures of Complexes (**1f**)—(**1h**).—The synthesis of complexes (**1f**)—(**1h**) was achieved by the reaction of the corresponding (**1c**)—(**1e**) with a 160-fold molar excess of MeI in MeCN in the presence of K_2CO_3 at reflux under Ar with stirring. The reaction mixture was filtered and evaporated to dryness. The residue was subjected to anion exchange with Dowex MSA-1 in Cl^- form (MeOH as the solvent) and then chromatographed on a SiO_2 column [eluants $CHCl_3$–acetone (9:1) for (**1f**) and (**1g**) and benzene–EtOH for (**1h**)]. Fractions containing initial and partially methylated complexes were collected and additionally methylated under the above conditions. The quaternized complex was eluted from the top of the chromatographic column by 30—50% aqueous acetic acid. The eluate was evaporated *in vacuo*, and the residue was purified on a LH-20 column (benzene–EtOH, 3:1).

(**1f**): Yield 60%, m.p. 141—144 °C (Found: C, 62.65; H, 5.70; N, 7.80. $C_{47}H_{50}ClN_5NiO_6$ requires C, 64.50; H, 5.75; N, 8.00%); $\lambda_{max.}$ (water) 500 (log ε 2.82), 390 (3.77), 325 (4.37), and 275 nm (4.44); $\lambda_{max.}(CHCl_3)$ 500 (log ε 2.76), 420 (3.72), 400 (3.68), 330 (4.25), and 250 nm (4.37); α (25 °C, *c* 0.022, $CHCl_3$) +455 (578), +864 (546), −1 364° (436 nm); $\delta_H(CDCl_3)$ 1.90—2.53 (6 H, m, aryl CH_3), 2.83—3.28 (6 H, m, OCH_3), 3.82, 394 and 3.98 (9 H, s, N–CH_3), 3.43—4.58 (11 H, m, aliphatic H), 5.78—7.38 and 7.88—8.70 (18 H, m, aryl H).

(**1g**): Yield 50%, m.p. 146—150 °C (Found: C, 60.05; H, 5.35; N, 7.40. $C_{47}H_{50}ClCuN_5O_6$ requires C, 64.15; H, 5.75; N, 7.95%); $\lambda_{max.}$(water) 500 (log ε 2.64), 400 (3.64), 350 (4.05), and 280 nm (4.61); $\lambda_{max.}(CHCl_3)$ 530 (log ε 2.41), 420 (3.53), 380 (4.08), and 285 nm (4.65); α (25 °C, *c* 0.022, $CHCl_3$) +1 818 (578), +455 (546), and −682° (436 nm).

(**1h**): Yield 55%, m.p. 118—120 °C (decomp.) (Found: C, 61.00; H, 6.40; N, 6.65. $C_{53}H_{63}ClN_5NiO_{10}$ requires C, 64.40; H, 6.40; N, 7.65%); $\lambda_{max.}$(water) 390 (log ε 3.78), 325 (4.30), and 275 nm (4.34); $\lambda_{max.}(CHCl_3)$ 500 (log ε 2.84), 410 (3.91), 390 (3.83), 330 (4.40), and 285 (4.48 nm); α (25 °C, *c* 0.036, in $CHCl_3$) +289 (589), +416.7 (578), and +1 016.7° (546 nm); $\delta_H(CDCl_3)$ 3.23—3.29 (6 H, m, aliphatic H) and 6.40—8.71 (20 H, m, aryl H).

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