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Self-Assembly in the Metallation of Bis(aminoaryl) Ethers

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Abstract: The dilithiation of 2,2'-bis(2-methoxyethylamino)diphenyl ether (**4**) and 2,2'-bis(*N,N*-dimethylethylenediamino)diphenyl ether (**7**) in the absence of any Lewis base donor resulted in the formation of dimeric complexes **8** and **9**, respectively, containing the unprecedented $Li_4O_2N_4$ "adamantanoid" metal core as a consequence of the self-recognition and self-assembly involving the two metallated subunits. In contrast, on monometallation using particular conditions, *e.g.* sodium hydride in the presence of Lewis base donor, the same ligands undergo a Smiles-type rearrangement, providing the first example of such a reaction involving an amine and a deactivated aromatic system. The conditions needed to promote this rearrangement have been investigated.

INTRODUCTION

Lithium amides and their complexes have aroused considerable interest, especially during the last decade. In major part, this interest has stemmed from their value as synthetic reagents.[1] Lithium amides tend to be employed for proton abstractions because of their strong basicities coupled with their relatively low nucleophilicities. This latter feature gives them an advantage over carbon-lithium reagents. It is now well established[2-4] that lithium amides generally exist as complex superstructures, held together by noncovalent bonds, *i.e.* they are supramolecular species. This complexity arises from the high propensity of amidolithium compounds to self-associate to form higher aggregates, a phenomenon which depends markedly upon the choice of the solvent and the precise reaction conditions. As a result, most amidolithium species are generated routinely *in situ* and used without any direct evidence of their solution state structures - or even of their existences. In spite of these complications, there has been growing interest shown by researchers[5,6] in the supramolecular structures of amidolithium complexes. They illustrate the general principle that, in assemblies of supermolecules involving metal ions and ligands, the ligands must contain the steric and electronic 'programme' that is 'read' by metal ions, following an algorithm represented by their coordination geometry.[7,8]

Until recently however, the structures of only simple monolithiated complexes of secondary amines were known.[9,10] Recently, we have described[11] the results of dilithiation of naphthylamine, providing the first example of a dilithiated primary amine. It is a Li_2O species held together by $(NaphN)^{2-}$ anions (Naph = naphthyl) and ether ligands. We have also obtained the structure of a solvated dilithiated diamine $(PhLiNCH_2CH_2NLiPh).3HMPA$ (HMPA = hexamethylphosphoric triamide), containing the commonly observed Li_2N_2 core.[12] Such a core is also featured in the first lithiated diazacrown.[13]

RESULTS AND DISCUSSION

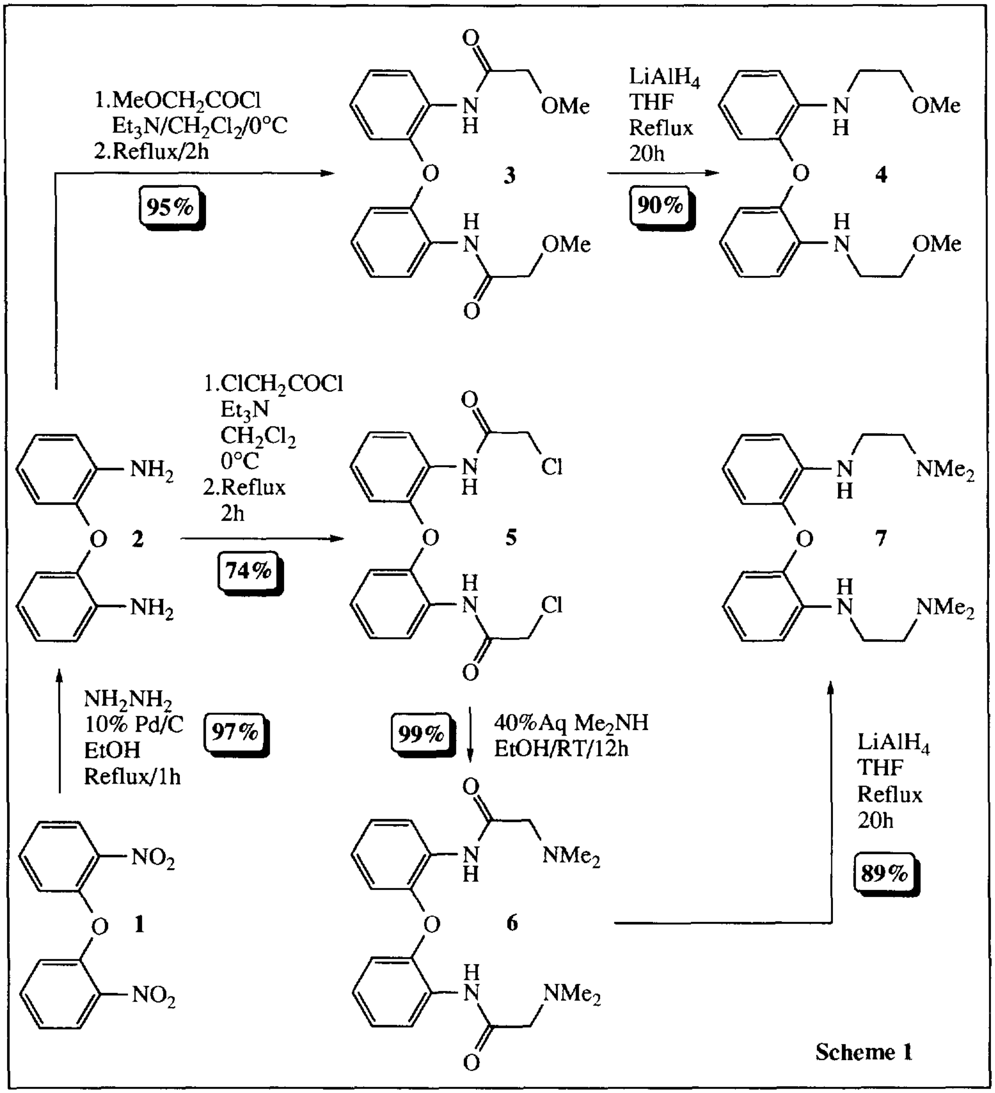
In extending this knowledge to include alkali metal complexes of a more diverse range of organic acids, we became interested[14,15] in the lithiation of 2,2'-bis(2-methoxyethylamino)diphenyl ether (**4**) and 2,2'-bis(*N*,*N*-dimethylethylenediamino)diphenyl ether (**7**) as ligands, that might offer great potential through their preorganisation for the self-assembly of defined superstructures. The aim of the research was to probe the intermolecular and intramolecular involvement of the heteroatoms in the OMe and NMe_2 groups in the side-arms with the N-coordinated Li atoms in the resulting lithium amide structures.

Synthesis of the Ligands

The syntheses (**Scheme 1**) of the ligands **4** and **7** start from the easily available (2-nitrophenyl)ether (**1**).[16] Reduction of **1** with hydrazine hydrate in the presence of 10% palladium on carbon in ethanol gave (2-aminophenyl)ether (**2**) in quantitative yield. Diamine **2** was reacted with commercially available methoxyacetyl chloride in dichloromethane in the presence of triethylamine as a base to give the bisamide **3** in 95% yield. An analogous reaction was carried out with chloroacetyl chloride to give the corresponding bis(chloroacetylamide) **5** in 75% yield after purification. Compound **5** was converted in 95-99% yield into the bis(*N*,*N*-dimethylacetamide) **6** with 40% aqueous dimethylamine in ethanol at room temperature. Reduction of **3** and **6** with lithium aluminium hydride in tetrahydrofuran afforded the diamines **4** and **7** in 90 and 89% yields, respectively.

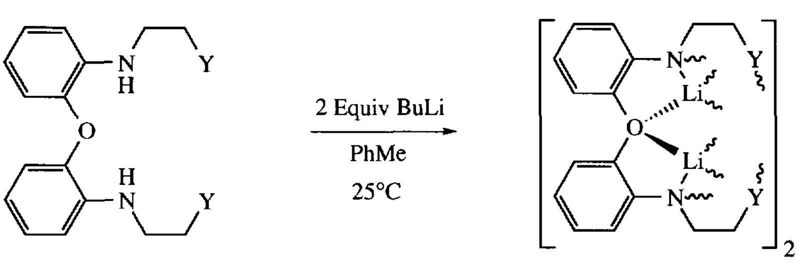
Preparation of Metal Complexes

Inspection of space-filling molecular models indicates that the ligands **4** and **7** have some special features. They include the fact that (i) the potential lithium binding sites are rigid on account of the diphenyl ether units and provide the appropriate sizes and shapes for the accommodation of Li atoms and (ii) the availability of additional internal donation sites [Ar-O-Ar and Y where Y=OMe in **4** and Y=NMe_2 in **7**] within the ligands, suggesting that the use of additional Lewis base donors (such as THF or HMPA) would not be necessary for the preparation of metal complexes involving these ligands.



Scheme 1

Dilithiation of the Ligands. Dilithiation (**Scheme 2**) of 2,2'-bis(2-methoxyethylamino)diphenyl ether (**4**) and 2,2'-bis(*N*,*N*-dimethylethylenediamino)diphenyl ether (**7**) and subsequent crystallisations of the derived lithium amides **8** and **9**, respectively, from toluene solutions were achieved in the absence of a Lewis base donor. The X-ray crystal structures of **8** and **9** revealed[14] that they both have an 'adamantanoid' metal core (**Figures 1** and **2**), a structural motif that is unprecedented in the chemistry of Group I metal complexes. **Figure 1** depicts the solid-state structure of the complex **8**. Each lithium is coordinated to its 'own' nitrogen and its 'own' oxygen (*i.e.* intramolecularly, with respect to the monomer involving Li1–O1, Li1–N1a, Li1a–O1, Li1a–N1) and then to nitrogen and the oxygen of the methoxy groups of the other ligand (Li1–N2, Li1–O4, Li1a–N2a, Li1a–O4a). The two monomer units slot together almost orthogonally–thus forming the adamantanoid core–encouraged by the tendency of the lithium atoms to attain their favoured four-fold



4: Y=OMe
7: Y=NMe_2

Scheme 2

8: Y=OMe
9: Y=NMe_2

coordination, without inducing any steric strain upon the framework of the organic ligands. In **9**, precisely the same intramonomer and intermonomer coordinations operate (**Figure 2**), except that the side arms are now terminated by dimethylamino groups instead of by methoxy groups. The conceptual view of this dimerisation as self-recognition of two monomers is supported by considering the bond lengths within the cores of the solid-state structures. In **Figure 3**, the bonds within one monomeric unit are highlighted in boldface. In **8**, the averaged[14] amide N–Li bonds within a monomer unit are shorter (196 pm) than the amide N–Li bonds between monomers (203 pm). The Li–O linkages between Li atoms of one monomer and the OMe groups of the other are considerably shorter (192 pm) than the intramonomer one involving the O atom of the Ar-O-Ar unit (207 pm). This difference is significant as it is these intermolecular Li–OMe interactions that clamp the two monomers together. Furthermore, of all the interactions between Li and the electronegative centres, only these Li–Y ones are terminal: all others involve *bridging* of two Li atoms. In **9**, where Y = NMe_2, however, these side-arm interactions are no longer the shortest bonds. This subtle difference in the binding between monomeric units in **8** and **9** is reflected in the solution studies. The room temperature ^{1}H NMR of **8** in C_6D_6

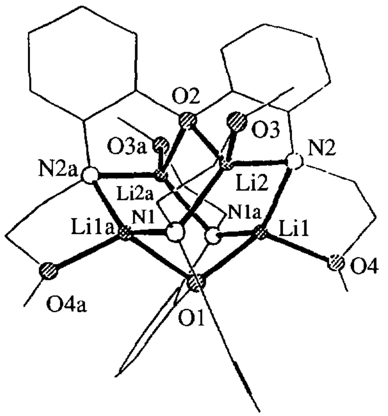


Figure 1. Molecular structure of **8** (for clarity, the carbon framework is not shown in detail and hydrogen atoms have been omitted).

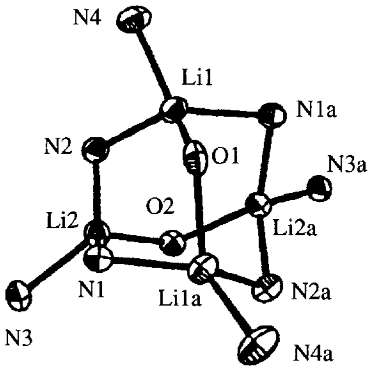
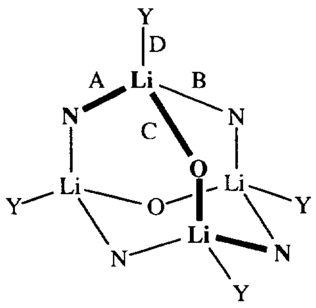


Figure 2. Adamantanoid $Li_4O_2N_8$ central core of **9** (thermal ellipsoids at the 50% probability level)

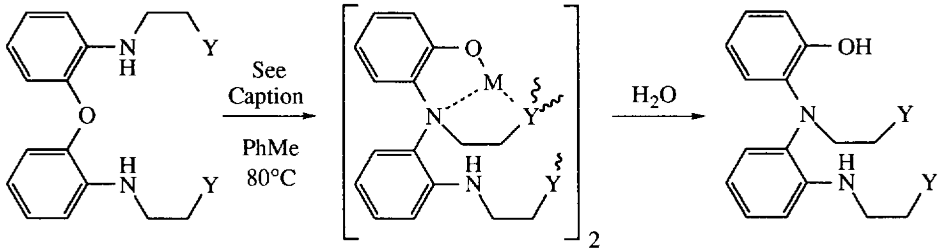
shows an ABCD system for the bismethylene protons in the side arm of the ligand, a fact that is consistent with persistence of the solid-state structure in solution. Cryoscopy[17] in benzene also indicates[14] that the dimer remains intact in solution [n = 1.97 ± 0.06 for a 0.025 M solution (concentration expressed in terms of monomer)]. In the case of **9**, the room temperature solution behaviour indicates a less rigid structure, consistent with the looser solid-state binding revealed by the data recorded in **Figure 3**.



	A	B	C	D
8 [Y = OMe]	196	203	207	192
9 [Y = NMe_2]	199	206	212	211

Figure 3. The core of complexes **8** and **9** showing average intramolecular (A and C) and intermolecular (B and D) bond lengths in pm. Bonds and atoms of one monomeric unit are in boldface.

The dimeric and geometric characteristics of the solid-state structures, portrayed in **Figures 1** and **2**, *together with the evidence for the persistence of the solid-state structures of* **3** *and* **4** *in solution*, suggest that a new family of molecular assemblies and supramolecular arrays can now be constructed around suitably chosen cyclic and acyclic ligands. This statement draws confidence from the fact that the two organic ligands arranged around the 'adamantanoid' $Li_4O_2N_4$ cores are (i) disposed orthogonally with respect to each other and (ii) carry functional groups which can clearly be modified without too much difficulty.



4: Y=OMe
7: Y=NMe_2

10: M = Na, Li; Y = OMe, NMe_2
10a: M = Na; Y = OMe

11: Y = OMe
12: Y = NMe_2

Scheme 3. The monometallation conditions were (1) 1 Mol Equiv BuLi/1 Mol Equiv HMPA, (2) 1 Mol Equiv NaH/2 Mol Equiv HMPA, or (3) 1 Mol Equiv $NaN(SiMe_3)_2$

Monometallation of the ligands. Dramatically different results (**Scheme 3**) were obtained on monometallation of the same ligands **4** and **7** with either (i) butyllithium or (ii) sodium hydride in toluene solution in the presence of the Lewis base donor, HMPA. The X-ray crystal structure (**Figure 4**) of the product revealed[15] that an *in situ* Smiles rearrangement of the ligands had taken place to afford the dimeric aryloxide metal complex **10.** The metal-free tertiary amines **11** and **12** which were obtained on hydrolysis, were fully characterised. The X-ray crystal structure indicated that **10a** is a monosodiated complex, not containing any HMPA in spite of its presence in the reaction solution. To our knowledge, this is the first dimeric sodium aryloxide to be isolated and characterised that is lacking external donor coordination. The structure is that of a ring dimer with each Na five–coordinate and approximately square pyramidal. The central Na_2O_2 ring is unsymmetrical but essentially planar [Na(1)-O(1) 227, Na(1)-O(1a) 221 pm, with Na(1)-O(1)-Na(1a) 91° and O(1)-Na(1)-O(1a) 89°]. Then additionally, each ligand uses the tertiary amine *ortho* to the phenoxide [N(1)] and its related methoxyethyl side-arm [O(2)] to chelate the Na in a bidentate fashion [Na(1)-N(1) 266, Na(1)-O(2) 232 pm]. The square pyramid is rendered complete by the second methoxyl group of the other ligand bridging across the dimer to Na [Na(1)-O(3a)] 236 pm. Of all the electronegative centres within the ligand, only N(2)(H)–which remains protonated in the complex–is not involved in coordination to Na. Its lone pair therefore interacts with the aryl π system rendering N(2) near planar. This behaviour is in contrast with N(1), which is approximately tetrahedral owing to its coordination to Na(1).

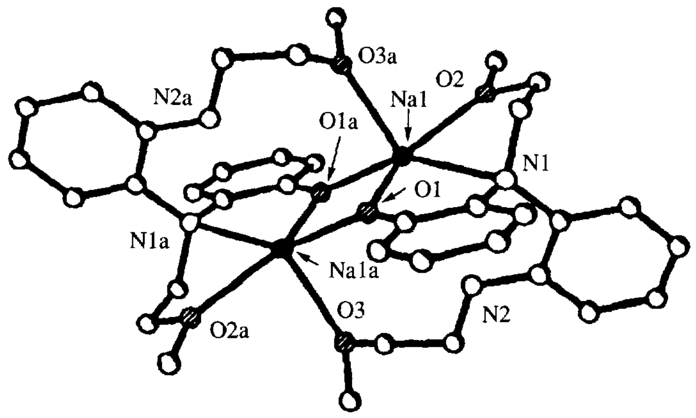
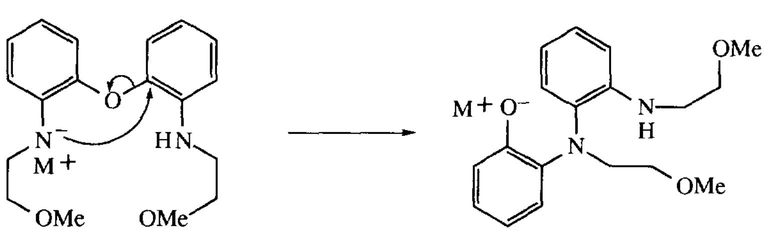


Figure 4. Molecular structure of the dimeric aryloxide complex **10a**



Scheme 4

The rearrangement (**Scheme 4**) of the original ligand, once metallated, to give the anionic ligand observed in Scheme 4 is an example of an intramolecular S_NAr reaction of the type known as a Smiles rearrangement.[18] Although displacement of aryloxide by aniline functionalities have been observed previously in diaryl ethers, such rearrangements are generally favoured when activation of the ring is provided by electron-withdrawing ortho and/or para substituents such as nitro groups or halogen atoms. The use of sodium hydride in the presence of HMPA or dimethylformamide, which are supposedly able to provide a 'naked anion', has been reported[19] to facilitate the Smiles rearrangement in non-activated and even deactivated systems, particularly when the anion is derived from an amide. The rearrangement we have observed in the present study appears to be the first example of a Smiles rearrangement involving an amine and a deactivated aromatic system. More importantly, it is the first such rearrangement in which the metal-ligand complex (usually not isolated and assumed to be present only as an intermediate prior to quenching) has been isolated and characterised. We have investigated the conditions needed to promote the Smiles rearrangement. Our findings are as follows (i) Addition of two equivalents of butyllithium to the ligand, even in the presence of HMPA, does not cause rearrangement. Clearly, the dianion is not susceptible to nucleophilic substitution, presumably owing to extreme deactivation of the aromatic rings. (ii) Monometallation with butyllithium solution or with a suspension of solid sodium hydride in toluene, in the presence of HMPA in each case, effects complete rearrangement of the ligand within 24 h at 80 °C (reaction monitored by TLC). (iii) Attempted monometallation by the same reagents as in (ii)-but in the absence of HMPA–failed. There is no reaction at all with solid sodium hydride, and with butyllithium the low-yield product is the dimetallated 'adamantanoid' complex (Figure 1) containing the unrearranged ligand. (iv) If one equivalent of the soluble sodium reagent sodium bis(trimethylsilyl)amide is used, then even in the absence of HMPA, complete rearrangement of the ligand occurs. (v) The use of the corresponding soluble lithium amide reagent, also without HMPA, does not cause rearrangement–at least over the same time-scale. However, if HMPA is added, the rearrangement occurs rapidly. These observations imply that the Smiles rearrangement can only proceed *via* monometallation, a strong complexant such as HMPA is always required in order for lithium to effect the rearrangement, and HMPA is only required in the case of an insoluble sodium reagent, *e.g.* sodium hydride. When a toluene-soluble reagent is used, sodium effects rearrangement in the absence of HMPA.

EXPERIMENTAL SECTION

Materials. Tetrahydrofuran and toluene were distilled from sodium benzophenone ketyl, triethylamine and dichloromethane from calcium hydride, and n-hexane from sodium wire. Hexamethylphosphoric triamide (HMPA) was stored over 4Å molecular sieves. All other solvents were of reagent grade.

n-Butyllithium in hexane, sodium hydride (dry, 95%), sodium hydride (80% in mineral oil), sodium- and lithium-bis(trimethylsilyl)amides in toluene, methoxyacetyl chloride, chloroacetyl chloride, dimethylamine (40% wt solution in water) were commercial products. Bis(2-nitrophenyl) ether was prepared according to a literature procedure[16].

General. All the metallations were carried out under an atmosphere of nitrogen using Schlenk tubes and glove box techniques. Thin-layer chromatography (TLC) was carried out on aluminium sheets coated with silica gel 60 (Merck 5554) or with neutral alumina 60 (Merck 5550). Compounds were detected by UV light or by development with Dragendorff's reagent prepared as described in the literature[20]. Flash column chromatography was performed on Merck TLC-Kieselgel 60H (15 μm) with the solvents specified. Bulb-to-bulb distillations were conducted in a Kugelrohr apparatus and the temperatures quoted refer to the oven temperature. Melting points, uncorrected, were taken in glass capillary tubes on an Electrothermal melting apparatus. Analytical samples were dried *in vacuo* (13.1 Pa) at 60-70° C. Microanalyses were performed on a Perkin-Elmer Model 1201 automatic analyzer. Electron-impact (EI, 70 eV) and chemical ionisation (CI) mass spectra were taken on a Kratos Profile instrument and fast atom bombardment (FAB) mass spectra (matrix: m-nitrobenzyl alcohol) on a Kratos MS 80 RF mass spectrometer with DS 90 data system. ^1H Nuclear magnetic resonance (NMR) spectra were recorded on either a Bruker AC 300 (300 MHz) or a Bruker AMX 400 (400 MHz) spectrometer. ^{13}C-NMR spectra were recorded on a Bruker AC 300 (75 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm), and coupling constants in hertz (Hz). The crystallographic data associated with the X-ray crystal structures of **8** and **9**, and **10a** have been reported in the preliminary communications.[14,15]

Bis(2-aminophenyl) Ether (2). Bis(2-nitrophenyl) ether (**1**) (33.0 g, 0.127 mol) in ethanol (900 ml) was warmed with magnetic stirring until complete dissolution of the solid occured. Catalyst (5.1 g, 10% Pd/C) was then added to the reaction mixture, followed by dropwise addition of hydrazine hydrate (38.1 g, 0.762 mol). The mixture was heated under reflux for 1 h before being cooled and filtered through a pad of Celite. The solvent was removed under reduced pressure, the residue was dissolved in chloroform, washed with water, brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the diamine **2** (24.7 g, 97%) as a thick liquid which, upon standing, crystallized, m.p. 61-63°C (lit.[21] m.p. 62.5-63.5°C). EIMS, *m/z* (relative intensity): 200 (M^+, 92%), 182 (29), 171 (12), 154 (12), 108 (76), 93 (100), 80 (88), 65 (65), 53 (42), 39 (44); ^1H NMR (300 MHz, $CDCl_3$) δ 3.89 (bs, 4H, NH_2), 6.67-6.74 (m, 2H, ArH), 6.78-6.84 (m, 4H, ArH), 6.92-6.99 (m, 2H, ArH).

2,2'-Bis(2-methoxyacetamido)diphenyl Ether (3). A solution of diamine **2** (7.4 g, 36.8 mmol) and triethylamine (11.6 g, 0.115 mol) in dry dichloromethane (100 ml) was added dropwise to an ice-cooled, stirred solution of methoxyacetyl chloride (10.0 g, 92.0 mmol) in dry dichloromethane (100 ml). The temperature was kept below 5 °C during the addition. The mixture was allowed to warm up to ambient temperature before being heated under reflux for 2 h, cooled, and treated with excess of dilute hydrochloric acid. The separated organic layer was washed with 5% aqueous sodium bicarbonate solution, water, brine, and dried ($MgSO_4$). Filtration and concentration gave the bisamide **3** (12.0 g, 95%), m.p. 144-145°C (EtOAc-light petroleum). CIMS, *m/z* (relative intensity): 345 ($M+H^+$, 61%), 318 (12), 299 (5), 270 (26), 258 (14), 243 (17), 228 (15), 166 (58), 151(35), 136 (100), 124 (29), 110 (81), 94 (83), 84 (39), 60 (99), 45 (73); ^1H NMR (300 MHz, $CDCl_3$) δ 3.36 (s, 6H, OCH_3), 3.98 (s, 4H, CH_2), 6.85 (dd, 2H, J 8Hz, J 1.5 Hz, ArH), 7.05 (dt, 2H, J 8Hz, J 1.5 Hz, ArH), 7.16 (dt, 2H, J 8Hz, J 1.5 Hz, ArH), 8.43 (dd, 2H, J 8Hz, J 1.5 Hz, ArH), 8.81 (bs, 2H, CONH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 59.3, 72.3, 117.7, 121.6, 124.7, 124.7, 128.8, 145.3, 167.8.. Anal. Calcd. for $C_{18}H_{20}N_2O_5$: C, 62.8; H, 5.85; N, 8.13%. Found: C, 62.6; H, 6.07; N, 8.16%.

2,2'-Bis(2-chloracetamido)diphenyl Ether (5). A stirred solution of **2** (15.0 g, 0.075 mol) and triethylamine (23.7 g, 0.235 mol) in dry dichloromethane (150 ml) was cooled in an ice-bath and treated under an atmosphere of nitrogen with a solution of chloroacetyl chloride (21.2 g, 0.188 mol) in dry dichloromethane (150 ml) in the manner described above for the preparation of **3**. However, the dark coloured crude product was first decolourised by passing it through a pad of alumina (eluant, $CHCl_3$-EtOAc). Concentration afforded the bisamide **5** (19.6 g, 74%), m.p. 163-164°C (EtOAc-light petroleum). CIMS (NH_3) *m/z* (relative intensity): 372 [M(^{37}Cl)+NH_4^+, <1%], 370 [M(^{35}Cl)+NH_4^+, <1%], 355 [M(^{37}Cl)+H^+, 5], 353 [M (^{35}Cl)+H^+, 8], 319 (8), 243 (31), 151 (78), 136 (100), 124 (41), 110(88), 94 (67), 84 (39), 77 (80), 60 (88); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.16 (s, 4H, CH_2), 6.82 (dd, 2H, J 8Hz, J 1.5 Hz, ArH), 7.09-7.21 (m, 4H, ArH), 8.19 (dd, 2H, J 8 Hz, J 1.5 Hz, ArH), 8.92 (bs, 2H, CONH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.1, 117.8, 122.6, 124.7, 125.9, 128.1, 146.1, 164.5. Anal. Calcd for $C_{16}H_{14}N_2O_3Cl_2$: C, 54.4; H, 4.00; N, 7.93%. Found: C, 54.5; H, 4.00; N, 7.97%.

2,2'-Bis(2,2-dimethylacetamido)diphenyl Ether (6). A 40% aqueous solution of dimethylamine (49.4 g, 0.439 mol) was added dropwise to a stirred solution of the bis(amidochloride) **5** (12.4 g, 0.035 mol) in ethanol (550 ml) and the resulting solution was stirred at 25 °C for 12 h. The reaction mixture was concentrated under reduced pressure and the residue was dissolved in chloroform and consecutively treated with 10% aqueous NaOH, water, brine and dried ($MgSO_4$). Filtration and concentration gave **6** (12.85 g, 99%) as a viscous oil which, upon standing, crystallised, m.p. 94-95°C (EtOAc-light petroleum). EIMS, *m/z* (relative intensity): 370 (M^+, 24%), 312 (32), 266 (12), 226 (19), 153 (11), 111 (15), 93 (25), 85 (32), 58 (100), 42 (51); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.18 (s, 12H, CH_3), 3.02 (s, 4H, CH_2), 6.80 (dd, 2H, J 8 Hz, J 1.5 Hz, ArH), 7.00 (dt, 2H, J 8Hz, J 1.5 Hz, ArH), 7.14 (dt, 2H, J 8 Hz, J 1.5 Hz, ArH), 8.45 (dd, 2H, J 8 Hz, J 1.5 Hz, ArH), 9.63 (bs, 2H, CONH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.7, 63.8, 117.6, 121.2, 124.3, 124.6, 129.2, 145.1, 168.9. Anal. Calcd for $C_{20}H_{26}N_4O_3$: C, 64.9; H, 7.07; N, 15.12%. Found: C, 65.1; H, 7.26; N, 15.11%.

2,2'-Bis(2-methoxyethylamino)diphenyl Ether (4). A hot solution of the bisamide **3** (11.8 g, 0.034 mol) in dry tetrahydrofuran (200 ml) was added dropwise with stirring to an ice-cooled slurry of lithium aluminium hydride (7.8 g, 0.206 mol) in dry tetrahydrofuran (300 ml). After addition, the reaction was stirred at reflux for 24 h, then cooled to 0°C, and excess of lithium aluminium hydride was destroyed by consecutive addition of water (8 ml), 15% aqueous sodium hydroxide solution (8 ml), and water (24 ml). The granular precipitate was removed by filtration and washed with ethyl acetate (2 x 100 ml) and toluene (3 x 100 ml). The combined filtrates were concentrated *in vacuo*, the residue was dissolved in toluene, dried (KOH pellets), and concentrated. Bulb-to-bulb distillation (160-163°C/0.07 torr) gave the diamine **4** (9.7 g, 90%) as a yellow oil which, upon standing, crystallised, m.p.42-43°C. CIMS; *m/z* (relative intensity): 317 (M+H^+, 100%), 259 (43), 201 (14), 186 (12), 166 (13), 152 (32), 132 (18), 120 (26), 110 (35), 94 (50), 76 (47), 59 (18), 44 (28); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.34 (s, 6H, OCH_3), 3.34 (t, 4H, J 5.5 Hz, CH_2), 3.59 (t, 4H, J 5.5 Hz, CH_2), 4.58 (bs, 2H, NH), 6.56-6.64 (m, 2H, ArH), 6.71-6.78 (m, 4H, ArH), 6.96-7.07 (m, 2H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.4, 58.8, 71.1, 111.4, 116.9, 117.7, 124.2, 139.9, 144.1. Anal. Calcd. for $C_{18}H_{24}N_2O_3$: C, 68.3; H, 7.65; N, 8.86%. Found: C, 68.1; H, 7.83; N, 8.94%.

2,2'-Bis(*N,N*-dimethylethylenediamino)diphenyl Ether (7). A solution of **6** (9.3 g, 0.025 mol) in dry tetrahydrofuran (100 ml) was added slowly to a stirred suspension of lithium aluminium hydride

(5.7 g, 0.15 mol) in dry tetrahydrofuran (250 ml) at 0°C. The work-up procedure was analogous to that for the reduction described in the previous reaction. Bulb-to-bulb distillation (158-162°C/0.1 torr) gave the diamine **7** (7.6 g, 89%) as a slightly yellow oil. CIMS, *m/z* (relative intesity): 343 ($M+H^+$, 100%), 298 (5), 272 (20), 181 (10), 165 (10), 110 (16), 94 (18), 72 (50), 58 (84), 46 (25); ^1H NMR (300 MHz, $CDCl_3$) δ 2.20 (s, 12H, CH_3), 2.53 (t, 4H, J 6 Hz, CH_2), 3.21 (q, 4H, J 5.5 Hz, CH_2), 4.70 (t, 2H, J 5 Hz, NH), 6.59 (dt, 2H, J 8 Hz, J 1.5 Hz, ArH), 6.73 (dt, 4H, J 8 Hz, J 1.5 Hz, ArH), 6.99 (dt, 2H, J 8 Hz, J 1.5 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.4, 45.3, 58.2, 111.3, 116.5, 117.5, 124.1, 140.1, 143.9. Anal. Calcd. for $C_{20}H_{30}N_4O$: C, 70.1; H, 8.83, N, 16.36%. Found: C, 69.8; H, 8.90; N, 16.06%.

Dilithium Complex 8. The diamine **4** (632 mg, 2.0 mmol), in a stirred solution of dry toluene (5 ml), was lithiated under nitrogen at 25 °C by addition of a 1.6 M solution of n-butyllithium in hexane (2.5 ml, 4.0 mmol). The separated solid was dissolved by warming the mixture to 80°C (oil bath). A crop of colourless crystals was deposited after standing at room temperature overnight. The air-sensitive solid was filtered off under nitrogen, washed with n-hexane, and dried *in vacuo* to yield **8** (0.322 g, 49%), m.p.>300°C. ^1H NMR (250 MHz, C_6D_6) δ 2.77 (s, 3H, OCH_3), 2.80, 2.92, 3.28, 3.45 (D, C, B and A respectively of ABCD system, 4 x 1H, $^2J_{AB}$ 7 Hz, $^3J_{AC}$ 17 Hz, $^3J_{AD}$ 16 Hz, $^3J_{BC}$ 28 Hz, $^3J_{BD}$ 7 Hz, $^2J_{CD}$ 7 Hz), 6.45 (t of d, 1H, aryl H *meta* to amide), 6.67 (dd, 1H, aryl H *ortho* to amide), 7.10-7.20 (m, 2H, other arene-H). Assignments were made by a combination of coalescence behaviour, selective decoupling and COSY experiments, and were confirmed using an NMR simulation programme. Anal. Calcd. for $C_{36}H_{44}N_4O_6Li_4$: C, 65.9; H, 6.76; N, 8.53%. Found: C, 65.6; H, 6.57; N, 8.78%.

Dilithium Complex 9. Diamine **7** (684 mg, 2.0 mmol) in a solution of dry toluene (12 ml) was lithiated in the manner described above for **8** to give the complex **9** (0.361 g, 51 %), m.p. 230-233°C. ^1H NMR (250 MHz, C_6D_6) δ 1.70 (s, 6H, Me_2N), 2.24, 2.89 (bs, 2 x 2H, CH_2CH_2), 6.23 (t of d, 1H, aryl *meta* to amide), 6.48 (dd, 1H, aryl *ortho* to amide), 6.95 (t of d, 1H, aryl *meta* to ether), 7.14 (dd, 1H, aryl *ortho* to ether). Anal. Calcd. for $C_{40}H_{56}N_8O_2Li_4$: C, 67.8; H, 7.96; N, 15.81%. Found: C, 66.4; H, 7.80; N, 16.38%.

[(2-Hydroxyphenyl)-(2-methoxyethylaminophenyl)-(2-methoxyethyl)]-amine (11)

Method A. A stirred solution of diamine **4** (632 mg, 2.0 mmol) in dry toluene (5 ml) was treated with 1.6 M butyllithium in hexane (1.25 ml, 2.0 mmol) under nitrogen at 25°C. After 1 h at 80°C (oil bath), hexamethylphosphoric triamide (0.35 ml, 2.0 mmol) was added and the mixture was heated at 80°C for 24 h (monitored by TLC, SiO_2, 5% EtOAc in CH_2Cl_2), before being cooled to room temperature and quenched with water. The organic phase was separated, washed with water, brine, dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by flash column chromatography (SiO_2, eluant CH_2Cl_2/EtOAc, 100:5) to give amine **11** (0.4 g, 63%) as a colouress thick oil. EIMS *m/z* (relative intensity): 316 (M^+, 48%), 284 (20), 269 (100), 239 (91), 224 (20), 211 (72), 196 (24), 132 (31), 106 (15), 77 (13), 45 (16); ^1H NMR (300 MHz, $CDCl_3$) δ 3.26 (q, 2H, J 5 Hz, NCH_2), 3.35 (s, 3H, OCH_3), 3.40 (t, 2H, J 5 Hz, NCH_2), 3.42 (s, 3H, OCH_3), 3.54 (t, 2H, J 5 Hz, OCH_2), 3.65 (t, 2H, J 5 Hz, OCH_2), 5.19 (bs, 1H, NH), 6.67-6.81 (m, 3H, ArH), 6.90-7.14 (m, 4H, ArH), 7.18 (dd, 1H, J 8 Hz, J 1.5 Hz, ArH), 8.08 (bs, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.3, 54.3, 58.8, 59.0, 70.3, 71.0, 111.6, 116.3, 117.3, 119.7, 123.4, 125.2, 125.3, 126.4, 133.6, 136.4, 144.9, 152.4. Anal. Calcd. for $C_{18}H_{24}N_2O_3$: C, 68.3; H, 7.65; N, 8.86%. Found: C, 68.3; H, 7.87; N, 8.75%.

Method B. A 0.6 M solution of sodium bis(trimethylsilyl)amide in toluene (2.5 ml, 1.5 mmol) was added to a solution of amine **4** (475 mg, 1.5 mmol) in dry toluene (4 ml) at 25°C and under nitrogen. This procedure yielded a grey precipitate. Stirring and heating at 80°C for 2 h gave a clear solution. The mixture was then maintained at 80°C for 24 h to complete the reaction (monitored by TLC), cooled and quenched with water. Using a work-up similar to that described in the **Method A** gave the amine **11** in 56% yield.

[(*N*,*N*-Dimethylethylendiaminophenyl)-(2-hydroxyphenyl)-(2-dimethylaminoethyl)]-amine (12). The preparation of the title compound from diamine **7** followed a procedure which was similar to that used above for the synthesis of amine **11** (monitored by TLC, SiO_2, $CH_2Cl_2/MeOH/NH_4OH$, 100:5:1). The crude product was purified by crystallisation (n-hexane, -20°C) to afford the amine **12** (0.45 g, 65%), m.p. 79-80 °C. EIMS, *m/z* (relative intensity): 342 (M^+, 62%), 284 (78), 239 (78), 225 (70), 211 (69), 196 (35), 133 (52), 91 (36), 72 (93), 58 (100), 42 (73); ^1H NMR (300 MHz, $CDCl_3$) δ 2.17 (s, 6H, CH_3), 2.37 (s, 6H, CH_3), 2.39 (q, 4H, CH_2), 3.08 (m, 2H, CH_2), 3.55 (t, 2H, J 5.5 Hz, CH_2), 4.95 (bs, 1H, NH), 6.58 (dd, 1H, J 8 Hz, J 1.5 Hz, ArH), 6.64-6.75 (m, 2H, ArH), 6.88-7.08 (m, 4H, ArH), 7.32 (dd, 1H, J 8 Hz, J 1.5 Hz, ArH), 12.4 (bs, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.8, 45.0, 45.5, 53.1, 57.2, 58.1, 110.8, 115.8, 117.5, 119.6, 122.9, 125.3, 125.9, 126.2, 135.4, 136.0, 144.5, 155.1. Anal. Calcd. for $C_{20}H_{30}N_4O$: C, 70.1; H, 8.83; N, 16.4%. Found: C, 70.2; H, 8.93; N, 16.3%.

Sodium Complex 10a. A suspension of sodium hydride (dry, 95%, 51 mg, 2.0 mmol) in dry toluene solution (4.5 ml) of amine **4** (632 mg, 2.0 mmol) was stirred at 80°C under dry nitrogen for one hour. Addition of hexamethylphosphoric triamide (0.7 ml, 4.0 mmol) caused vigorous reaction and, after stirring for a further hour at 80°C, near complete dissolution was achieved. The red-brown solution was filtered whilst hot. Refrigeration of the solution at -5 °C for 48 hours yielded a crop of colourless, cubic crystals **10a** (0.23 g, 35%), m.p. 215-217 °C. ^1H NMR (250 MHz, CD_3SOCD_3) δ 3.05 (q, 2H, $HNCH_2CH_2$), 3.18 (s, 3H, OMe), 3.22 (s, 3H, OMe), 3.3-3.5 (m, 6H, 3 x CH_2), 5.87 (t), 6.26 (d), 6.40 (d), 6.49 (t), 6.60 (d), 6.79 (t), 6.92 (t), 7.13 (d) (8 x 1H, ArH). Anal. Calcd. for $C_{18}H_{23}N_2O_3Na$: C, 63.9; H, 6.85; N, 9.40%. Found: C, 63.3; 6.66; N, 9.66%.

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