Formation of Exocyclic Olefinic Groups *via* Stereoselective Nitrosations: a New Route Towards Pendant Arm Macrocyclic Ligands

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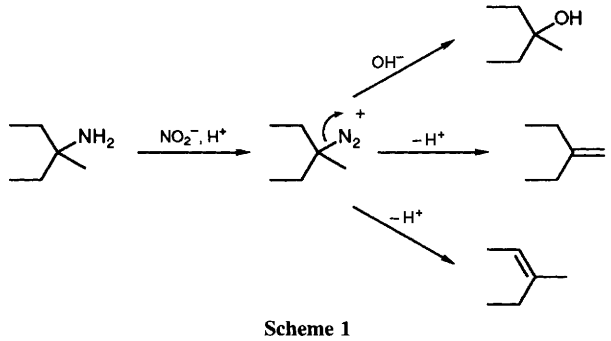
Nitrosation of the Cu^{II} and Pd^{II} complexes of *trans*-6,13-dimethyl-1,4,8,11-tetraazacyclotetradecane-6,13-diamine results in new macrocyclic complexes bearing exclusively exocyclic olefinic groups as shown by an X-ray crystal structure and NMR spectroscopy.

Although reactions of aliphatic primary amines with nitrite salts in dilute aqueous acid (commonly referred to as nitrosations) have been extensively studied,[1] rarely has a high degree of stereoselectivity been a feature. Upon departure of the N_2 leaving group from the presumed diazonium intermediate, substitution, usually by the solvent is one possible course that the reaction can take (Scheme 1). Another possibility is elimination of a proton accompanying loss of the N_2 group to form an alkene. In addition, rearrangement of proposed carbocation intermediates is a commonly observed, but undesirable, feature of such reactions and hence, unlike aromatic relatives, the nitrosation of aliphatic primary amines is a seldom recommended synthetic procedure.

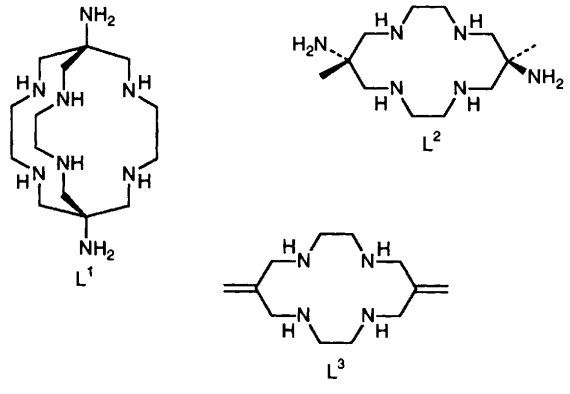
We are aware of but one other report[2] concerning the nitrosation of a coordination compound bearing one or more primary amine groups attached to the ligand framework. In that case, nitrosation of the Co^{III} complex of the ligand L^1 yielded a vast array of substitution and rearrangement products necessitating extensive chromatographic separation of the reaction mixture. We have pursued a similar study with the Cu^{II} complex of the known[3] diamino-substituted macrocycle L^2 and have found that a high degree of selectivity is resultant upon nitrosation.

Reaction of $[Cu(H_2L^2)]^{4+}$ with an excess of sodium nitrite in dilute aqueous perchloric acid (pH 3) at 5 °C yielded the dialkene $[CuL^3]^{2+}$ in *ca.* 30% yield (not optimised). Purification was achieved with column chromatography, and recrystallisation of $[CuL^3](ClO_4)_2$ from water afforded X-ray quality crystals.‡ Inspection of Fig. 1 reveals that both olefinic groups of $[CuL^3]^{2+}$ are exocyclic to the fourteen-membered macrocyclic ring. That this was not merely a phenomenon of selective crystallisation of exocyclic in preference to any endocyclic species (where the C=C double bonds would be included in the macrocycle) was proven by precipitation of the metal ion with aqueous sodium sulfide followed by NMR analysis of the reaction mixture. No trace of any lower symmetry endocyclic olefinic species was found in the ^{13}C NMR spectrum, although some hydrated products (alcohols) were identified amongst the reaction products.§ The nitrosation reaction was performed under identical conditions with the diamagnetic $[Pd(H_2L^2)]^{4+}$ complex,[4] which allowed an NMR of the coordinated ligands. The proton-decoupled ^{13}C NMR spectrum of the reaction mixture is shown in Fig. 2. The four marked resonances are consistent with the C_{2h} symmetry of the ligand L^3. Traces of the hydrated, alkene-ol complex can be seen in Fig. 2 from the appearance of resonances at *ca.* δ 56, 60 and 72, respectively (a methyl resonance also appears at δ 26, which is not shown in Fig. 2). Therefore, it appears that the reaction is clean in terms of (*i*) the absence of any rearranged species; (*ii*) the stereoselective elimination to the exocyclic product and (*iii*) the preference for elimination over substitution, at least as far as the Pd^{II} directed reaction is concerned.

The exclusive formation of the exocyclic olefinic groups in $[CuL^3]^{2+}$, without rearrangement, is remarkable when one makes comparisons with earlier results of nitrosation reactions of primary amines both with and without a metal ion being



Scheme 1



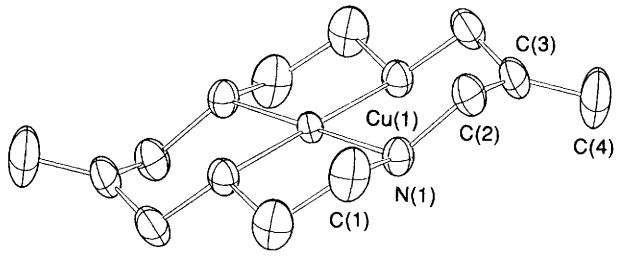


Fig. 1 ORTEP drawing of the $[CuL^3]^{2+}$ cation. Selected bond lengths (Å) and angles (°) Cu(1)–N(1) 2.010(2), C(2)–C(3) 1.467(5), C(3)–C(4) 1.307(7); N(1)–C(2)–C(3) 111.8(3), C(2)–C(3)–C(4) 121.4(2).

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‡ *Crystal Data*: $C_{12}H_{24}Cl_2CuN_4O_8$, M = 486.80, monoclinic, space group *C2/m*, a = 13.481(6), b = 9.312(2), c = 9.052(3) Å, β = 116.99(2)°, U = 1012.7(7) Å^3, D_c (Z = 2) = 1.596 g cm^{-3}, $F(000)$ = 502, μ = 13.43 cm^{-1}, λ(Mo-Kα) 0.71069 Å. Reflections were measured on an Enraf-Nonius CAD4 diffractometer. The structure was solved by direct methods and refined by full-matrix least-squares analysis to an R of 0.044, R_w 0.045 on 1254 $F[I > 2.5\sigma(I)]$. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

§ The ^{13}C NMR spectrum of the free ligand L^3 (in ^2H_2O) exhibited resonances at δ 45.4, 51.3, 114.6 and 143.8 *vs.* $SiMe_4$. The spectrum of the mono-hydrated adduct of L^3 (an alkene-ol) displayed resonances at δ 24.9, 46.4, 47.2, 52.7, 56.7, 71.7, 115.6 and 144.5 *vs.* $SiMe_4$.

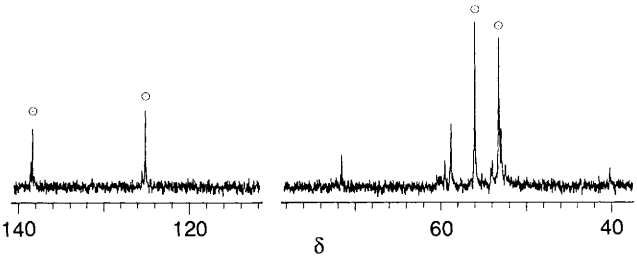

Fig. 2 Proton-decoupled ^{13}C NMR spectrum $[(CD_3)_2SO]$ of the solution resulting from reaction of $[PdL^2]^{2+}$ with acidified $NaNO_2$ solution

present in an active role. One might have expected that the endocyclic alkene would be more stable considering the general trend that alkyl substitution stabilises alkenes.[5] In the present case, the Cu^{II} centre forms part of a six-membered chelate ring to which the original primary amine is attached, and this apparently directs the chemistry towards formation of an exocyclic C=C double bond. The metal ion also plays a vital role in protecting the secondary amines, *via* coordination, from the formation of *N*-nitroso species.

The exocyclic olefinic functional groups in $[CuL^3]^{2+}$ offer a wide range of possibilities for derivitisation of the macrocyclic ligand at its apical C atoms *via* conventional organic synthetic procedures. Although *N*-alkylation of aliphatic, polyazamacrocyclic ligands has been thoroughly studied, the *C*-functionalisation of similar ligands is a more challenging task,[6] and ligands such as L^3 should provide relatively straightforward routes to new macrocyclic ligands bearing pendant functional groups.

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