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Unusual Specificity in Alkylation Reactions of a Nickel(II) Cyclidene Macrocyclic Complex

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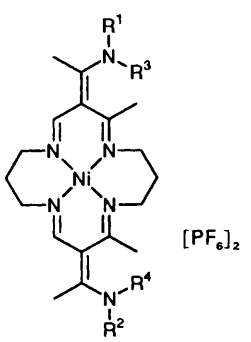
Alkylation reactions of a nickel(II) cyclidene macrocyclic complex occur with kinetic control of the reaction products, allowing the selective preparation of a series of macrocyclic complexes with variable and useful structural features.

The structural chemistry of the cyclidene macrocyclic ligands originally developed by Busch has attracted a great deal of interest, not least because these molecules contain a protected cavity at the metal binding site which guest molecules may enter.[1] Busch and co-workers[2] have reported widely on the behaviour of a range of both bridged and unbridged examples. We have recently reported on the structural modification of various macrocyclic ligands, including cyclidenes, to allow their incorporation into the matrix of a range of synthetic polymers.[3] Of key importance to this is the ability to have a single site on the complex for reaction with the polymer, otherwise the complexes act as cross-linking agents and produce insoluble polymer/complex mixtures that are difficult to process.[4]

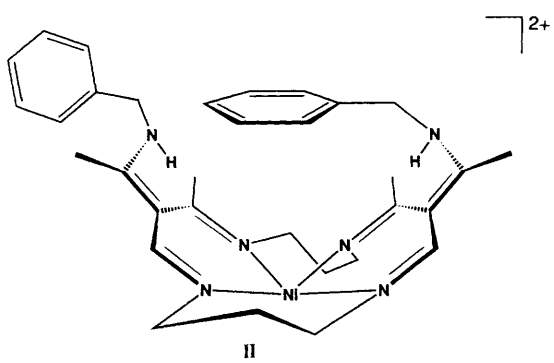
Although normally drawn flat for convenience, and nominally possessing a plane of symmetry, complex **1**, (structure **I**), in common with other unbridged cyclidenes, has a well defined three dimensional geometry[5] and the ^{1}H NMR spectrum in CD_3CN solution indicates that there is a degree of asymmetry associated with the orientation of the two benzyl groups, with the aliphatic protons of the benzyl groups giving rise to two signals in the ratio of 3:1. This is interpreted as arising because one of the benzyl aromatic rings points inwards and effectively caps the pseudo-cavity of the molecule, while the other points outwards, into the solution (structure **II**). A very similar phenomenon is seen in the crystal structure of a cyclidene compound bearing pyrazole substituents.[5] The ^{1}H and ^{13}C NMR spectra indicate that **1** is fluxional on the NMR time-scale and that the benzyl group 'in' the cavity is replaced by the group 'out' of the cavity. This, and other data,[6] indicate that there is a strong preference for a phenyl ring to be 'in' the cavity and that, on steric grounds, only one ring at a time may be accommodated.

This has important consequences upon the reactivity of complex **1**. Alkylation of **1** with *n*-propyl bromide produced in high yield only a monoalkylated product, **2**, rather than the expected product, **3**.* In contrast, both methyl iodide and benzyl bromide reacted smoothly and quickly with deprotonated **1** to produce the dialkylated products, **4** and **5** respectively. Since the dialkylated product **3** was readily prepared by treating complex **6** with an excess of benzyl bromide, the failure to produce it from complex **1** is interpreted as arising from kinetic control of the reaction. In the monoalkylated product the benzyl group at the tertiary amine end of the molecule lies in the cavity inhibiting the entry of any other group. During the



I

	R^1	R^2	R^3	R^4
1	CH_2Ph	CH_2Ph	H	H
2	CH_2Ph	CH_2Ph	Pr^n	H
3	CH_2Ph	CH_2Ph	Pr^n	Pr^n
4	CH_2Ph	CH_2Ph	Me	Me
5	CH_2Ph	CH_2Ph	CH_2Ph	CH_2Ph
6	Pr^n	Pr^n	H	H
7	CH_2Ph	CH_2Ph	Pr^n	$CH_2C_6H_4CH{=}CH_2$



II

* Alkylations of complex **1** were carried out by the same general procedure. In a typical experiment a solution of **1** (1.5 g, 1.75 mmol) in MeCN (100 cm^3) was heated at reflux with $KOBu^t$ (0.39 g, 3.5 mmol). To the resulting dark brown solution was added *n*-propyl bromide (1 cm^3, 11 mmol) and the mixture was heated at reflux for several h. The volume of the solution was reduced and the residue chromatographed on neutral alumina with MeCN as eluent. The fast moving dark orange band was collected and the solvent removed to yield the product as an orange solid (1.23 g, 78%). All of the new complexes described in this work gave satisfactory elemental analyses and the ^{13}C and ^{1}H NMR spectra were in accord with the suggested structures.

second alkylation reaction, the secondary amine end of the molecule is subjected to a twist to reduce the steric repulsion effects between the amino substituents and the macrocyclic methyl groups.[5] This has the effect of placing the new alkyl group in close proximity to the phenyl ring already within the cavity. With *n*-propyl bromide, steric repulsion between the phenyl ring and the alkylating agent increases the activation energy for the reaction, effectively inhibiting the process. For smaller, or more reactive alkylating agents, these steric effects are less important in contributing to the activation energy, and in those cases the second alkylation of **1** occurs readily.

The monoalkylated species **2** displays the same selectivity in its reaction as does **1**. It can only be alkylated at the secondary amine group by either small or rather reactive alkyl halides. For example reaction of **2** with 1-chloromethyl-3-vinylbenzene produces complex **7**, a species bearing a single co-polymerizable side chain for incorporation into polymer synthesis.

This remarkable control of reactivity allows the selective preparation of a family of macrocyclic complexes with a range of desirable features. By judicious choice of reagents and reaction sequence, it is possible to prepare asymmetric monofunctionalized, and asymmetric or symmetric difunctionalized macrocyclic species having a variety of desired structural characteristics. The nickel(II) ion may be readily removed from the macrocycles by treatment with strong acid, following the literature procedure,[4] and the corresponding free ligands may then be isolated. The ligands may then be re-metallated with a range of metal ions; for example we have introduced cobalt(II), producing a family of macrocycles capable of the reversible binding of dioxygen. A detailed study of the synthesis, characterization and reactions of these interesting materials will form the basis of a separate report.

Acknowledgements

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