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SYNTHESIS OF A CHLOROPHYLL WHICH DOES NOT AGGREGATE

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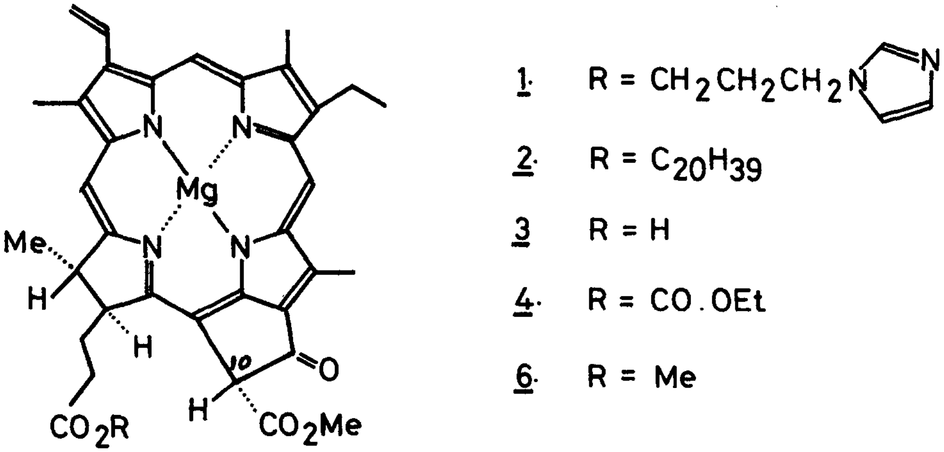
The solution chemistry of chlorophylls is dominated by the coordination demands of the central magnesium ion. In the absence of added ligands, the Lewis acidity of the metal is satisfied by binding to a carbonyl oxygen of another chlorophyll molecule. This leads to the formation of dimers and higher aggregates, and a correspondingly complex chemistry.[1,2] In order to simplify, or at least render more amenable to analysis, the behaviour of the system, we have modified chlorophyll-a to give it a "built-in" imidazole tail (1). This tail binds intramolecularly to the magnesium, preventing aggregation in solution.



1. R = $CH_2CH_2CH_2N$

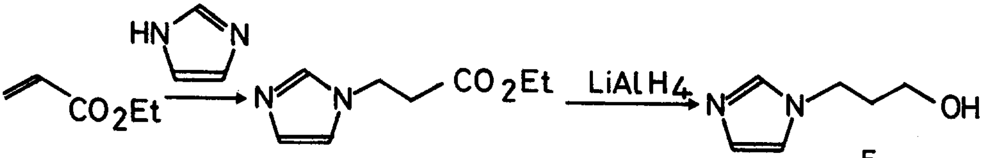
2. R = $C_{20}H_{39}$

3 R = H

4. R = CO.OEt

6. R = Me

The phytyl group of chlorophyll-a (2) was removed with spinach beet chlorophyllase in aqueous acetone[3,4] to give the acid 3. This was converted to the mixed anhydride 4 with triethylamine/ethyl chloroformate in dry THF at -10° C. Addition at -10° of 5 in dry DMF to the reaction mixture gave 1 (together with some of the chlorophyll-b analogue) which was purified by sucrose chromatography. For comparison, 6 was prepared by methylation of 3 with diazomethane.



5.

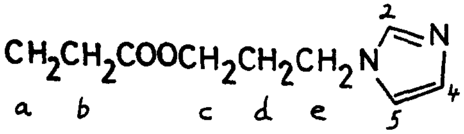
Chlorophylls 2 and 6 are highly aggregated in CD_2Cl_2 and give poorly resolved NMR spectra. In contrast, 1 gave well resolved spectra indicating the absence of aggregation. The chemical shifts and coupling constants of the imidazole-bearing chain are similar to those found in bridged porphyrins[4,5] and clearly indicate intramolecular binding to the magnesium ion. J and δ for the 'b' protons are particularly characteristic for a fixed conformation.

TABLE

Chemical Shifts and Coupling Constants for the Bound Tail of 1

Proton	δ	Complexation Shift (p.p.m.)*	J (Hz)
2	4.0	3.4	-
4	2.8	4.0	-
5	5.7	1.5	-
a	2.3	?	13.4, 7.5, 7.5
	2.8	?	13.4, 7.5, 5.3
b	0.5	1.7	18.0, 7.5, 7.5
	1.7	0.5	18.0, 7.5, 5.3
c	2.85		
	2.95		
d	1.3	*ca* 0.7	
e	3.5	*ca* 0.7	

* Upfield shift relative to unbound tail displaced by added ligands.



2 and 6 are disaggregated in acetone-d_6, a solvent which competes effectively for the metal, but the imidazole tail of 1 remains bound (Table). In acetone, chlorophylls are normally in equilibrium with 10-15% of their C-10 epimers but when the tail of 1 is bound the epimer is not detectable by NMR. This is presumably due to steric interaction between the tail and carboxymethyl group as the epimer is present as normal when the tail is displaced by added pyridine.

Similarly, the radical cations $2^{+\cdot}$ and $6^{+\cdot}$ decay rapidly in acetone-d_6, probably to "allomerised" chlorophylls,[6,7] whilst $1^{+\cdot}$ is relatively stable. As the oxidation potentials are undoubtedly the same, the stability of $1^{+\cdot}$ is presumably kinetic.

Addition of pyridine or N-methylimidazole to 1 in CD_2Cl_2 and acetone-d_6 has been accompanied by NMR monitoring of added ligand and tail over a range of temperatures. The major binding process for the added ligand has $\Delta H = -4$ to -8 kcal/mole and $\Delta S = -20$ to -30 e.u., showing that these molecules are adding as sixth ligands to 5-coordinate 1 and that solvent is not being displaced from magnesium coordination. The uv/visible spectra of 1 in these solvents are also consistent with 5-coordination.[2] A minor competing process most easily monitored by the built-in imidazole resonances is displacement of the tail: as expected this occurs with smaller ΔH and ΔS than the major process, but in the presence of a large excess of ligand yields a 6-coordinate species with unbound tail. The imidazole-tailed compound 1 is clearly the first of a series of chlorophylls whose coordination and aggregation behaviour can be tailored at will.

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REFERENCES

1. J. J. Katz in "Inorganic Biochemistry" ed. G. L. Eichhorn, Elsevier, p. 1022, (1973).
2. L. L. Shipman, T. M. Cotton, J. R. Norris, J. J. Katz, J. Amer. Chem. Soc., **98**, 8222 (1976).
3. M. Holden, Biochem. J., **78**, 359 (1961).
4. J. K. M. Sanders, J. C. Waterton, I. S. Denniss, to be published.
5. A. R. Battersby, D. G. Buckley, S. G. Hartley, M. D. Turnbull, J. C. S. Chem. Comm., 879 (1976).
6. J. K. M. Sanders, Chem. Soc. Reviews. In Press.
7. G. R. Seely in "The Chlorophylls" ed. L. P. Vernon and G. R. Seely, Elsevier, p. 91 (1966).