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THE AUSTRALIAN NATIONAL UNIVERSITY

JOHN CURTIN SCHOOL OF MEDICAL RESEARCH

BIOLOGICAL INORGANIC CHEMISTRY UNIT

ANNUAL REPORT - 1963

STAFF

Fellow:

A. M. Sargeson, B.Sc., Ph.D.

Senior Research Fellow:

B. Halpern, B.Sc., Ph.D. (to October).

Senior Technical Officer:

I. K. Reid (to November).

STUDENTS

The Unit supervised two students for the degree of Doctor of Philosophy, Mr. G.H. Searle who submitted his thesis entitled "Cobalt(III) Triethylenetetramine Complexes" in September and Mr. K.R. Turnbull (jointly with the School of General Studies) who is working on the resolution and reactivity of coordinated amino acids.

Both students and staff gave two seminars each during the year on their research and related subjects.

RESEARCH PROGRAMME

The Unit's research programme for the study of synthetic procedures for metal complexes and coordinating agents, their properties, reactions and possible applications to biology, was continued. In the past year a study of the metal salicylidene residue as a protecting group for amino acid esters in amidation reactions and peptide synthesis has been carried out. The residue was found effective for the facile preparation of amino acid amides but was too labile for peptide synthesis, (Naida Gill*, Halpern, Sargeson, Turnbull). However, by replacing the metal arylidene group with dimedone, well defined crystalline enamines were obtained and dipeptides were readily prepared using the protected esters. Optically active peptides were obtained from the active amino acids, the reaction was rapid and the dimedone residue was readily removed with full retention of optical activity, (Halpern, James). The amidation reaction is now being studied in more detail.

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The rate...

The rate of an aldol type condensation of aldehydes with active methylene groups in coordinated ligands was shown to be strongly dependent on the charge of the complex. The result was consistent with the generation of a coordinated carbanion as the rate determining step and this is in agreement with the mechanism proposed for the normal organic aldol reaction (Naida Gill*, Halpern, Sargeson, and Turnbull).

Several stereospecific quadridentates based on optically active amino acids were prepared but they were shown to be poor coordinating agents and unsuitable for making optically active complexes to be used as stereospecific reaction sites.

A study of the kinetics and stereochemical changes in the aquation of cobalt(III) complexes has led to a clearer understanding of the part played by water in these reactions. By indirectly producing the five coordinate intermediate $[Coen_2Cl]^+$ it was shown that the final aquation products differed widely from the normal aquation products. It was deduced then that some bond forming is required of water in the activated state, for the latter reaction and that the mechanism is not S_N1 limit, (Sargeson).

On the other hand the aquation of the <u>trans</u> dichloro triethylenetetramine cobalt(III) ion was shown to be S_N2 and the bond making by water led the fission of the cobalt chloride bond (Sargeson, Searle).

Not only has the study of these systems given information about the mechanism of aquation but the concomitant rotatory dispersion and circular dichroism studies have established the absolute configurations of these complexes, (Searle).

The kinetics and mechanism of the formation of cobalt(III) carbonato complexes has been established. The rate determining step is the addition of free CO_2 to the metal hydroxy conjugate base without fission of the Co —— O bond, (pH 6.5 - 8.5). At high pH however the mechanism appears to alter and carbonate ion probably replaces the coordinated water or hydroxyl ion directly, (Amling, Dwyer).

The study of the fundamental chemistry and preparative procedures for cobalt(III) complexes has been continued, with the preparation and resolution of sodium bis(oxalato) glycinato cobalt(III), sodium bis(oxalato) acetylacetonato cobalt(III), sodium bis(acetylacetonato) oxalato cobalt(III), sodium bis-(oxalato) carbonato cobalt(III) and sodium bis(malonato) glycinato cobalt(III), (Reid).

The factors which give rise to stereospecificity in cobalt(III) ethylenediamine and propylenediamine complexes are now clearly understood. The dominant terms are, the conformational effects due to chelate rings and the statistical distribution of the coordinated ligands, (Dwyer, Sargeson and James).

OTHER ACTIVITIES

Joint research projects with Professor G.B. Kauffman, Fresno State College, California, and with Dr. J. Garnett, University of New South Wales, were completed and the research results will be published in the ensuing year.

In August Dr. A. Sargeson gave a lecture to the Canberra Branch of the Royal Australian Chemical Institute entitled "Metal Ion Induced Organic Reactions". Dr. B. Halpern resigned in October to take up a research post with Syntex, New Mexico.

In October Dr. A. Sargeson left Canberra to spend twelve months on Study Leave at the Department of Chemistry, Stanford University, Palo Alto, California.

*A member of the Department of Chemistry, School of General Studies.

.../4 Publications

PUBLICATIONS

BUCKINGHAM, D.A.**, DWYER F.P., SARGESON, A.M.

'Disproportionation in synthetic reactions with cobalt(III) complexes.' Aust. J. Chem. 16, 921.

DWYER, F.P., BROOMHEAD, J.A.**

'The mechanism of racemisation of the 2,2'-bipyridine bis(1,10-phenanthroline) nickel (II) ion and the 1,10-phenanthroline bis(2,2'-bipyridine) nickel (II) ion.' Aust. J. Chem. 16, 51.

DWYER, F.P., GOODWIN, H.*, GYARFAS, E.C.*

'Mono and bis(2,2'-bipyridine) and (1,10-phenanthroline) chelates of ruthenium and osmium. II Bis chelates of bivalent and tervalent ruthenium.' Aust. J. Chem. 16, 544.

DWYER, F.P., HALPERN, B., TURNBULL, K.R.

'Resolution of racemic α-amino acids I. Neutral α-amino acids.' Aust. J. Chem. 16, 510.

'Resolution of racemic α-amino acids II. Acidic α-amino acids.' Aust. J. Chem. 16, 727.

DWYER, F.P., MACDERMOTT, T.E.**

'The stereospecific preparation of L-carbonato bis(l-propylenediamine) cobalt(III) iodide.' Inorganic Chemistry, 2, 871.

'Stereospecific influences in metal chelates containing optically active ligands.' VIII. J. Amer. Chem. Soc. 85, 2916.

DWYER, F.P., MACDERMOTT, T.E.**, SARGESON, A.M.

'Stereospecific influences in metal complexes containing optically active ligands.' VI. J. Amer. Chem. Soc. 85, 661.

'Stereospecific influences in metal complexes containing optically active ligands.' VII. J. Amer. Chem. Soc. 85, 2913.

DWYER, F.P., REID, I.K., SARGESON, A.M.

'Mechanism of the inversion reaction between d cis-dichloro bis(ethylenediamine) cobalt(III) ion and silver carbonate.' J. Amer. Chem. Soc. 85, 1215.

HALPERN, B., SARGESON, A.M., TURNBULL, K.R.

'A simple resolution of β-phenylalanine.' Chem. and Ind. 33, 1399.

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MACDERMOTT, T.E.**, SARGESON, A.M.

'Rotatory dispersion and configuration of cobalt(III) complexes.' Aust. J. Chem. 16, 334.

SARGESON, A.M.

'The rate of racemisation and isomerisation of the cis chloroaquo bis(ethylenediamine) cobalt(III) ion.' Aust. J. Chem. 16, 352.

SARGESON, A.M., SEARLE, G.H.

'An S_N2 mechanism for the aquation of the trans dichloro triethylenetetramine cobalt(III) ion.' Nature, 200, 356.

WHITE, D.O.*, HARRIS, A.W.*, DWYER, F.P., SHULMAN, A.*

'Action of metal chelates of substituted 1,10-phenanthrolines on viruses and cells. I. Inactivation of viruses.' Aust. J. Exptl. Biol. 41, 517.

*Not a member of this University.

**Based on work done while a member of the Department.