

The Preparation and Testing of Some Cyanoborane Complexes of Gold

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In recent years, a number of papers have been published [1] describing the possible therapeutic use of some substituted cyanoboranes for the treatment of, amongst other diseases, rheumatoid arthritis. Since gold complexes are currently used in the treatment of rheumatoid arthritis [2], it is of interest to examine the possibility of forming gold complexes of these cyanoboranes and examining their activity.

One problem with the testing of gold compounds for use in rheumatoid arthritis is that many anti-rheumatic drugs, including Myocrysin (sodium gold thiomalate), are not active in acute inflammatory animal tests. The results of these latter tests, therefore, may or may not be instructive. However, to be active, gold must be absorbed; thus we were interested in the extent of the oral absorption of gold.

Experimental

Preparations

Starting with sodium cyanotrihydroborate, dimethylamine and trimethylamine cyanoboranes were prepared by standard methods [3] and confirmed by elemental analysis. The three ligands were refluxed with both triphenylphosphine gold(I) chloride and sodium tetrachlorogold(III) in the ratio of 3:1 in THF for the former and acetone for the latter. The reactions of dimethylamine and trimethylamine cyanoboranes with triphenylphosphinegold(I) chloride gave colloidal gold. With sodium cyanoborane the product analysed for $(\text{Ph}_3\text{P})_4\text{Au}_9\text{Cl}_6(\text{BH}_3\text{CN})_4$ (Found: C, 28.5; Cl, 6.2; B, 1.2; N, 1.7; H, 2.0. Theory: C, 28.5; Cl, 6.6; B, 1.3; N, 1.7; H, 2.2.)

Attempts to prepare the corresponding triethylphosphine derivative resulted in the formation of colloidal gold.

Using tetrachlorogold(III) and sodium cyanoborane, the gold(III) was reduced to colloidal gold. With the substituted cyanoboranes, however, complexes of the type LAuCl_3 precipitated. Found for $(\text{CH}_3)_3\text{NBH}_2\text{CNAuCl}_3$: C, 12.3; N, 6.9; H, 2.7; Cl, 26.5. Theory: C, 12.0; N, 7.0; H, 2.7; Cl, 26.5.

Found for $(\text{CH}_3)_2\text{NHBH}_2\text{CNAuCl}_3$: C, 9.3; N, 7.6; H, 2.6; Cl, 26.6. Theory: C, 9.3; N, 7.2; H, 2.3; Cl, 27.3.

Infrared Spectra

The infrared spectra of the above compounds were run as Nujol mulls and the values (cm^{-1}) obtained for the $\text{C}\equiv\text{N}$ stretching modes were as follows:

$\text{N}_m\text{BH}_3\text{CN}$	2179
$(\text{Ph}_3\text{P})_4\text{Au}_9\text{Cl}_6(\text{BH}_3\text{CN})_4$	2220
$(\text{CH}_3)_3\text{NBH}_2\text{CNAuCl}_3$	2240
$(\text{CH}_3)_2\text{NHBH}_2\text{CNAuCl}_3$	2245

Animal Tests

The activities of the gold complexes were measured using the rat-paw kaolin oedema model [4]. They were all inactive when administered orally; however, in each case gold was detected (using atomic absorption) in the blood of the rats. For example, the result of the analysis of the pooled sera of five rats each given orally 20 mg of the complex $(\text{Ph}_3\text{P})_4\text{Au}_9\text{Cl}_6(\text{Bu}_3\text{CN})_4$ was 0.64 ppm.

Results and Discussion

The cyanotrihydroborate anion and the amino-cyanoboranes are well-known reducing agents. With many of the gold complexes examined, colloidal gold(0) was the product. However, using cyanotrihydroborate and triphenylphosphine gold(I) chloride, a complex of empirical formula $(\text{Ph}_3\text{P})_4\text{Au}_9\text{Cl}_6(\text{Bu}_3\text{CN})_4$ was isolated. This is likely to be a gold cluster several of which have previously been prepared by reducing phosphine gold complexes with sodium tetrahydroborate [6]. It is reddish-brown in colour, insoluble in water and air-stable. It is interesting that either it or a metabolite is apparently ingested by rats, as a significant concentration of gold was found in their blood although no positive effect was observed in the rat-paw kaolin oedema model. The complexes of the type LAuCl_3 , where L was trimethylamine cyanoborane and dimethylamine cyanoborane, are probably square planar gold(III) complexes bonded through the nitrogen, as has been previously described for other cyanoborane complexes [7].

In conclusion, the preparation of simple gold(I) and gold(III) complexes with cyanoborane-type ligands suitable for therapeutic use appears to be unlikely, due to the tendency for reduction of the gold ions present to the metal. It is of interest, however, that the gold cluster gives rise to significant oral absorption of gold — whether as a polymer or dissociated monomer is as yet unknown. Since the

nature of the complexed gold affects its therapeutic properties, both beneficial and toxic, the cyanoborane cluster complexes could provide a possible alternative group of complexes worthy of further investigation.

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