

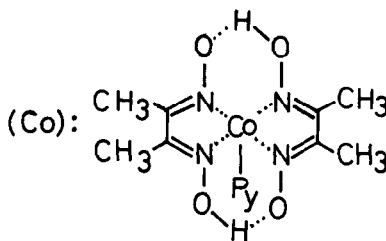
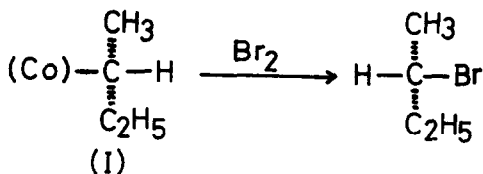
STEREOCHEMISTRY OF S_E2 REACTION OF ALKYL COBALOXIME,
 ALKYL BIS(DIMETHYLGLYOXIMATO)COBALT PYRIDINE

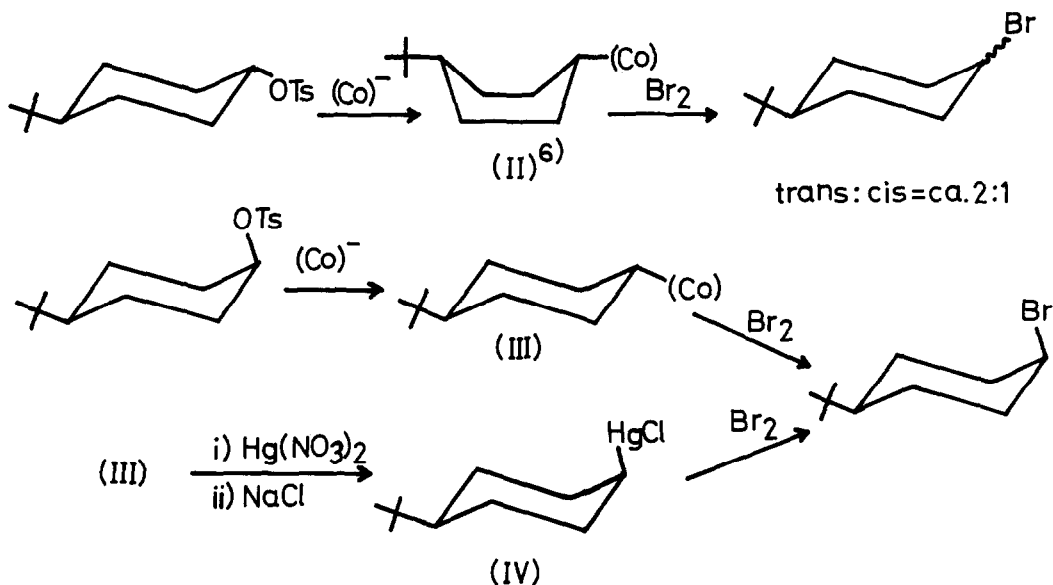
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It has been established by Schrauzer and his coworkers that alkyl bis(dimethylglyoximato)cobalt (alkyl cobaloxime, thereafter) constitutes a good model system of a biologically important alkyl cobalamin, coenzyme B_{12} analogue.¹⁾ Methyl cobalamin has been recognized to be responsible for the production of dimethyl mercury in the sludge of rivers and seas which caused a serious pollution problem.²⁾ S_E2 nature has been settled for the reaction forming alkyl mercury from mercuric ion and alkyl cobalamin and alkyl cobaloxime.³⁾ In S_E2 reaction, electrophilic reagent usually approaches from the same side to a leaving group giving the product with retention of configuration.⁴⁾ S_E2 reaction of sec-butyl cobaloxime (I) with bromine, however, has been reported to occur with inversion at the reaction center.⁵⁾ In this communication we like to add more examples of S_E2 reaction of alkyl cobaloximes with bromine and report about the steric course of the formation of alkyl mercurials from alkyl cobaloxime.

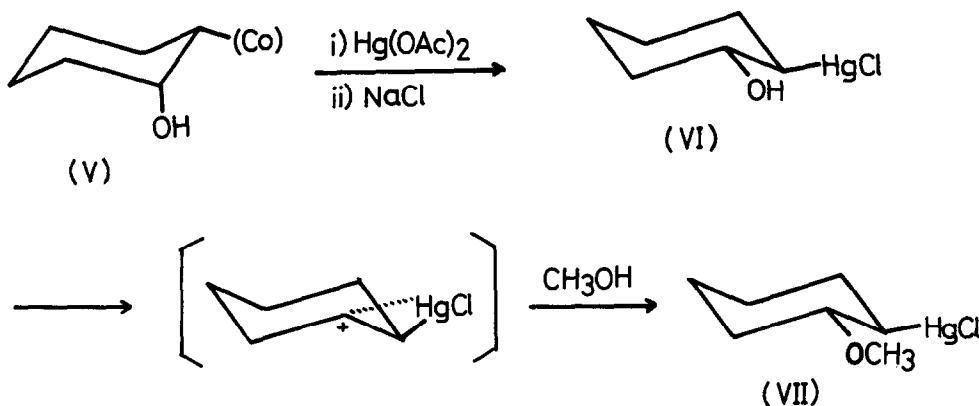




cis and trans-4-tert-Butylcyclohexyl cobaloximes (II and III) were synthesized by S_N2 displacement of trans and cis-4-tert-butylcyclohexyl tosylates with cobaloxime anion prepared in situ by NaBH_4 reduction of cobaloxime. The steric course of this reaction has been settled to proceed with inversion,⁷⁾ and the difference in the reactivity of the present reactions ---II, 7.7 and III, 40.7%⁸⁾ yields under the same reaction conditions --- is a good reflection of S_N2 nature.

Treatment of II dissolved in dichloromethane with 2.5 equivalents of bromine at -5°C gave a 2:1 mixture of trans-4-tert-butylcyclohexylbromide and its cis isomer in high yield. Same treatment of III afforded cis-4-tert-butylcyclohexylbromide exclusively in high yield. Treatment of III dissolved in methanol containing small amount of acetic acid (0.2 mol/l) with 2 equivalents of mercuric nitrate for 120 hr followed by treatment with aqueous sodium chloride gave organomercurial IV in poor yield. The product IV was identified to be cis-4-tert-butylcyclohexyl mercuric chloride by comparison with the authentic sample prepared from the corresponding Grignard reagent.⁹⁾ To ascertain a stereochemistry, product IV was further transformed into cis-4-tert-butylcyclohexylbromide by treatment with bromine in pyridine. The latter transformation has been proven to

proceed with retention of configuration.¹⁰⁾ Mercuration of cis-2-hydroxycyclohexyl cobaloxime (V)^{7,11)} with mercuric acetate for 22 hr followed by treatment with aqueous sodium chloride gave trans-2-methoxycyclohexyl mercuric chloride (VII) in 67 % yield. Methoxy derivative VII must be derived from hydroxy derivative VI formed initially, since β -effect of mercury facilitates extensively an ionization of the hydroxy group by perturbation with a filled d-orbital of mercury.¹²⁾ This type of displacement perturbed by transition metal retains the original configuration.¹³⁾ Compound VI, prepared independently by oxymercuration of cyclohexene, can be easily converted to VII by dissolving VI in methanol-acetic acid. The stereochemistry of the primary product VI, therefore, is most likely trans and the mercuration must take place with inversion of configuration.



Bromination and mercuration described in this communication proceed in highly stereospecific manner, inversion at the reaction center, and this feature of alkyl cobaloxime is in sharp contrast to most S_E2 reaction. Formation of cis-4-tert-butylcyclohexyl bromide from II as a minor product might be due to a homolytic fission of carbon cobalt bond of II. Another possibility is the partial racemization of II during its preparation since the epimer thus formed can not be differentiated by chromatography and spectroscopic analysis.

S_E2 reaction has been reported to proceed preferentially with inversion in some special cases such as brominations of alkyl tin compounds,¹⁴⁾ norbornyl lithium,¹⁵⁾ and tri-norbornyl borane assisted by sodium methoxide.¹⁶⁾ In general,

S_E2 reaction proceeds with retention of configuration but experimental findings described in this paper support further that the reaction can take place with inversion in special cases. Blocking of the front side by the large leaving group, bis(dimethylglyoximate)cobalt, enforces the reaction to take a different steric course, inversion. These properties of alkyl cobaloxime must be taken into account in considering the chemical nature of alkyl cobalamin, too.

References and Footnotes

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