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ARYLMERCURY COMPOUNDS

VI* A PROPOSED MECHANISM FOR THE SYMMETRIZATION OF ARYLMERCURIC SALTS IN THE PRESENCE OF CHELATING AGENTS

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Summary

A mechanism is proposed for the symmetrization of arylmercuric salts in the presence of chelating agents The roles of the chelating agent and auxiliary ligand (which is necessary in most cases) are considered The proposed mechanism includes three main steps (*i*) dissociation of the arylmercuric salt, (*ii*) formation of a reactive complex between the ionized arylmercuric salt and the chelating agent, (*iii*) an electrophilic substitution at a C—Hg bond via a two electron, three-center bond type transition state

Introduction

Most of the studies of the mechanism of symmetrization of organomercuric salts have involved RHgX in which R is an aliphatic group in reactions carried out in the presence of ammonia The exact nature of this reaction and the role of each of the reactants are still unresolved [2]

Reutov, Nesmeyanov et al [3-12] have shown that there is retention of configuration during the cleavage of the C—Hg bond Reutov and Beletskaya [5 7] have reported the reaction to be second order in the alkylmercuric halide, second order in ammonia (at least a 15 fold excess of ammonia is needed), reversible in each step and inhibited by the product Jensen [2, 13] concludes that the reaction is stereospecific, the kinetic expression for the reaction rate is $R = k[NH_3]^2\,[RHgBr]^2$, the reaction is irreversible, the ammonia has an important role in the course of the reaction, in addition to forming a complex with the mercuric salt produced

* For part IV see ref 1

Reutov et al [9-12, 14-17] suggested a four-center type transition state for the reaction but Jensen [2], who is critical of this description, suggests a "two-electron three-center bond" type transition state We have been concerned with the symmetrization of arylmercuric salts, in the presence of a chelating agent, such as ethylenediaminetetraacetic acid(EDTA) and an auxiliary ligand nucleophile as represented in eqn 1, and have undertaken a detailed study of the mechanism

$$2ArHgX + Che \xrightarrow{\text{nucleophile}} Ar_2Hg + Hg\ Che \qquad (1)$$

Che = chelating agent

We describe below our observations on the role of each of the reactants and our proposed multi step mechanism for the symmetrization

Results

Ionization of the arylmercuric salt (ArHgX) is an important feature of the symmetrization process The yield under identical conditions, benzene/H_2O (95/5) mixture for C_6H_5HgX falls in the order (X =) NO_3, ClO_4 (95%) > OAc (90%) > OH (80%) > BO_2 (60%) > BzO (45%), Cl (45%) > Br (20%) (No reaction occurs for X = I)

Because of the solubility characteristics of the chelating agent (sodium salt) the reaction is carried out under basic conditions Addition of excess hydroxide ions slows down the reaction (as shown in Table V in ref 18) Addition of common ion, e g OAc^- to the reaction mixture of ArHgOAc, causes a similar decrease in rate (Table 1) Furthermore, addition of Cl^- or Br^- ions to an aqueous reaction mixture stops the symmetrization process because of immediate precipitation of ArHgCl or ArHgBr The symmetrization rate is affected by the nature of the reaction medium with mixtures of organic solvents and water, the rate and yield decrease along with the dielectric constant of the organic solvent (Table 2)

An aqueous solution of phenylmercuric acetate has an absorption at λ = 241 nm ($\log \epsilon$ = 2 02) at this wavelength The UV spectra of aqueous solutions of phenylmercuric acetate and EDTA Na_4 in various ratios show the complex ArHg EDTA is formed (see Fig 1)

TABLE 1

COMMON ION EFFECT ON THE REACTION YIELD AFTER 15 MIN AT A CONSTANT pH (11 42 ± 0 02)

$$2\,C_6H_5HgOAc - 10\,n\text{-}BuNH_2 + EDTA\ Na_4 \xrightarrow{OAc^-} (C_6H_5)_2Hg$$

Added OAc^- (M) (from C_6H_5HgOAc (M))	Yield (%)
—	55
10	48
50	37
100	30

TABLE 2

EFFECT OF SOLVENT ON THE SYMMETRIZATION OF C_6H_5HgOAc

$2\ C_6H_5OAc + EDTA\ Na_4 + 10\ n\ BuNH_2 \rightarrow (C_6H_5)_2Hg$

Organic solvent [a]	Yield [b] (%)
Acetone	27
Ethanol	20
DMSO	19
THF	12
Dioxane	12

[a] Organic solvent/H_2O = 7/1 (v/v) [b] After 15 min

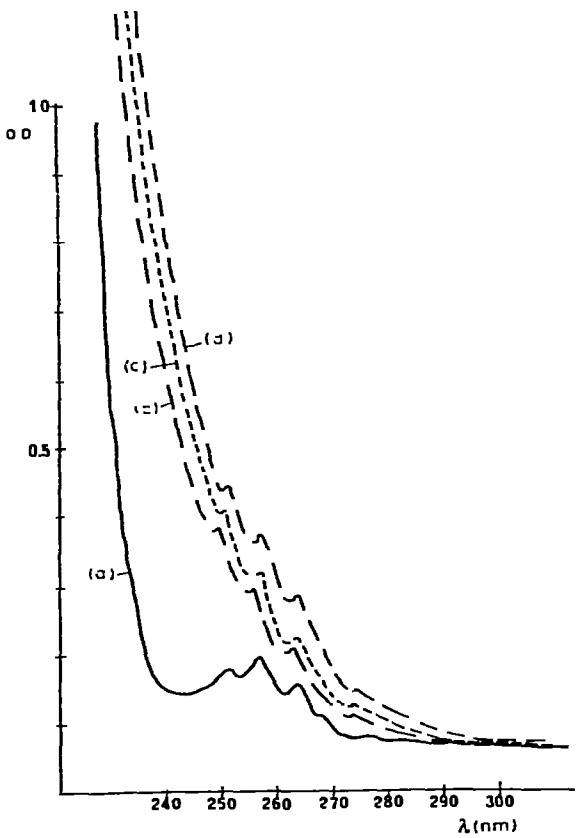


Fig 1 UV spectra of C_6H_5Hg EDTA complex in various ratios of C_6H_5HgOAc and EDTA Na_4 in aqueous solution (a) C_6H_5HgOAc alone (b) C_6H_5HgOAc/EDTA Na_4 3/1 (*M/M*) (c) C_6H_5HgOAc/EDTA Na_4 2/1 (*M/M*) (d) C_6H_5HgOAc/EDTA Na_4 1/1 (*M/M*)

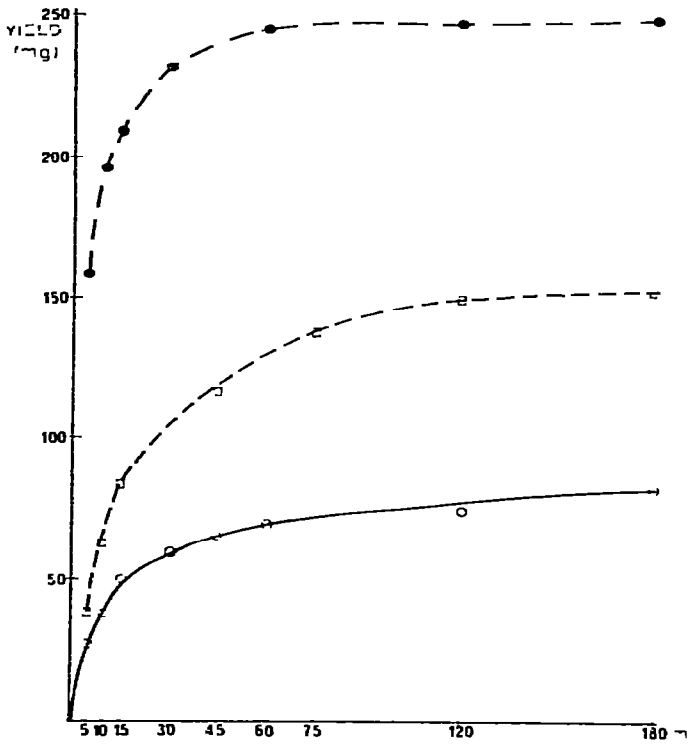


Fig. 2 Symmetrization of C_6H_5HgOAc in the presence of EDTA Na_4 (●) detarex Na_5 (○) and detarol Na_3 (▽) in aqueous solution and in the presence of n butylamine

The symmetrization proceeds faster and with higher yields when EDTA is present than when detarex (diethylenetriaminopentaacetic acid $(HOOCCH_2)_2N(CH_2)N(CH_2COOH)(CH_2)_2N(CH_2COOH)_2$) or detarol (*N*-hydroxyethylenediaminoethanetriacetic acid $HOCH_2CH_2\ HOOCCH_2N(CH_2)N(CH_2COOH)_2$) is present as shown by Fig 2 for the symmetrization of phenylmercuric acetate with n-butylamine as auxiliary ligand

The above three chelating agents were also used in symmetrizations of phenylmercuric acetate in which an excess of sodium thiocyanate was used as the auxiliary ligand Addition of thiocyanate to phenylmercuric acetate solution before addition of a chelating agent, causes the precipitation of phenylmercuric thiocyanate On the other hand, addition of the thiocyanate to phenylmercuric acetate solution containing a chelating agent causes coprecipitation of phenylmercuric thiocyanate and diphenylmercury Both the relative and the absolute amount of the two compounds in the precipitate are functions of the efficiency of the chelating agent and of its concentration in the reaction mixture, provided a constant initial concentration of the thiocyanate is used Table 3 summarizes the results obtained after 5 min reaction time in the symmetrization of phenylmercuric acetate in the presence of various amounts of EDTA, detarex and detarol with an excess of NaCNS to provide the auxiliary ligand

TABLE 3

INFLUENCE OF THE CHELATING AGENT (NATURE AND CONCENTRATION) ON THE SYMMETRIZATION YIELD IN THE PRESENCE OF EXCESS THIOCYANATE

$$2\ C_6H_5HgOAc + Che \xrightarrow{CNS^-} (C_6H_5)_2Hg$$

Chelating agent	Che (M)/ C_6H_5HgOAc (M)	Yield of product mixture [a] (mg)	$(C_6H_5)_2Hg$ in product mixture [a] [b] (%)	Yield of $(C_6H_5)_2Hg$ (%)
EDTA	0 25	313	12 5	11 0
	0 50	168	51 0	24 0
	1 00	45	66 0	8 5
Detarex	0 25	93	20 0	5 2
	0 50	52	63 0	14 0
	1 00	34	74 0	6 9
Detarol	0 25	185	8 4	4 4
	0 50	39	72 0	8 1
	1 00	30	56 4	4 6

[a] After 5 min [b] Calculated from the C H and N elemental analysis

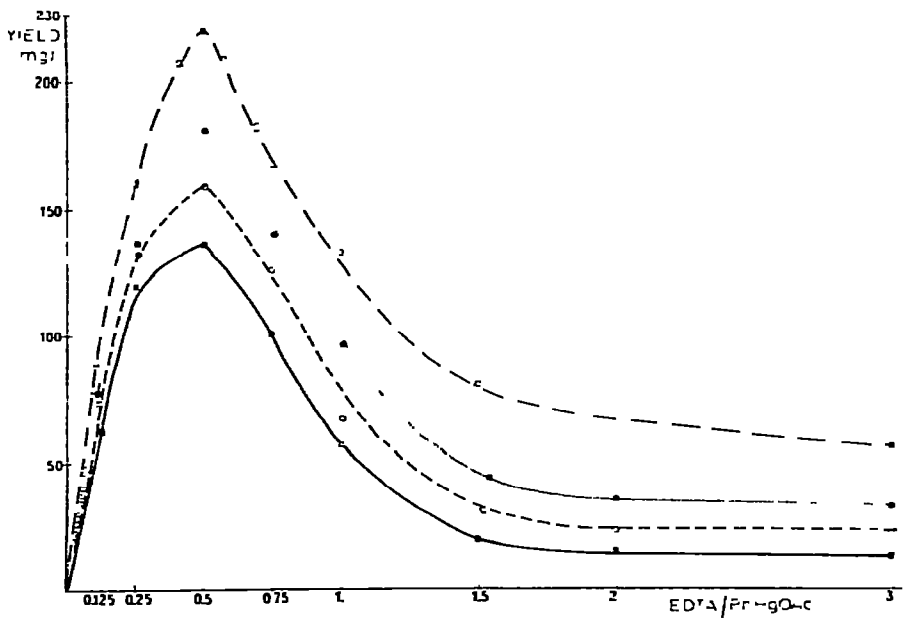


Fig 3 Influence of EDTA Na_4 concentration on the symmetrization of C_6H_5HgOAc in aqueous solution (pH 11 45 = 0 05) and in the presence of piperidine [piperidine/C_6H_5HgOAc 5/1 (M/M)] ▫ after 20 h ● after 120 min ○ after 30 min ■ after 15 min

TABLE 4

INFLUENCE OF EDTA Na_4 RELATIVE CONCENTRATION ON THE SYMMETRIZATION OF C_6H_5HgOAc [a]

$$2\,C_6H_5HgOAc + 10\,n\,BuNH_2 \xrightarrow{EDTA\ \ Na} (C_6H_5)_2Hg$$

EDTA - Na_4 (M)/C_6H_5HgOAc (M)	Yield [b] (%)
0 3	45
0 5	55
1 0	29
1 5	12

[a] At constant pH (11 45 - 0 03) [b] After 15 min

It was found that the concentration of the chelating agents has a marked effect in increasing both the reaction yield and rate when it is increased up to a molar ratio of 0 5/1 (chelating agent = arylmercuric salt), but further increase in this ratio, leads to a decrease in the reaction rate with no significant change in yield This behaviour is illustrated in Fig 3 for the symmetrization of phenyl mercuric acetate with EDTA Na_4 with piperidine as auxiliary ligand

The same effect is observed when n $BuNH_2$ is used as an auxiliary ligand (Table 4) and also in the absence of an auxiliary ligand (Table 5) With ammonia as an auxiliary ligand, the reaction reaches completion (95% yield) after a few seconds and no suitable method was found for following its process Replacing the ammonia hydrogens by alkyl groups on going to primary and secondary amines causes a decrease in the reaction rate and lowers the yield The symmetrization is slower with primary than with secondary amines present, while nucleophiles containing no amino group have even greater retarding effect (see Fig 3 and Table VII of ref 18)

Increasing the amount of the auxiliary ligand up to a molar ratio of 5/1 (auxiliary ligand = arylmercuric acetate) causes an increase, both in the symmetrization yield and rate Further increase of this ratio slows the reaction but

TABLE 5

SYMMETRIZATION OF m $(CH_3)_2C_6H_3HgOAc$ IN THE PRESENCE OF EDTA Na_4 AND THE ABSENCE OF NUCLEOPHILE [a] [b]

$$2m\ (CH_3)_2C_6H_3HgOAc \xrightarrow{EDTA\ \ Na_4} [m\ (CH_3)_2C_6H_3]_2Hg$$

EDTA Na_4 (M)/m-$(CH_3)_2C_6H_3HgOAc$ (M)	Yield [c] (%)
0 5	24
0 75	16
1 00	8
1 25	6

[a] In a H_2O/EtOH (3/2 V/V) mixture [b] At a constant pH (11 45 + 0 05) [c] After 15 min.

has no effect on the yield These findings are summarized in Fig 1 of ref 18 For the arylmercuric acetates, the greater electron releasing power of the substituent C_6H_4HgOAc the higher is the rate and the yield (after 24 h) (see Fig 3 of ref 18) Additional electron donating substituents also further increase the rate $(CH_3)_3C_6H_2 > (CH_3)_2C_6H_3 > CH_3C_6H_4 > C_6H_5$

The same yield (45 ± 1%, after 45 min at pH 11 4) was obtained for the following pairs of reaction systems

Phenylmercuric acetate mixed with piperidine for either one minute or 24 h, before adding EDTA Na_4

Phenylmercuric acetate mixed with EDTA Na_4 for either one minute, or 24 h, before adding piperidine No ring isomerization was found during the symmetrization of substituted arylmercuric salts, e g *ortho*- or *para*-substituted salts yield the di-*ortho* or di-*para* symmetrization products, respectively

Analysis of residual solution in those experiments in which the final yield (after 96 h) reaches only 80%, reveals the presence of starting material which does not react further but which can be precipitated quantitatively as ArHgCl by adding HCl Furthermore, addition of further starting material after the reaction has ceased leads to formation of more symmetrization product On the other hand, no more symmetrization is brought about by adding more EDTA · Na_4 or auxiliary ligand

Discussion

Based on the results of this work and related studies [1, 18] we propose below a mechanism for the symmetrization process of arylmercuric salts in the presence of a chelating agent together with (or in some cases in the absence of) an auxiliary ligand

The overall reaction (eqn 1) can be divided into 3 main steps

Ionization of the arylmercuric salt $ArHgX \rightleftharpoons ArHg^+ + X^-$

Complexation of the arylmercuric cation with the chelating agent $ArHg^+ + Che^{n-} \rightleftharpoons ArHgChe^{+1-n}$

Electrophilic substitution at the C—Hg bond $ArHg^+ + ArHgChe^{+1-n} \rightarrow ArHgAr + HgChe^{+2-n}$

Ionization

The ionization process is an essential step in the first stages of the reaction Compounds having a covalent Hg—X bond (e g phenylmercuric iodide [19]) do not symmetrize under these conditions The need for initial ionization is indicated by the following observations

Changing of the anion in C_6H_5HgX from X = OAc or NO_3 to anions such as borate, benzoate or chloride which form a partly covalent bond [19] causes a decrease in the reaction yield

With ArHgOAc, increasing the pH above 11 5 causes a decrease in both yield and rate The decrease results from the reaction between $ArHg^+$ and OH^- to form ArHgOH which is less ionized than ArHgOAc [19]

In a mixture of water and organic solvents, use of organic solvents having a low dielectric constant, e g THF or dioxane, leads to lower rates and yields than use of acetone, ethanol, or DMSO which have higher dielectric constants (see Table 2)

Addition of anions such as carbonate, thiocyanate, sulfide, and thiosulfate causes the precipitation of the corresponding arylmercuric salts

It is worthwhile to note that the influence of both thiosulphate and thiocyanate (which can also serve as an auxiliary ligand) on the course of the reaction is a function of the pH, their concentration to that of the arylmercuric salt and the presence or absence of EDTA Na_4. Addition of thiosulphate to PhHgOAc solution before addition of EDTA Na_4 or at an acidic pH causes immediate precipitation of $(PhHg)_2S_2O_3$. On the other hand, addition of the same anion to a basic solution of $PhHgOAc_2$, or after the addition of EDTA Na_4 leads to formation of the complex $\left[PhHg(S_2O_3)_2\right]^{3-}$ which participates in the symmetrization

The addition of thiocyanate to a reaction mixture containing EDTA Na_4 causes the formation of symmetrization product without formation of arylmercuric thiocyanate only if it is added in no more than five fold excess relative to the arylmercuric salt. At higher ratios, a substantial amount of PhHgCNS is coprecipitated with the symmetrization product

The existence of the reversible ionization reaction is revealed also by the common ion effect found in the symmetrization process (Table 1). The reversible ionization process is further indicated by the fact that in no case does the symmetrization yield the stoichiometric amount of diarylmercury compound, even though unchanged ArHgX is found after a long reaction time, when no further increase in the yield is taking place. The formation of Ar_2Hg tends to shift the equilibrium for the ionization process to the right by reducing the amount of free $ArHg^+$ cations, this leads to a progressive increase in the anion concentration which in turn causes the reversible association reaction to predominate. Hence the whole symmetrization process is self retarded

Complex formation

Following the ionization step, the $ArHg^+$ cation forms a complex with the chelating agent (step 2). Complexes of Hg^{2+} with different ligands (poly or mono-dentate) including EDTA are described in the literature [20-23]. In addition, complexes of $PhHg^+$ with various nucleophiles are known [24-26]. Although no complexes of arylmercuric salts with chelating agents are described in the literature, the enhancement in the UV absorption of ArHgX in the presence of EDTA · Na_4 (as is shown in Fig. 1 for phenylmercuric acetate) indicates the formation of such a complex

Formally the symmetrization takes place through a reaction between two electrophiles ($ArHg^+$) with expulsion of the Hg^{2+} cation. The contribution of EDTA · Na_4 to this process is to convert one of the electrophiles into a nucleophile through complex formation

The reversibility of this step is indicated by the observation that an excess of chelating agent, e.g. [chelating agent]/[ArHgX] > 0.5 decreases the rate but has no effect on the yield (Tables 4 and 5 and Fig. 3). This result indicates that a reversible, 1/1 (chelating agent/$ArHg^+$) complex is formed. The highest rate is obtained when $[ArHgX]_0 = 2[\text{chelating agent}]_0$

Excess of chelating agent reduces the concentration of $ArHg^+$ (via complexation) and hence slows the reaction, but because of the reversibility of the complexation no change in the final yield is observed Furthermore, the finding that the yield is unaffected by the order of introduction of the reactants, shows that the two initial steps (ionization and complex formation) are reversible

Electrophilic substitution

This step involves an electrophilic attack of $ArHg^+$ on a chelate having a nucleophilic character

The three factors which influence the nucleophile and the electrophile are described below

The influence of the chelating agent on the nucleophilicity of the formed chelate The factors influencing both the stability and reactivity of the ArHg Che^{-n+1} are consistent with those known for Hg Che^{-n+2} The analogy is explained by Jensen [2] who has suggested that the structure of $ArHg^+$ is basically $Ar^{\delta-}$ $Hg^{+(\delta+)}$ which is similar to Hg^{2+} EDTA, a hexadentate chelating agent, forms a chelate having four stable five member rings, formally reducing the charge on the mercury atom by four charge units Detarol, a five dentate chelating agent, is less effective than EDTA since it forms a chelate having only three heterocyclic rings and reduces the formal charge by only three charge units This correlation between number of rings in the chelate, formal reduction of charge on the mercury atom and efficiency in the symmetrization is manifested in Table 3 and also in the results obtained with NTA and MIDA [18] The same explanation accounts for the fact that no symmetrization takes place in the presence of ligands in which the carboxylic groups are replaced by alkyl, cyano or alcoholic groups [18]

Arylmercuric salts symmetrize less effectively with detarex than with EDTA present This is because the surplus negatively charged coordination dentates form an envelope which traps the electrophile before it reaches the reaction center, viz the C—Hg bond

When the chelating agent carries large groups (DATA) [18], steric effects prevent the formation of a stable complex with $ArHg^+$ [24] and no symmetrization takes place

The influence of the aromatic substituent and the nature of the auxiliary ligand on the nucleophilicity of the chelate The electron donating ability of the aromatic substituent has a substantial effect on the nucleophilicity of the chelate This effect is evident in the correlation between the nature of the substituent and the rate and yield When the aromatic ring bears more than one electron donating group (xylyl, mesityl, duryl, etc) a highly nucleophilic chelate is formed which reacts with the weak electrophile ($ArHg^+$) in the absence of an auxiliary ligand When the aromatic ring bears an electron withdrawing group (Cl or Br) or even weak electron donating groups (CH_3, OCH_3, $N(CH_3)_2$) the nucleophilicity of the formed chelate is too small to allow the symmetrization In these cases the presence of an auxiliary ligand (ammonia, amine, etc) is needed The auxiliary ligand donates its lone-pair electrons to the mercury atom in the chelate and enhances the C—Hg bond nucleophilicity so that attack by the weak electrophile can take place

At low concentrations the auxiliary ligand contributes only slightly to the

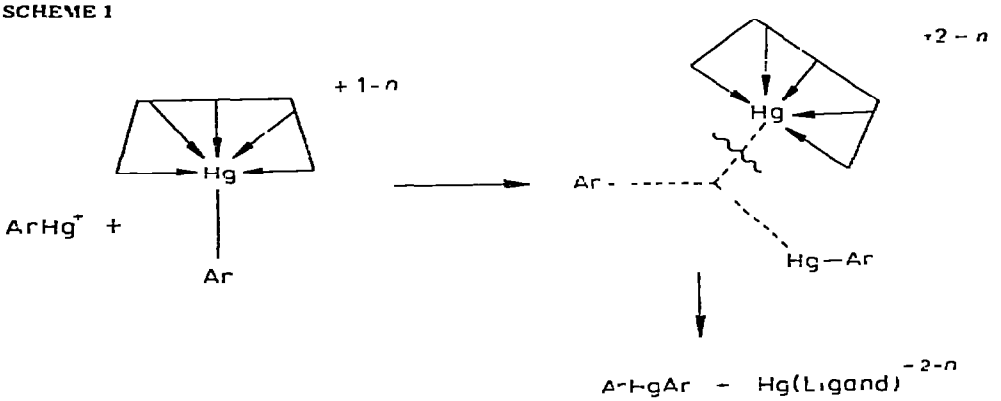
enhancement of the nucleophilicity of the chelate, and hence the efficiency of the process is low An increase in the reaction rate and yield is observed upon increasing the auxiliary ligand concentration up to a ratio of 5/1 (molar ratio of auxiliary ligand/ArHgX) A further increase of that ratio causes a decrease in the reaction efficiency (Fig 1 of ref 18) possibly due to a decrease in the electrophilicity of $ArHg^+$ because of its association with surplus auxiliary ligand These findings are in agreement with those described by Jensen [2]

The overall efficiency of an auxiliary ligand is determined by two opposing effects its ability to enhance the nucleophilicity of the formed chelate and its ability to reduce the electrophilicity of $ArHg^+$

Electrophilic substitution The third step of the reaction involves cleavage of a C—Hg bond (in the arylmercuric salt) and formation of a new C—Hg bond (in the symmetrization product) The fact that no isomerization occurs excludes an S_E1 mechanism This conclusion is in agreement with those of other investigators [3, 10-12, 14 16] According to Nesmeyanov et al , [3, 4] a back side S_E2 route is also excluded Reutov [9 12, 14-17] has proposed a four center, concerted transition state This mechanism, which according to Jensen [2] has not been confirmed, seems unlikely in our system because of steric interference by the bulky chelate

In the light of our work, it seems that a three-center two electron transition state of the type shown in Scheme 1, best describes the mechanism of the electrophilic substitution step This mechanism is consistent with Jensen's description of the transition state for the symmetrization of alkylmercuric salts [2] and with Olah's conception of σ bond nucleophilicity [28, 29]

SCHEME 1



Experimental

Materials

Phenylmercuric salts, PhHgX (where X = NO_3, OH, OAc, OBz, Br, I) were C P grade, commercially available materials The other arylmercuric salts were prepared by established methods All the arylmercuric salts were recrystallized from organic solvents

The ligands, EDTA, detarex, detarol, were obtained as commercial samples

as the free acids, and were converted into the suitable sodium salts by adding the necessary amount of NaOH solution All the amines were commercial samples of C P grade, and were freshly distilled before use

Methods and instruments

All the compounds mentioned were analyzed by the following methods melting point, elemental analysis, PMR (Varian T-60), IR (Perkin—Elmer grid IR model 457), mass spectra (Varian Mat model 311 mass spectrometer) and UV (Varian Cary 17 spectrophotometer)

pH measurements were carried out with a Coleman Metrion IV pH meter

Procedures

For details of experimental procedures see ref 18

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