BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 1050—1054 (1971)

The Solvent Effect on the Reaction of 1,1,4,4-Tetraphenyl-2-halobuta-2,3-dien-1-ol with Mercuric Halide

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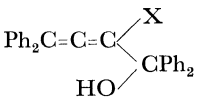
(Received August 3, 1970)

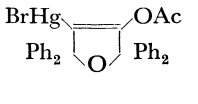
The reaction of the title compound (I) with mercuric halide in an aprotic and in a protic solvent afforded the fulvene derivative (VII) and the dihydrofuran derivative (VIII or IX) respectively. Both the cross-reactions (bromo-analog of I (Ia)+$HgCl_2$, chloro-analog of I (Ib)+$HgBr_2$) in an aprotic solvent afforded the chloro-fulvene derivative (VIIb). However, when the above reactions were carried out in a protic solvent, the product was the dihydrofuran derivative (IX), in which the halogen combining with carbon is chlorine and that combining with mercury is bromine. On the basis of the results of those cross-reactions, the reaction mechanism will be discussed. Acetonitrile showed distinctive behavior. In acetonitrile, the bromine of Ia was easily exchanged with the chlorine of sodium chloride at room temperature, and Ib was obtained quantitatively.

In a previous paper,[1] we have reported the reaction of the bromo-analog of the title compound (Ia) with mercuric acetate to afford various reaction products, depending on the nucleophilicity of the solvent used. When the reaction was carried out in acetic acid, the acetoxymercuration product II was obtained as the sole product. The reaction in alcohol, however, afforded the corresponding alkoxy acetylene alcohol (III), derived by the retropropargyl rearrangement,[2] and the mercurated dihydrofuran derivative (IV), derived by mercuration, followed by intramolecular cyclization, in various ratios depending on the bulkiness of the alkyl of the alcohol used. In the solvent with which it is not necessary to take account of its nucleophilicity, such as acetone, the reaction of Ia with mercuric acetate afforded the naphthalenone derivatives (V and VI), probably *via* an allenic epoxide intermediate.

In order to clarify the role of a protic solvent on the reaction of I with mercuric salt, we have studied the halomercuration of I in various protic and aprotic solvents. We have found that the variation in the main reaction product depends on whether the solvent used is protic or aprotic.



(I) a: X=Br; b: X=Cl



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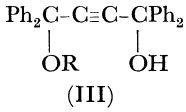

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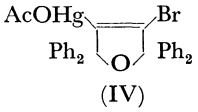

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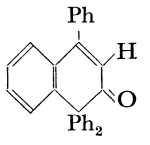
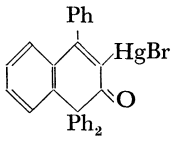


(V)



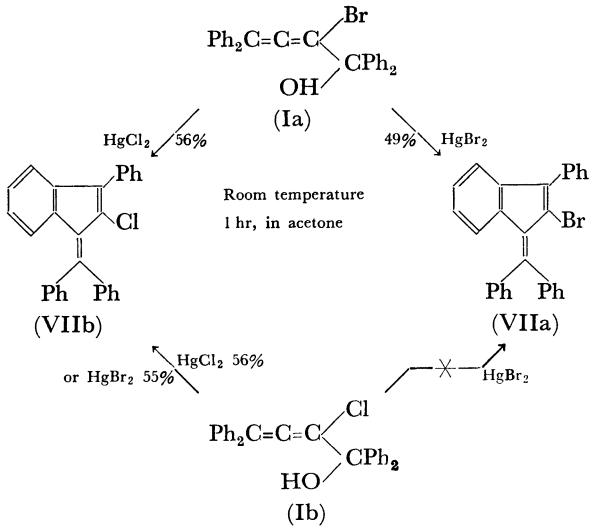
(VI)

Results. The treatment of an acetone solution of I with an equimolar amount of mercuric halide (HgX_2) for 1 hr at room temperature afforded mainly the fulvene derivative (VII) in the yields shown in Scheme 1 in addition to a small amount of the dihydrofuran derivative (VIII or IX). The structures of the main products were determined by a comparison of their mp's and infrared spectral data with those of

1) F. Toda and K. Akagi, *Tetrahedron*, **25**, 3795 (1969).
2) F. Toda, M. Higashi, and K. Akagi, This Bulletin, **42**, 829 (1969).

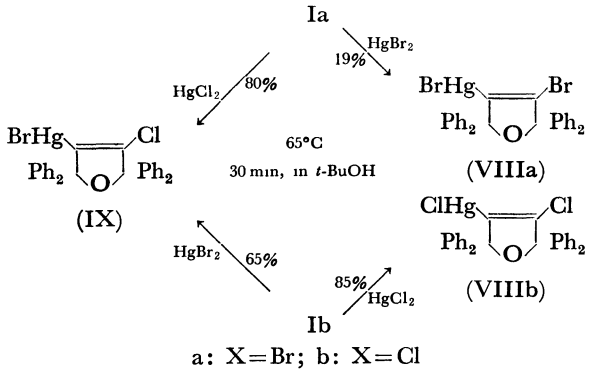
the corresponding authentic samples, VIIa[3] and VIIb.[4] Since both the cross reactions, Ia+$HgCl_2$ and Ib+$HgBr_2$ yielded the same product, VIIb, and since the VII product did not exchange the halogen upon treatment with HgX_2 under the same conditions as those employed for the halomercuration reaction, the reaction must proceed through a process in which halogen-exchange is possible. The above observation is important in order to clarify the reaction mechanism. It will be discussed in the following section.

The same treatment of I with HgX_2 in *t*-butanol as that employed for the reaction in acetone afforded VIII or IX in the yields shown in Scheme 2. The reaction of Ia+$HgBr_2$ and Ib+$HgCl_2$ afforded di-dibromo (VIIIa) and dichloro-derivatives (VIIIb) respectively. The two cross reactions, Ia+$HgCl_2$ and Ib+$HgBr_2$, however, yielded the same product, bromochloro derivative (IX), in which the halogen combining with carbon is chlorine and that combining with mercury is bromine. The results show again that the reaction proceeds *via* an intermediate in which halogen-exchange occurs. The reaction mechanism will be described in detail in the Discussion section.



Scheme 1

The structures of VIII and IX were determined by the methods shown in Scheme 3. The infrared spectral data of VIIIa thus obtained were identical with those of an authentic sample[1] prepared by shaking an acetone solution of IV with aqueous potassium bromide. The treatment of VIIIa with sodium borohydride in alcohol at room temperature afforded a demercurated product,



Scheme 2

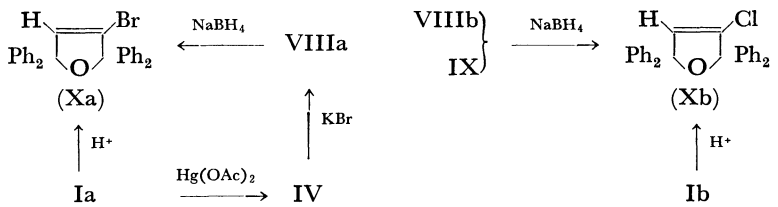
Xa, quantitatively. The spectral data of Xa were identical with those of an authentic sample prepared according to a previously-reported method[3], the acid-catalyzed cyclization of Ia. The sodium borohydride reduction of VIIIb and IX gave the same product, Xb, and its spectral data were identical with those of an authentic sample prepared by the acid-catalyzed cyclization of Ib.

As was described above, the type of the main product of the reaction of I with HgX_2 depends on the solvent used. In order to test the generality of the solvent effect on the reaction, several aprotic and protic solvents were employed for the reaction. The yields of the products of the reaction of Ia and $HgCl_2$ are summarized in Table 1, together with the reaction conditions. Because of the difference in the solubility of the reactants and in the reaction rate, the reaction condition differs slightly from each other. However, the product ratio was slightly affected by the reaction temperature and the time.

In all the aprotic solvents, the major product was VIIb. In some cases, however, IX was isolated as a minor product in addition to VIIb. Reversely, the major product of the reaction in a protic solvent, such as *t*-amyl, *t*-butyl and cyclohexyl alcohol, was IX. The anomalous behavior of acetic acid, phenol, and acetonitrile was also observed.

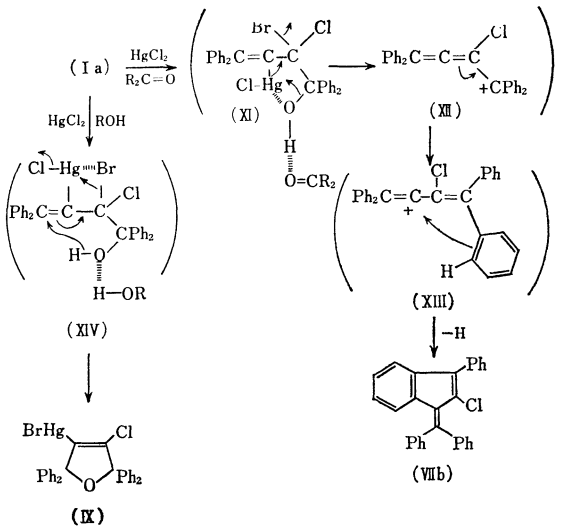
Discussion. On the basis of the finding that the reaction of Ia with $HgCl_2$ in aprotic and protic solvests afforded mainly the fulvene derivative (VIIb) and dihydrofuran derivative (IX) respectively (Table 1), and of the results of the cross reactions (Schema 1,2), the reaction mechanism which is shown in Scheme 4 was postulated. In Scheme 4, ketone is representative of the aprotic solvent.

For the intermediate (XI) initially produced by



Scheme 3

3) F. Toda, T. Komoda, and K. Akagi, *ibid.*, **41**, 1493 (1968).



Scheme 4

Table 1. Yield of the products of the reaction of Ia and $HgCl_2$

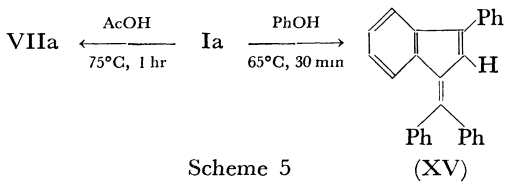
Reaction condition			Product (%)	
Temp.	Time (hr)	Solvent	VIIb	IX
r. t.[a]	1	Me_2CO	56	12
65°C	0.5	$(t\text{-Bu})_2CO$	95	—
65°C	0.5	cyclohexanone	82	—
refl.[b]	0.5	THF	71	6
refl.	0.5	Et_2O	82	9
r. t.	1	CS_2	56	6
r. t.	0.5	MeCN	77	(VIIIb, 6)
refl.	0.5	MeCN	97	—
r. t.	0.5	$MeCO_2H$	66	—
65°C	0.5	PhOH	61 (XV, 11)	—
65°C	0.5	*t*-AmOH	—	84
65°C	0.5	*t*-BuOH	15	80
65°C	0.5	cyclohexanone	15	42

a) Room temperature, b) Reflux.

the chloromercuration on Ia, an aprotic solvent serves as an electron-donor species and coordinates with the hydrogen of the hydroxyl group. The hydrogen bonding increases the electron density around the oxygen of the hydroxyl, and facilitates the coordination between mercury and the hydroxyl oxygen. Dechloromercuration, followed by the dehydroxylation of XI, affords the cation (XII). It is reasonable to consider that Br^- is more facile at leaving a moiety than Cl^- and that XI affords the chlorine-substituted cation (XII). The intramolecular cyclization of the cation (XIII) derived by the migration of the double bond of allene in XII affords VIIb.

In a protic solvent, however, the mercury-oxygen coordination in the chloromercurated intermediate (XIV) is inhibited because of the decreased electron density around the hydroxyl oxygen resulting from hydrogen bonding between the protic solvent and the hydroxyl oxygen. Therefore, the coordination between mercury and bromine is preferable. Intramolecular coordination between mercury and bromine has been postulated.[1,5] Of two halogens on the carbon of XIV, the elimination of Br^- occurs predominantly. Therefore, the reaction can be interpreted by a combination of the following two main processes: the Br^- attacks the mercury, and then the Cl^- leaves the mercury. The migration of the double bond and the intramolecular cyclization yields IX.

Of the five protic solvents cited in Table1, acetic acid and phenol differed widely from the others in the mode of reaction. In those solvents, the main reaction product was VIIb, not IX. A strong acid, such as acetic acid or phenol, would promote the dehydroxylation of the intermediate XI and finally afford VIIb *via* XII. The observation that the heating of Ia in acetic acid for 1 hr at 75°C afforded VIIa in a 68% yield, supports the above assumption. The conversion of I into VII by treatment with sulfuric acid has been reported.[2] Nevertheless, since the reaction of Ia with $HgCl_2$ in acetic acid afforded the halogen-exchanged product VIIb, but not VIIa, the process must also contain a halomercurated intermediate such as XI. The same interpretation is applicable to the reaction in phenol, which affords mainly a halogen-exchanged product VIIb and a small amount of halogen-free fulvene (XV). The process giving XV must proceed by a direct reaction of Ia and phenol, since the treatment of Ia with phenol at 65°C for 30 min afforded XV in an 90% yield (Scheme 5), even though its mechanism is not clear.



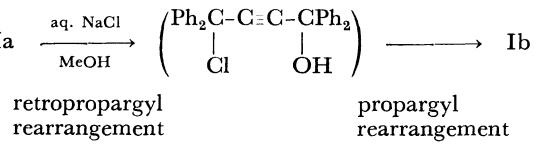
Scheme 5 (XV)

It is reasonable to assume that the halogen-exchange process on the reaction of I and HgX_2 is a part of the reaction, as has been discussed above, since neither of the reaction products, VII and VIII, exchanged its halogens with those of HgX_2 under the same conditions as were employed for the halomercuration. Nevertheless, the possibility that the exchange occurs before the reaction starts cannot be ruled out. If the halomercuration process of I to afford XI or XIV is reversible, halogen-exchange will occur before the reaction starts. This possibility can, however, be disregarded on the basis of the following observation. The reaction of Ia with five molar amounts of $HgCl_2$ in *t*-butyl alcohol afforded IX, but not any detectable VIIIb. If the halogen-exchange process precedes the reaction to afford the dihydrofuran derivative, the reaction product might be VIIIb or, at least, might be contaminated with VIIIb.

The reaction of Ia and $HgCl_2$ in acetonitrile is distin-

4) E. D. Bergmann, E. Fischer, and J. H. Jaffe, *J. Amer. Chem. Soc.*, **75**, 3230 (1953).

5) E. F. Kiefer and W. Gericke, *ibid.*, **90**, 5131 (1968).



Scheme 6

guishable from those in other aprotic solvents. The reaction at room temperature in acetonitrile afforded VIIIb (6%) instead of IX, in addition to VIIb (77%). Since shaking an acetonitrile solution of IX with $HgCl_2$ did not yield VIIIb, and since IX was recovered quantitatively, the complete halogen-exchange leading to VIIIb should occur before the completion of reaction. It can reasonably be assumed that the chloro-analog of Ia (Ib) initially formed by a halogen exchange between Ia and $HgCl_2$ reacts with $HgCl_2$ to afford VIIIb. This assumption was certified by shaking an acetonitrile solution of Ia with sodium chloride at room temperature for 30 min; this afforded Ib quantitatively. The halogen-exchange probably proceeds by the sequence of retropropargyl-propargyl rearrangements shown in Scheme 6. The exchange, however, was not observed in other aprotic solvents tested, such as acteone and tetrahydrofuran. The treatment of Ib with aqueous potassium bromide in acetonitrile, however, did not afford Ia.

Experimental

All the melting points were uncorrected. The infrared spectra were recorded in Nujol mull on a spectrophotometer, IR-E, of the Japan Spectroscopic Co. The molecular weights were determined by means of a molecular-weight apparatus of Hitachi-Perkin Elmer, model 115, in benzene.

1,1,4,4-Tetraphenyl-2-halobuta-2,3-dien-1-ol (I). The bromo-analog (Ia) was prepared according to a previously-reported method.[3] The chloro-analog (Ib) was prepared by a modified version of that method used for the preparation of Ia. Into an ice-cooled solution of 1,1,4,4-tetra-phenyl-but-2-yne-1,4-diol (5 g, 13 mmol) in acetic acid (30 m*l*) - benzene (12 m*l*), concentrated hydrochloric acid (5 m*l*) dissolved in acetic acid (20 m*l*) was stirred drop by drop, over a period of 10 min. After the stirring had then been continued for a further 30 min, ice water (100 m*l*) was added to the reaction mixture. The crude product which separated was extracted with ether. The ether solution was washed with water, aqueous sodium bicarbonate, and water successively, and dried over sodium sulfate. The crude crystals obtained by the evaporation of the solvent were recrystallized from benzene - petroleum ether to afford Ib as colorless prisms (2.7 g) (51%); mp 100—101°C. IR 3400 (OH) and 1945 cm^{-1} (C=C=C).

Found: C, 82.16; H, 5.38%. Calcd for $C_{28}H_{21}OCl$: C, 82.25; H, 5.14%.

Acid-catalyzed Intramolecular Cyclization of Ib. A solution of Ib (0.1 g) in acetone (3 m*l*) containing two drops of concentrated hydrochloric acid was heated under reflux for 10 min. The crude crystals obtained by the evaporation of the solvent were washed with water and recrystallized from methyl alcohol to give Xb as colorless needles (0.03 g) (30%); mp 169—169.5°C. IR 1630 (C=C) and 1020 cm^{-1} (C–O).

Found: C, 81.98; H, 5.07%. Calcd for $C_{28}H_{21}OCl$: C, 82.25; H, 5.14%.

General Procedure of the Reaction of I and HgX_2. A mixture of I (1 mmol), HgX_2 (1 mmol), and solvent (5 m*l*) was treated under the reaction conditions summarized in Table 1 and in Scheme 1 and 2. When the reaction was carried out in a solvent with a boiling point lower than 100°C, such as all the aprotic solvent used except di-*t*-butyl ketone and cyclohexanone, the reaction product was isolated by the evaporation of the solvent. On the other hand, when the reaction was carried out in a solvent which boils at temperature higher than 100°C, the reaction product was isolated by adding petroleum ether to the reaction mixture.

The crude product thus obtained was purified by recrystallization or was fractionated into components by fractional recrystallization.

Some examples of each case are shown in the following columns.

Reaction of Ia and $HgCl_2$ in Acetone. A solution of Ia (0.46 g, 1 mmol) and $HgCl_2$ (0.28 g, 1 mmol) in dry acetone stirred at room temperature for 1 hr. The crude product obtained by the evaporation of the acetone was extracted with petroleum ether (20 m*l*). The evaporation of the solvent afforded VIIb as red prisms (0.22 g) (56%); mp 158°C (lit,[4] mp 159—160°C). The spectral data of VIIb were identical with those reported in the literature.[4] The residue remaining after the extraction with petroleum ether was extracted with cyclohexane (20 m*l*). The removal of the solvent of the cyclohexane solution afforded IX as colorless plates (0.08 g) (12%); mp 194—195°C. IR 1610 (C=C) and 1015 cm^{-1} (C–O).

Found: C, 48.67; H, 2.92%; mol wt (benzene), 696. Calcd for $C_{28}H_{20}OHgBrCl$: C, 48.84; H, 2.91%; mol wt 688.

The reaction of IX by sodium borohydride in ethyl alcohol yielded Xb in an almost quantitative yield.

By the same procedure, Ib was treated with $HgBr_2$ in acetone to afford VIIb (55%) and IX (9%).

Under the same conditions, Ia reacted with $HgBr_2$ to give VIIa (49%) as red prisms; mp 160°C (lit,[3] mp 160—161°C).

Under the same conditions, Ib reacted with $HgCl_2$ and yielded VIIb (56%) and VIIIb (4%) as colorless plates; mp 253—260°C. IR 1615 (C=C) and 1020 cm^{-1} (C–O).

Found: C, 52.85; H, 3.23%; mol wt (benzene), 669. Calcd for $C_{28}H_{20}OHgCl_2$: C, 52.26; H, 3.11%; mol wt, 644.

The sodium borohydride reduction of VIIIb afforded Xb quantitatively.

Reaction of Ia and $HgCl_2$ in t-Butyl Alcohol. A mixture of Ia (0.46 g, 1 mmol), $HgCl_2$ (0.28 g, 1 mmol), and *t*-butyl alcohol (5 m*l*) was stirred at 65°C for 30 min. The crystals which separated out upon the addition of petroleum ether (20 m*l*) to the reaction mixture were collected by filtration and were recrystallized from cyclohexane to afford IX (0.48 g) (70%). The petroleum ether solution remaining after the removal of IX was concentrated to dryness. The fractional recrystallization of the residue from petroleum ether afforded VIIb (0.06 g) (15%) and some additional IX (0.07 g) (10%).

By the same procedure as was employed for the above reaction, Ia was treated with $HgBr_2$ in *t*-butyl alcohol to afford VIIIa (19%) and (2%). The structure of VIIIa was determined by a comparison of its infrared spectrum (1620 (C=C) and 1015 cm^{-1} (C–O)) with that of an authentic sample prepared according to the previously-reported method,[1] as is shown in Scheme 3. The sodium borohydride reduction of VIIIa gave Xa quantitatively.

The reactions of Ib+$HgCl_2$ and Ib+$HgBr_2$ in *t*-butyl alcohol afforded VIIIb (85%), and VIIIb (65%) and VIIb (15%), respectively.

Reaction of Ia and $HgCl_2$ in Phenol. A mixture of Ia (0.46 g, 1 mmol), $HgCl_2$ (0.28 g, 1 mmol), and phenol (5 m*l*) was stirred at 65°C for 30 min. After cooling, water was added to the reaction mixture, the product which was crystallized out was fractionated by fractional recrystallization from *n*-hexane to afford VIIb (0.24 g, 61%) and XV (0.05 g, 11%) as yellow prisms; mp 204°C (lit,[3,6] mp 204—205°C). The infrared spectral data of XV were identical with those of an authentic sample prepared according to the literature.[3]

Reaction of Ia and Phenol. A solution of Ia (0.23 g, 0.5 mmol) in phenol (2.5 m*l*) was heated at 65°C for 30 min. After cooling, the reaction mixture was diluted with water to give XV (0.16 g) (90%).

Reaction of Ia with Acetic Acid. A solution of Ia (0.23 g, 0.5 mmol) in acetic acid (2.5 m*l*) was heated at 75°C for 1 hr. The evaporation of the solvent gave VIIa, after recrystallization from acetone (0.15 g) (68%).

Reaction of Ia with Five Molar Amounts of $HgCl_2$ in t-Butyl Alcohol. A mixture of Ia (0.46 g, 1 mmol), $HgCl_2$ (1.35 g, 5 mmol) and *t*-butyl alcohol (5 m*l*) was heated at 65°C under stirring for 30 min. The residue remaining after evaporation of the solvent under reduced pressure was extracted with cyclohexane (20 m*l*). The evaporation of the solvent of the cyclohexane solution afforded IX (0.688 g) (100%). The bromochloro compound (IX) thus obtained was proven, by a careful infrared spectral study, not to be contaminated with any detectable amount of dichloro-analog (VIIIb).

Reaction of Ia with Aqueous Sodium Chloride in Acetonitrile. A solution of Ia (0.23 g, 0.5 mmol) in acetonitrile (2.5 m*l*) was shaken with saturated aqueous sodium chloride (2.5 m*l*) at room temperature for 30 min. An acetonitrile layer was then separated and concentrated to dryness to afford Ib (0.19 g) (97%).

Reaction of Ia with Aqueous Sodium Chloride in Acetone (or Tetrahydrofuran). The same treatment of Ia as above with aqueous sodium chloride in acetone (or tetrahydrofuran) gave the recovered Ia in a quantitative yield in both cases.

The authors wish to express their thanks to Mr. Shoichi Kato for the elemental analyses, and to Miss Toshiko Matsumoto for her measurement of the molecular weights.

6) J. Salkind and A. Kruglo, *Ber.*, 61, 2306 (1928).