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*Dedicated to Full Member of the Russian Academy of Sciences
I. P. Beletskaya on occasion of her jubilee*

Reaction of Catalytic Olefination of Hydrazones with Polyhaloalkanes. Investigation of Alkene Formation Chemoselectivity

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Abstract—Hydrazones of carbonyl compounds at treatment with polyhaloalkanes in the presence of CuCl as catalyst are converted into substituted alkenes with formation of a new C=C bond.

We recently found a new reaction for olefinating carbonyl compounds: Catalytic Olefination Reaction (COR) [1–7]. It was demonstrated that the treating of N-unsubstituted hydrazones of aromatic aldehydes and ketones with carbon tetrachloride in the presence of catalytic amounts of CuCl afforded the corresponding β,β-dichlorostyrenes [2, 7]. Thus a new carbon-carbon double bond is created as a result of redox reaction. This approach to olefination of carbonyl compounds is totally new and has no published analogs. It was shown that catalytic olefination is a general process. Alongside the carbon tetrachloride as olefination reagents are suitable the other polyhaloalkanes: carbon tetrabromide [5, 7], bromoform [4, 7], Freones CF_3CCl_3 and $CF_2Cl–CFCl_2$ [6]. The corresponding polyhaloalkanes in the reaction play the role of C_1- and C_2-building blocks. It turned out that variation of haloalkanes in reaction with hydrazone provided different types of di-, tri-, and tetra-substituted alkenes; therewith the structure of arising alkenes **II** depended on the character of the halogen-containing reagent. Alongside alkenes the COR affords symmstrical azines **III** (Scheme 1).

This method of alkene synthesis has obvious advantages of simple apparatus and easy isolation of the reaction products, mild conditions and high yields of the target substances. These features characterize the new reaction as very promising and easy for use in the organic synthesis.

Formal result of the reaction is a elimination of two halogen atoms from the molecule of the poly-haloalkane. Under COR conditions occurs the rupture of C–Br [4, 5], C–Cl [2, 3], and even C–F [6] bonds in the molecule of the initial halogen-containing compound although the energies and bond lengths of C–Hlg bonds significantly differ: C–Br, bond length 1.938 Å, bond energy 70 kcal mol^{-1}; C–Cl, bond length 1.767 Å, bond energy 83.5 kcal mol^{-1}; C–F, bond length 1.379 Å, bond energy 108 kcal mol^{-1} [8]. Consequently, in the presence of different halogen atoms in a molecule the competitive elimination thereof under reaction conditions is possible which might provide different alkene types. Thus the establishing of factors governing the laws of halogens elimination and the reaction chemoselectivity is of fundamental theoretical and practical importance.

Scheme 1.
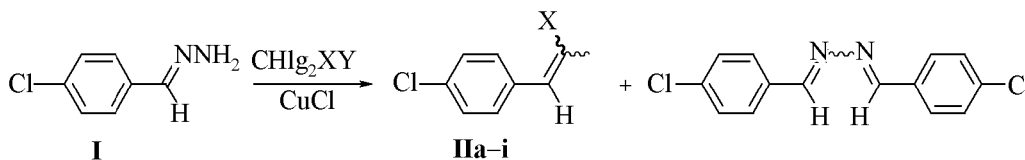
II, Hlg = Y = X = Cl (**a**); X = Br, Y = Hlg = Cl (**b**); Hlg = Y = X = Br (**c**); X = H, Y = Hlg = Cl (**d**); X = F = Br (**e**); X = F, Y = Hlg = Cl (**f**); X = CF₃, Y = Hlg = Cl (**g**); X = F, Y = CClF₂, Hlg = Cl (**h**).

Reaction of hydrazone **I** with polyhaloalkanes

| Polyhaloalkane | Yield of reaction products, % | | | | | |
| | DMSO–aqueous ammonia | | | ethanol–ethylenediamine | | |
	alkene (II)	Molar ratio of products[a]	azine (III)	alkene (II)	Molar ratio of products[a]	azine (III)
CCl_4	74	**IIa**	21	92	**IIa**	5
$CBrCl_3$	71	**IIa, IIb** (98 : 2)	20	54	**IIa**	37
CBr_2Cl_2	82	**IIa, IIb** (95 : 5)	10	78	**IIa, IIb** (71 : 29)	17
CBr_4	89	**IIc**	7	55	**IIc**	23
$CHCl_3$	0	–	56	0	–	73
$CHBrCl_2$	44	**IId, IIe** (98 : 2)	52	32	**IIe**	55
$CHBr_2Cl$	41	**IId, IIe** (84 : 16)	53	41	**IIe, IIe** (71 : 29)	41
$CHBr_3$	67	**IIe**	26	30	**IIe**	65
$CFCl_3$	Traces	**IIg**	30	58	**IIg**	17
$CCl_3\text{-}CF_3$	63	**IIh**	21	64	**IIh**	33
$CCl_2F\text{-}CClF_2$	20	**IIi**	21	49	**IIi**	44

[a] According to the data of ^{1}H NMR spectra.

We have chosen 4-chlorobenzaldehyde hydrazone (**I**) as a model compound for investigation of factors affecting the chemoselectivity of COR. A wide range of polyhaloalkanes of different character was used as olefinating reagents: tetrahalomethanes CBr_nCl_{4-n} (n = 0, 1, 2, 4; products of successive replacement of chlorine with bromine in carbon tetrachloride: CCl_4, $CBrCl_3$, $CBr2Cl_2$, CBr_4); haloforms $CHBr_nCl_{3-n}$ (n = 0, 1, 2, 3; products of successive replacement of chlorine with bromine in chloroform: $CHCl_3$, $CHBrCl_2$, $CHBr_2Cl$, $CHBr_3$); Freons CCl_3F, CCl_3CF_3, $CCl_2F–CClF_2$, CBr_2F_2.

We formerly showed that the character of solvent and of base used in the reaction significantly affected the yield of the target alkenes. Two types of optimal reaction conditions were selected for different poly-haloalkanes. When polychloro- and polybromo-methanes CCl_4, CBr_4, $CHBr_3$ were applied the best yields of the target alkenes were obtained at reaction in DMSO with aqueous ammonia used as base [2]. In reaction with Freons optimal solvent and base were respectively ethanol and 1,2-ethylenediamine [6]. Thus these two reaction systems supplement each other and cover the whole range of halogen-contain-ing COR reagents we have studied. Therefore the reactions with the model hydrazone **I** were performed in both systems.

The reaction was cariied out in the presence of CuCl as catalyst (10 mol%). Polyhaloalkenes were used in 5-fold excess with respect to hydrazone **I**. The

structures of the formed alkenes **IIa–I** were studied by GC-MS method and ^{1}H NMR spectroscopy.

It was established that the treatment of hydrazone **I** with tetrahalomethanes in all cases afforded β,β-di-halostyrenes (**IIa–c**) and azine **III** as only products. The overall yield of the two COR products, alkene **IIa–c** and azine **III**, was close to quantitative yield (see the table).

The thorough investigation of reaction mixtures composition revealed that at the use bromotrichloro-methane $CBrCl_3$ and dibromodichloromethane CBr_2Cl_2, which contained simultaneously chlorine and bromine, alongside the main product, dichloro-alkene **IIa**, arose also some bromochloroalkene **IIb**. It was demonstrated that at successive replacement of bromine for chlorine the fraction of alkene **IIb** increased. Consequently, under COR conditions in the reagent molecule are cleaved prevailingly the C–Br bonds in keeping with the strength of the C–Hlg bonds.

The treating of hydrazone **I** with tetrahalomethanes in the reaction system ethanol–ethylenediamine were obtained the same products (see the table). However in reaction with dibromodichloromethane CBr_2Cl_2 the chemoselectivity sharply decreased as compared with the process in DMSO, and bromo-chloroalkene **IIb** was obtained in 29% yield.

Similarly occurs reaction between haloforms and hydrazone **I** in the presence of CuCl. Therewith the

corresponding vinyl halides **IId** and **IIe** and also azine **III** are formed (see the table). At the use of chloroform in both reaction systems no β-chlorostyrene was detected, the only reation product was azine **III**. However replacement of one chlorine by bromine (at the use of CHBrCl$_2$) resulted in a good yield of the target alkene **IIg**; therewith the yield of product in DMSO is higher than in ethanol. The *E*-isomer of alkene prevailed in the product.

The use of dichlorobromomethane CHBrCl$_2$ as olefinating reagent in COR opens a convenient preparative route to β-chlorostyrenes. In going from CHBrCl$_2$ to dibromochloromethane CHBr$_2$Cl the fraction of β-bromostyrene **IIf** considerably increased (see the table).

The chemoselectivity of reaction with compounds containing fluorine, chlorine, and bromine was studied on a series of Freons, namely on CCl$_3$F, CCl$_2$F–CClF$_2$, CCl$_3$–CF$_3$, and CF$_2$Br$_2$. The same systems were used for olefination. It turned out that reaction of hydrazone **I** with chlorofluoroalkanes gave rise to fluoroalkenes (**IIf–h**) and azine **III**.

The formation of fluoroalkenes **IIf–h** occurred stereoslectively. The composition of reaction mixtures was additionally studied by GC-MS method. The application for olefinating Freones CCl$_3$F and CCl$_3$–CF$_3$ afforded only alkenes **IIf** and **IIg** evidencing especially high selectivity of reaction with these Freones. With Freon CCl$_2$F–CClF$_2$ traces of alkene **IIi** (*m/z* 256) were detected in the reaction mixture; the product resulted from rupture of chlorine and fluorine from the Freon molecule.
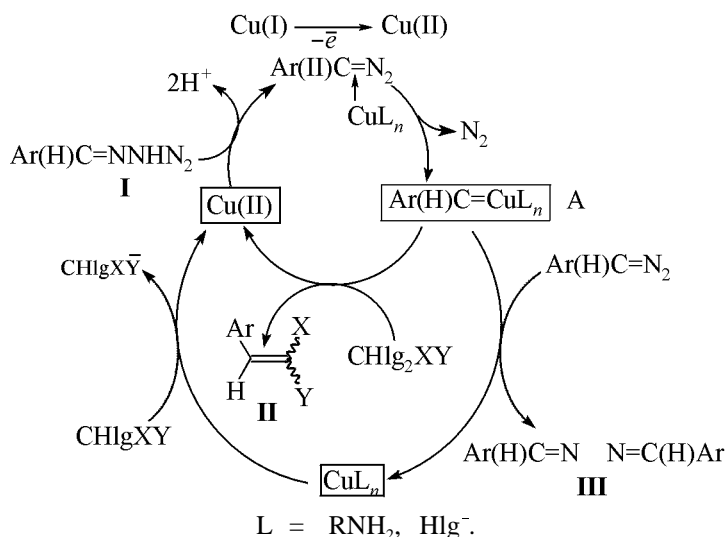
Reactions of hydrazone **I** with all polyhaloalkanes studied in this work (excluding CBr$_2$F$_2$) in the presence of CuCl gave rise to the same comounds: alkenes **II** and azine **III**. As a rule the overall yield of COR products is close to quantitative, no other compounds resulting from hydrazone **I** transformations were found in the reaction mixtures. These facts led us to an assumption that in all cases the reactions between hydrazone **I** and the halogen-containing reagents followed the same mechanism (Scheme 2).
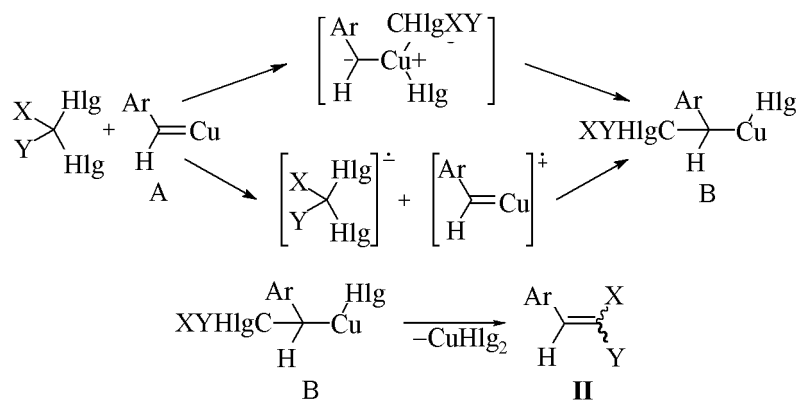
We previously studied the COR mechanism and explained the processes occurring in the system and providing the reaction products, alkenes **II** and azine **III** [2, 4, 7]. In the first stage hydrazone **I** is oxidized by Cu(II) compounds arising in the system furnishing the corresponding diazoalkane. Further decomposition of diazoalkane catalyzed by copper results in formation of a copper-carbene complex A, a key reaction intermediate. The reaction of the complex with polyhaloalkanes affords alkenes **II** with regeneration of Cu(II) thus starting the new catalytic cycle (inner cycle). Complex A also reacts with diazoalkane furnishing azine **III** (outer cycle).

The relations found in elimination of halogens from polyhaloalkanes containing simultaneously various halogen atoms required that the mechanism of alkene formation be supplemented. A more detailed consideration of interaction between copper-carbene complex A and polyhaloalkanes provides an understanding of the observed chemoselectivity. A reaction of CCl$_4$ and other polyhaloalkanes addition to double carbon-carbon bonds in the presence of CuCl furnishing 1:1 adducts is studied in detail and well documented [9 11]. Two possible mechanisms were suggested for this reaction. The reaction either proceeds along radical mechanism [11]

Scheme 2.

$$Cu(I) \xrightarrow{-\bar{e}} Cu(II)$$

Ar(II)C=N$_2$

CuL$_n$ → N$_2$

2H$^+$

Ar(H)C=NNHN$_2$

I

Cu(II)

$\boxed{Ar(H)C=CuL_n}$ A

Ar(H)C=N$_2$

CHlgX$\bar{Y}$

CHlg$_2$XY

Ar X

H Y

II

CHlgXY

CuL$_n$

Ar(H)C=N N=C(H)Ar

III

L = RNH$_2$, Hlg$^-$.

Scheme 3.

or through intermediate formation of Cu(III) compounds [12, 13]. We assume that similarly reacts the copper-carbene complex with polyhaloalkanes under the COR conditions. In the first stage arises an organocopper compound B either via addition of polyhaloalkane to copper-carbene complex A by insertion of copper into the C–Hlg bond, or through a preliminary one-electron transfer resulting in formation of a pair "cation-radical—anion-radical" that subsequently undergoes dimerization in the solvent cage (Scheme 3). Subsequent elimination of Cu(II) salt from B intermediate results in alkene **II** formation.

The chemoselectivity is very high in reactions with polyhaloalkanes containing a single bromine atom ($CBrCl_3$, $CHBrCl_2$): Only traces of bromine-containing alkenes **IIb** and **IIe** are formed (see the table).

However the replacement of one more chlorine by bromine in the reagent molecule causes increase in the amount of bromine-containing alkenes out of proportion. It seems that in the first stage almost exclusively C–Br bonds in the polyhaloalkane are disrupted with Cu–Br bond formation in keeping with the published data on the bromochloroalkanes addition to olefins [9, 10]. Thus the first stage procceds selectively: when the initial reagent contains a single bromine atom the subsequent β-elimination of CuBrCl from B intermediate results in the only chlorocontaining alkene **II**. When the initial reagent contained more than one bromine atom (CBr_2Cl_2, $CHBr_2Cl$) the subsequent elimination of Cu(II) salt may occur by two routes affording two different alkenes (Scheme 4). Therefore the overall chemoselectivity of the reaction depends on the decomposition of intermediate B. Apparently the elimination of
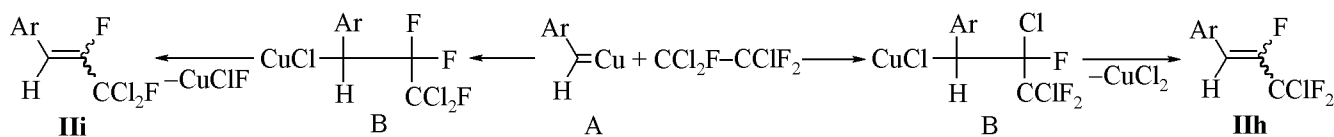
Scheme 4.

$$X = H, Cl.$$
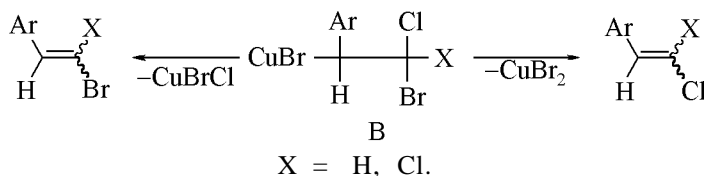
$CuHlg_2$ from intermediate B occurs significantly faster and less selectively, probably due low stability of **B**.

The comparison of two reaction systems studied (DMSO aqueous ammonia and ethanol–ethylenediamine) shows that in the latter system the reaction is less chemoselective. The most probable cause thereof is the higher nucleophilicity of ethylenediamine as compared with ammonia. As a result the intermediate B in the second system decomposes faster, and consequently the reaction is less selective.

The excellent chemoselectivity of olefination with Freons CCl_3F, CCl_3CF_3 also originates from significantly higher strength of the C–F bond as compared to that of C–Cl bond. However unsymmetrical Freon CCl_2F–$CClF_2$ can react with copper-carbene complex A at two different ends affording two different intermediates B and C. The subsequent elimination of $CuHlg_2$ fom intermediates B and C results in two different alkenes **IIh** and **IIi** although the formation of compound **IIi** occurred as a minor process (Scheme 5).

Scheme 5.

$$\underset{\textbf{IIi}}{\overset{Ar}{\underset{H}{>}}=\overset{F}{\underset{CCl_2F}{<}}} \xleftarrow{-CuClF} \underset{B}{CuCl-\overset{Ar}{\underset{H}{|}}-\overset{F}{\underset{CCl_2F}{|}}-F} \longleftarrow \underset{A}{\overset{Ar}{\underset{H}{>}}=Cu} + CCl_2F-CClF_2 \longrightarrow \underset{B}{CuCl-\overset{Ar}{\underset{H}{|}}-\overset{Cl}{\underset{CClF_2}{|}}-F} \xrightarrow{-CuCl_2} \underset{\textbf{IIh}}{\overset{Ar}{\underset{H}{>}}=\overset{F}{\underset{CClF_2}{<}}}$$

EXPERIMENTAL

^{1}H NMR spectra were registered on spectrometer Varian VXR-400 (operating frequency 400 MHz) in CDCl$_3$, internal reference TMS. GC-MS measurements were carried out on HP5890 instrument (ionization by electron impact, 70 eV) using 5989x-G detector. TLC analyses were carried out on Merck 60 F$_{254}$ plates, column chromatography was performed on silica gel Merck (63-200 mesh). 4-Chlorobenzaldehyde hydrazone (**I**) was prepared by procedure [2]. Commercial polyhaloalkanes were used without additional purification.

Reaction of hydrazone (I) with polyhaloalkanes in DMSO. To a solution of freshly prepared hydrazone **I** (309 mg, 2 mmol) in DMSO (2 ml) was added a concn. aqueous ammonia (0.68 ml) and freshly purified CuCl (20 mg, 0.2 mmol, 10 mol%) and then the corresponding polyhaloalkane (10 mmol) maintaining the temperature at 20°C. The reaction mixture was stirred for 20 h and then poured in water (200 ml). The reaction products were extracted into dichloromethane (3–20 ml), the combined extract were dried over sodium sulfate, the dichloromethane was evaporated, and the reaction products were separated by column chromatography on silica gel. We failed to separate *E*- and *Z*-isomers of alkenes by means of column chromatography.

Reaction of hydrazone **I** with CBr$_4$ was performed similarly using a solution of CBr$_4$ (3.32 g, 10 mmol) in DMSO (8 ml).

Reaction of hydrazone (I) with polyhaloalkanes in ethanol. To a solution of freshly prepared hydrazone **I** (309 mg, 2 mmol) in ethanol (20 ml) was added ethylenediamine (10 mmol, 0.67 ml) and freshly purified CuCl (20 mg, 0.2 mmol, 10 mol%) and then the corresponding polyhaloalkane (10 mmol) maintaining the temperature at 20°C. The reaction mixture was stirred for 24 h and then worked up as described above. Reaction of hydrazone **I** with CBr$_4$

was performed similarly using a solution of CBr$_4$ (3.32 g, 10 mmol) in ethanol (30 ml).

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