# Catalytic olefination reaction of carbonyl compounds. A study on stereoselectivity of alkene formation

*V. G. Nenaidenko,[a]* V. N. Korotchenko,[a] A. V. Shastin,[b] D. A. Tyurin,[a] and E. S. Balenkova[a]*

*[a]Department of Chemistry, M. V. Lomonosov Moscow State University, Leninskie Gory, 119992 Moscow, Russian Federation. Fax: +7 (095) 932 8846. E-mail: nen@acylium.chem.msu.ru*
*[b]Institute of Problems of Chemical Physics, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation. E-mail: shastin@icp.ac.ru*

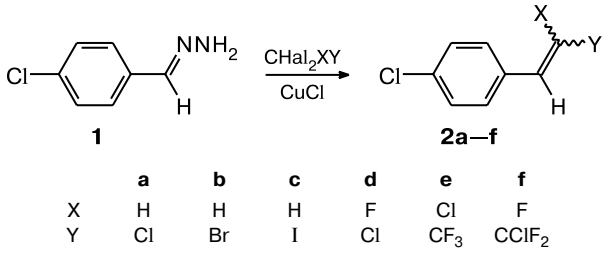
The mechanism of formation of alkene stereoisomers in the catalytic olefination reaction of carbonyl compounds was studied. 4-Chlorobenzaldehyde hydrazone **1** stereoselectively reacts with a number of F-, Cl-, Br-, and I-containing polyhaloalkanes in the presence of catalytic amounts of CuCl to give ω-substituted styrenes **2** with the more thermodynamically stable alkene isomer being the major product. A model for the formation of the stereoisomers of alkenes **2** in the olefination reaction is proposed. Stereoselectivity of the reaction is determined by elimination of copper(II) halides from the lowest-lying conformers of organocopper intermediates **II**. According to quantum-chemical calculations, the elimination should involve the staggered conformations with antiperiplanar arrangement of C—Hal and C—Cu bonds and proceed by the *E*2 *anti*-elimination mechanism. The results of quantum-chemical calculations are in good agreement with the experimental *E*/*Z* alkene isomer ratios.

**Key words:** catalysis, copper salts, carbonyl compounds, hydrazones, carbenes, alkenes, olefination, elimination, stereoselectivity.

Recently,[1—4] we have reported on a new catalytic olefination reaction (COR) of carbonyl compounds. It was shown that *N*-unsubstituted hydrazones of aromatic aldehydes and ketones treated with polyhaloalkanes in the presence of catalytic amounts of CuCl are transformed into corresponding substituted alkenes. Stereoselective formation of the double carbon—carbon bond, resulting in the more thermodynamically stable alkene isomer as the major product was also observed. In this work we elucidate factors responsible for stereoselectivity of alkene formation.

4-Chlorobenzaldehyde hydrazone (**1**) was chosen as the model compound for studying stereoselectivity of the COR. The olefinating agents were polyhaloalkanes of different nature, namely, chloroform ($CHCl_3$); bromodichloromethane ($CHBrCl_2$); bromoform ($CHBr_3$); iodoform ($CHI_3$); trichlorofluoromethane ($CCl_3F$); 1,1,1-trichloro-2,2,2-trifluoroethane ($CCl_3CF_3$); and 1,1,2-trichloro-1,2,2-trifluoroethane ($CCl_2FCClF_2$). Reactions of hydrazone **1** with polyhaloalkanes were studied using two systems: (1) DMSO (solvent)—aqueous ammonia (base) and (2) ethanol—1,2-ethylenediamine. Earlier,[1,2] these reaction systems were shown to provide optimum conditions for olefination. The reactions were carried out in the presence of catalyst (CuCl, 10 mol.%). Polyhaloalkanes were taken in a five-fold excess with respect to hydrazone **1**, which reacts with these compounds to give a mixture of *E*- and *Z*-isomers of alkenes **2a—f** (Scheme 1).

**Scheme 1**




**1** **2a—f**

| | a | b | c | d | e | f |
|---|---|---|---|---|---|---|
| X | H | H | H | F | Cl | F |
| Y | Cl | Br | I | Cl | $CF_3$ | $CClF_2$ |

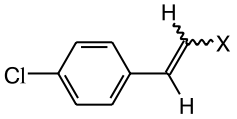
Hal = Br, Cl

No target β-chlorostyrene was obtained in the reaction of $CHCl_3$ with hydrazone **1**. This is apparently due to very low reactivity of $CHCl_3$ in the olefination reaction. Treatment of hydrazone **1** with other haloforms results in the corresponding β-halostyrenes **2a—c**. The reactions in DMSO are characterized by higher yields. For instance. the reaction of hydrazone **1** with $CHBrCl_2$ results in

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1740—1745, August, 2003.

1066-5285/03/5208-1835 $25.00 

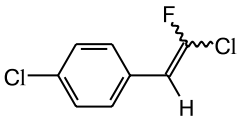
β-chlorostyrene **2a** while the reactions with $CHBr_3$ and $CHI_3$ result in β-bromostyrene **2b** and β-iodostyrene **2c**, respectively. It is quite unexpected that stereoselectivity of the formation of haloalkenes in system 1 reduces as follows: **2a** > **2b** > **2c** (Table 1), whereas the reverse order should be expected from consideration of steric factors (volumes of halogen atoms at the double bond).[5]



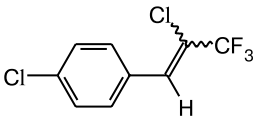
**2a—c**

X = Cl (**a**), Br (**b**), I (**c**).

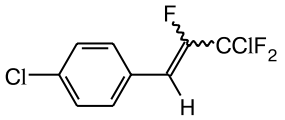
System 2 was found to provide optimum conditions for the reactions with freons, resulting in the corresponding fluorine-containing alkenes **2d—f**.



**2d**



**2e**

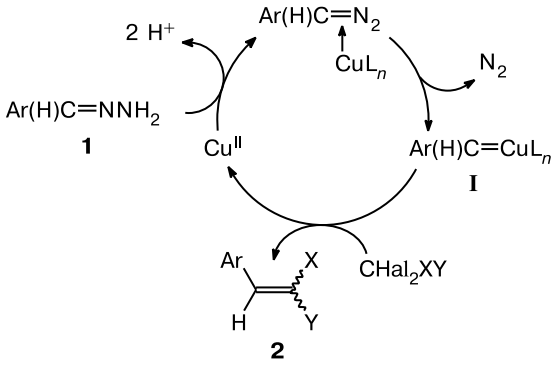


**2f**

The nature of the solvent and the base has a strong effect on both the yields of the target alkenes **2a—f** and the ratio of the isomeric products (see Table 1). However, this influence is ambiguous. For instance, treatment of hydrazone **1** with bromoform enhances the reaction stereoselectivity on going from DMSO to ethanol, whereas the formation of alkene **2e** in the reaction of the model compound with $CCl_3CF_3$, becomes a less stereoselective process. The *E*/*Z* ratios obtained for the reactions with $CHBrCl_2$, $CHI_3$, and freon $CCl_2FCClF_2$ are nearly independent of the reaction medium. Probably, this variety of effects is due to different solvation of reaction intermediates and to the influence of the ligand environment of the catalyst. In particular, the solvent nature is known to have a very strong and ambiguous effect on stereoselectivity of the Wittig reaction involving α-haloylides, resulting in vinyl halides.[6—8]

Earlier,[2,4] we have proposed a catalytic cycle, which describes the mechanism of alkene formation upon treating hydrazones of carbonyl compounds with polyhaloalkanes. The key reaction stage involves a copper—carbene complex **I** generated in the oxidation of hydrazone (Scheme 2). Similar copper—carbene complexes are conventional intermediates of carbene transfer reactions catalyzed by copper compounds.[9] Subsequent reactions of complex **I** with polyhaloalkanes results in the target alkenes.

**Scheme 2**



Ar = 4-$ClC_6H_4$; L = $NH_3$, en, solv, $Hal^-$.

However, the scheme proposed gives no explanation for the preferred formation of a particular alkene stereoisomer in a given reaction. Therefore, we placed special emphasis on the reaction of the copper—carbene complex **I** with polyhaloalkanes assuming that it involves copper insertion into the carbon—halogen bond with the formation of an organocopper compound **II** (Scheme 3). Analogous copper[10,11] or nickel[12] insertions into the carbon—halogen bond are assumed to be the key stages of

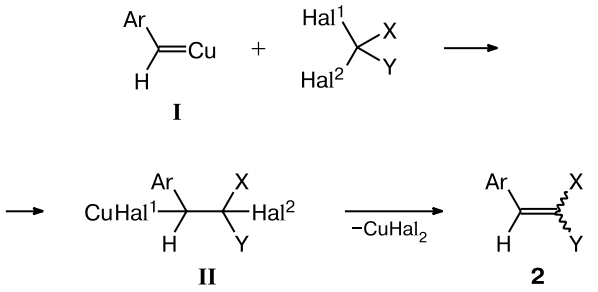
**Table 1.** Parameters of reactions of hydrazone **1** with polyhaloalkanes

| Reagent | DMSO—ammonia | | Ethanol—ethylenediamine | | $\Delta E$ [a] /kcal mol$^{-1}$ | $E : Z$ [a] |
|---|---|---|---|---|---|---|
| | Yield of **2** (%) | $E : Z$ [b] | Yield of **2** (%) | $E : Z$ [b] | | |
| $CHCl_3$ | 0 | — | 0 | — | — | — |
| $CHBrCl_2$ | 44 | 93 : 7 | 32 | 91 : 9 | 0.71 | 77 : 23 |
| $CHBr_3$ | 67 | 86 : 14 | 30 | 95 : 5 | 0.67 | 71 : 29 |
| $CHI_3$ | 40 | 81 : 19 | 11 | 80 : 20 | — | — |
| $CFCl_3$ | Traces | — | 58 | 77 : 23 | 0.70 | 77 : 23 |
| $CCl_3CF_3$ | 63 | 12 : 88 | 64 | 22 : 78 | 1.89 | 4 : 96 |
| $CCl_2FCClF_2$ | 20 | 14 : 86 | 49 | 13 : 87 | 1.21 | 11 : 89 |

[a] Calculated.
[b] According to $^1$H NMR spectroscopy data.

transition-metal catalyzed addition of polyhaloalkanes to olefins resulting in 1 : 1 adducts. Copper insertions into the carbon—halogen bond of alkyl halides and allyl halides in the reactions with copper—isonitrile complexes producing intermediates of the type **II** are also known. Subsequent β-elimination of the $Cu^{II}$ salt gives alkene **2**. It should be noted that elimination of halogen atoms from the polyhalo compound occurs chemoselectively. Recently,[13] we have shown that if the reactant molecule contains several types of halogen atoms, the process almost exclusively involves cleavage of the weakest carbon—halogen bond with the heavier halogen atom.

**Scheme 3**

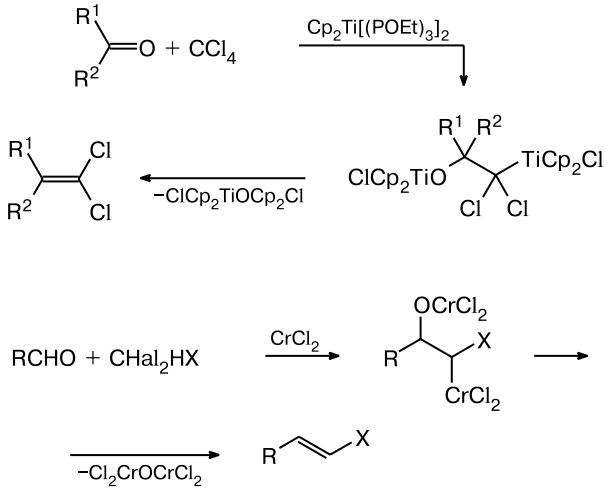



Ar = 4-$ClC_6H_4$

$E_{C-Hal^1} < E_{C-Hal^2}$

A large number of reductive coupling reactions of polyhaloalkanes with carbonyl compounds in the presence of equimolar amounts of reducing agents (compounds of chromium[14,15] and titanium[16] in the lowest oxidation states) have been reported. Here, the formation of the double bond involves β-elimination of metal salts from organometallic intermediates (Scheme 4).

**Scheme 4**




It was reasonable to assume that stereochemistry of alkene formation should be consistent with the laws of bimolecular elimination reaction, *E*2. To confirm the applicability of our model to the observed stereoselectivity of the reaction, we carried out quantum-chemical calculations of the conformational energies[17—22] of intermediates of the type **II** (Fig. 1 and 2).

The molecule of intermediate **II** can adopt several conformations; in this case elimination of $Cu^{II}$ salt from different conformers can result in different isomers of alkene **2**. Our model assumes that intermediate organocopper compounds **II** are rather stable and can reach a thermodynamic conformational equilibrium and that elimination itself occurs from the lowest-lying conformer. In this case the alkene isomer ratio is determined by the relative energies of conformers **II**. An analogous approach was also applied to elimination from isomeric 2,3-dibromobutanes.[23] According to our calculations (see Fig. 1), the energy difference between the eclipsed and staggered conformations of intermediates **II** is rather large (6—8 kcal $mol^{-1}$). This allowed us to assume that elimination of copper(II) halides should occur in the staggered conformers with antiperiplanar arrangement of the carbon—halogen and carbon—copper bonds by the *anti*-elimination mechanism *E*2. Conformational energy minima (see Fig. 1 and 2) correspond to the staggered conformations from which elimination of copper halides does occur to give the olefination products. We believe that the activation energy for elimination of copper(II) halides should be the same for different conformers, since the corresponding transition states of *anti*-elimination are structurally similar.

At equal rates of elimination of copper(II) chloride from the intermediate organocopper compound, the ratio of alkene isomers and the reaction stereoselectivity should be determined by the energy difference between two antiperiplanar conformers of intermediates of the type **II**, which correspond to minima on the conformational curves and give two alkene isomers. Using the energy difference between the minima on conformational curves, we calculated the theoretical ratios of alkene isomers **2** (see Table 1) assuming that conformers of the type **II** are in thermodynamic equilibrium. The formula for calculations was as follows: $K = \exp[-\Delta E/(RT)]$, where $\Delta E$ is the energy difference between the corresponding minima on the conformational curves and $K$ is the ratio of conformers. Comparison shows that the calculated and experimental isomer ratios are in good agreement. For instance, calculations predict a lower stereoselectivity of the formation of β-bromostyrene (**2b**) in the reaction with bromoform compared to the formation of β-chlorostyrene (**2a**), as is observed experimentally.

Calculations for the reactions involving $CFCl_3$ and $CCl_2FCClF_2$ give excellent agreement with the experimental data. Two diastereomeric intermediates of the

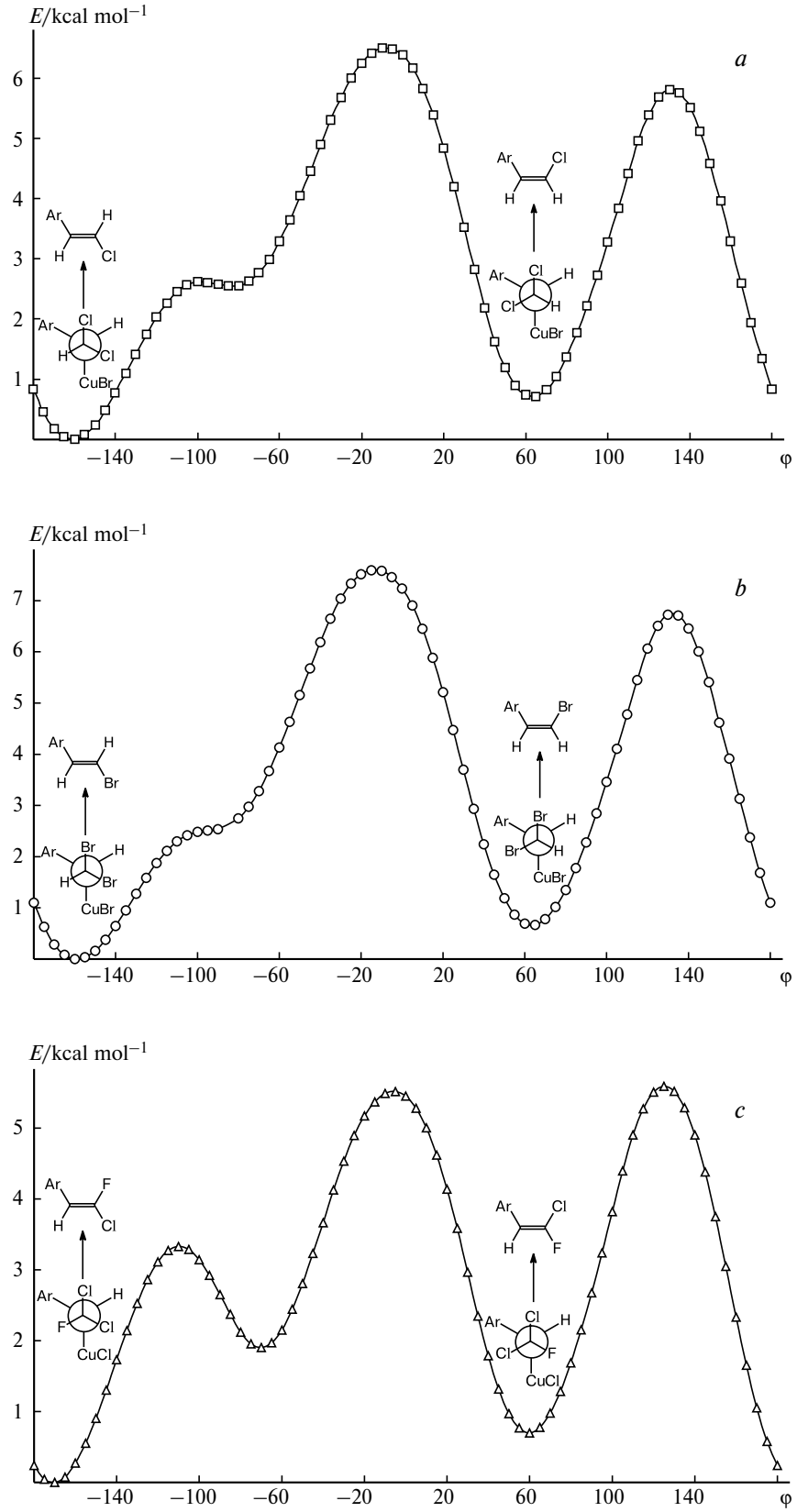



**Fig. 1.** Conformational energies (*E*) of intermediates of the type **II** plotted *vs*. dihedral angle φ for the reactions with bromodichloromethane (*a*), bromoform (*b*), and trichlorofluoromethane (*c*); φ is the angle Ar—C—C—Cl (*a*, *c*) or Ar—C—C—Br (*b*).

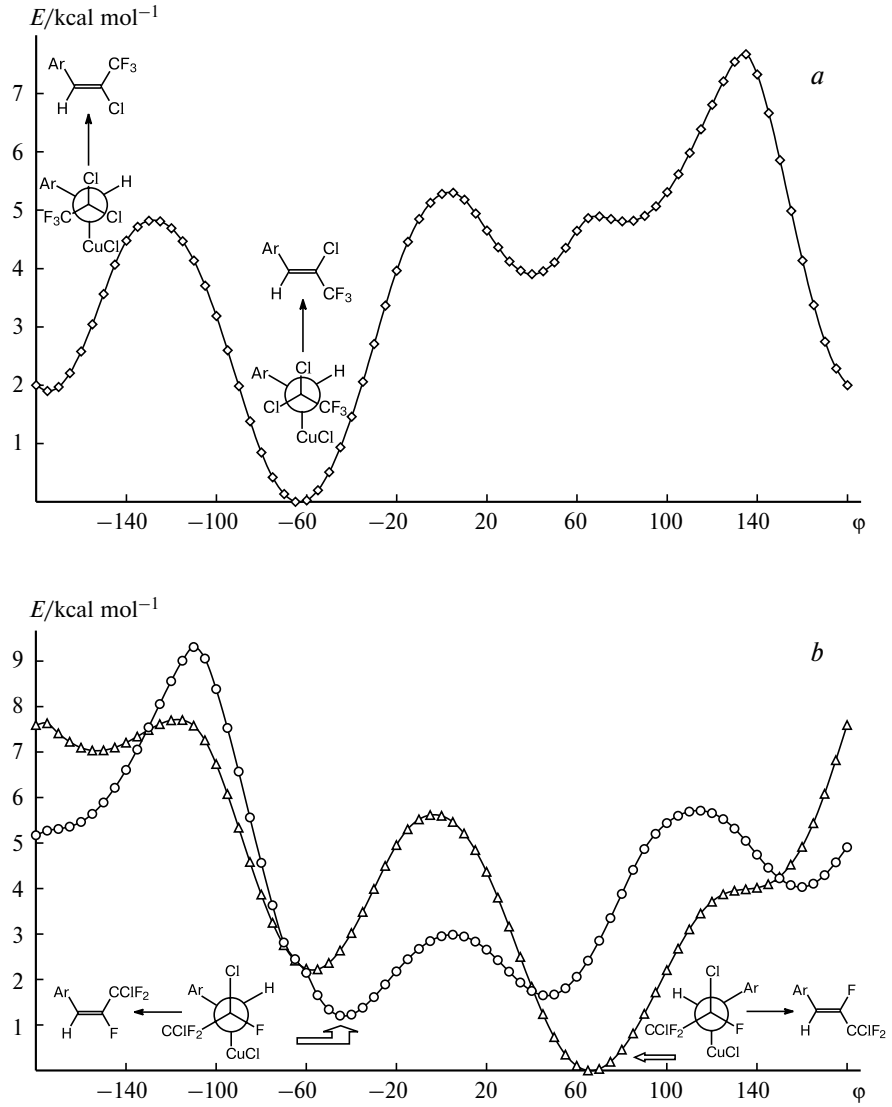



**Fig. 2.** Conformational energies ($E$) of intermediates of the type **II** plotted *vs.* dihedral angle φ for the reactions with 1,1,1-trichloro-2,2,2-trifluoroethane (*a*) and 1,1,2-trichloro-1,2,2-trifluoroethane (two diastereomers) (*b*); φ is the angle Ar—C—C—Cl.

type **II** can be formed in the latter case and each of them is characterized by one conformational energy minimum corresponding to elimination of $CuCl_2$. Therefore, the ratio of alkene isomers **2f** is determined solely by the energy difference between the diastereomers. The largest difference between the predicted isomer ratio and the experimental data was found for the reaction with $CCl_3CF_3$. Here, calculations predict a higher stereoselectivity of the formation of alkene **2e** compared to that observed experimentally. This is likely due to some limitations of our computational model, which ignores the effect of different solvation of the initial compounds, intermediates, and the ligand environment of the catalyst. In particular, freon $CCl_3CF_3$ contains a hydrophobic trifluoromethyl group, which should have a dramatic effect on the behavior of this compound in the reaction.

Thus, we analyzed the factors responsible for stereoselectivity of alkene formation in the catalytic olefination reaction. Our quantum-chemical calculations confirmed the assumption of the formation of intermediates **II** followed by *trans*-elimination of $Cu^{II}$ compounds. By and large, conformational energy calculations allow a reasonably correct prediction of the ratio of alkene isomers **2a—f**. This enables us to conclude that the model proposed in this work can be used to describe the reactions of carbene complex **I** with polyhaloalkanes and subsequent alkene formation. The results obtained give a better insight into the mechanism of the COR and the nature of the accompanying processes.

## Experimental

In this work we employed the nonempirical generalized gradient approximation of the exchange-correlation functional PBE 96.[17,18] Calculations were carried out using the "PRIRODA" code written by D. N. Laikov[19] and extended orbital basis sets of contracted Gaussian functions. The contraction patterns were as follows: (5s1p):[3s1p] for H, (11s6p2d):[4s3p2d] for C, (11s6p2d):[4s3p2d] for F, (16s12p2d):[5s4p2d] for Cl, (17s13p8d):[6s5p3d] for Cu, and (19s16p9d):[6s5p3d] for Br. Earlier,[20—22] this computational method proved itself in calculations of complex organometallic systems containing various metal and nonmetal atoms (Cr, Ti, Zr, Si, Sb, Bi) including systems with non-classical interactions as highly efficient technique. The conformational energies were calculated by scanning the dihedral angle formed by the leaving halogen atom, the carbon atoms of the double bond, and the carbon atom of the aromatic ring. At each value of the dihedral angle, calculations were carried out with full optimization of the remaining geometric parameters of the molecule. The vibrational frequencies at the minima of the potential curves were calculated using analytical expressions for the first and second derivatives.

$^1$H NMR spectra were recorded on a Varian VXR-400 spectrometer in $CDCl_3$ with $SiMe_4$ as internal reference. TLC was performed on Merck 60 $F_{254}$ plates while column chromatography was carried out on Merck silica gel (63—200 mesh). 4-Chlorobenzaldehyde hydrazone **1** was synthesized following the known procedure.[1] The commercially available polyhaloalkanes were used as received.

**Reaction of hydrazone 1 with polyhaloalkanes in DMSO (general procedure).** To a solution of freshly prepared hydrazone **1** (309 mg, 2 mmol) in DMSO (2 mL), concentrated aqueous ammonia (0.68 mL) and freshly purified CuCl (20 mg, 0.2 mmol, 10 mol.%) were added, followed by the addition of the corresponding polyhaloalkane (10 mmol) in one portion. The temperature was maintained at 20 °C. The reaction mixture was stirred for 24 h and poured into water (200 mL). The reaction products were extracted with methylene chloride (3×20 mL), the combined extracts were dried over sodium sulfate, methylene chloride was evaporated, and the reaction products were isolated using column chromatography ($SiO_2$). The *E*- and *Z*-alkene isomers cannot be separated by column chromatography.

**Reaction of hydrazone 1 with polyhaloalkanes in ethanol (general procedure).** To a solution of freshly prepared hydrazone **1** (309 mg, 2 mmol) in ethanol (20 mL), ethylenediamine (0.67 mL, 10 mmol) and freshly purified CuCl (20 mg, 0.2 mmol, 10 mol.%) were added, followed by the addition of the corresponding polyhaloalkane (10 mmol) in one portion. The temperature was maintained at 20 °C. The reaction mixture was stirred for 24 h and poured in water (500 mL). The reaction products were extracted with methylene chloride (3×30 mL), the combined extracts were dried over sodium sulfate, methylene chloride was evaporated, and the reaction products were isolated using column chromatography ($SiO_2$).

The spectral and physical characteristics of compounds **2a—f** are in agreement with the published data.

This work was carried out with the financial support of the Russian Foundation for Basic Research (Project Nos. 03-03-32052a and 03-03-32024a).

## References

1. A. V. Shastin, V. N. Korotchenko, V. G. Nenajdenko, and E. S. Balenkova, *Tetrahedron*, 2000, **56**, 6557.
2. V. N. Korotchenko, A. V. Shastin, V. G. Nenajdenko, and E. S. Balenkova, *Tetrahedron*, 2001, **57**, 7519.
3. A. V. Shastin, V. N. Korotchenko, V. G. Nenaidenko, and E. S. Balenkova, *Izv. Akad. Nauk, Ser. Khim.*, 2001, 1334 [*Russ. Chem. Bull., Int. Ed.*, 2001, **50**, 1401].
4. V. N. Korotchenko, A. V. Shastin, V. G. Nenajdenko, and E. S. Balenkova, *J. Chem. Soc., Perkin Trans. 1*, 2002, 883.
5. A. J. Gordon and R. A. Ford, *The Chemist´s Companion*, Wiley-Interscience, New York, 1972.
6. X.-P. Zhang and M. Schlosser, *Tetrahedron Lett.*, 1993, **34**, 1925.
7. G. Stork and K. Zhao, *Tetrahedron Lett.*, 1989, **30**, 2173.
8. M. Matsumoto and K. Kuroda, *Tetrahedron Lett.*, 1980, **21**, 4021.
9. M. P. Doyle, *Chem. Rev.*, 1986, **86**, 919.
10. P. Martin, E. Steiner, J. Streith, T. Winkler, and D. Bellus, *Tetrahedron*, 1985, **41**, 4057.
11. M. Mitani, I. Kato, and K. Koyama, *J. Am. Chem. Soc.*, 1983, **105**, 6719.
12. L. A. van de Kuil, D. M. Grove, R. A. Gossage, J. W. Zwikker, L. W. Jenneskens, W. Drenth, and G. van Koten, *Organometallics*, 1997, **16**, 4985.
13. V. N. Korotchenko, A. V. Shastin, V. G. Nenaidenko, and E. S. Balenkova, *Zh. Org. Khim.*, 2003, **30**, 433 [*Russ. J. Org. Chem.*, 2003, **30** (Engl. Transl.)].
14. A. Furstner, *Chem. Rev.*, 1999, **99**, 991.
15. D. M. Hodgson and L. T. Boulton, in *Preparation of Alkenes*, Ed. J. M. J. Williams, Oxford University Press, Oxford, 1996, p. 89.
16. T. Takeda, Y. Endo, A. Chandra Sheker Reddy, R. Sasaki, and T. Fujirawa, *Tetrahedron*, 1999, **55**, 2475.
17. J. P. Perdew, K. Burke, and M. Ernzerhof, *Phys. Rev. Lett.*, 1996, **77**, 3865.
18. M. Ernzerhof and G. E. Scuseria, *J. Chem. Phys.*, 1999, **110**, 5029.
19. D. N. Laikov, *Chem. Phys. Lett.*, 1997, **281**, 151.
20. O. I. Trifonova, E. A. Ochertyanova, N. G. Akhmedov, V. A. Roznyatovsky, D. N. Laikov, N. A. Ustynyuk, and Yu. A. Ustynyuk, *Inorg. Chim. Acta*, 1998, **280**, 328.
21. Yu. A.Ustynyuk, L. Yu. Ustynyuk, D. N. Laikov, and V. V. Lunin, *J. Organomet. Chem.*, 2000, **597**, 182.
22. P. L. Shutov, S. S. Karlov, K. Harms, D. A. Tyurin, A. V. Churakov, J. Lorberth, and G. S. Zaitseva, *Inorg. Chem.*, 2002, **41**, 6147.
23. E. L. Eliel, N. L. Allinger, S. J. Angyal, G. A. Morrison, *Conformational Analysis*, J. Wiley and Sons, New York, 1965.

*Received January 24, 2003;*
*in revised form April 8, 2003*