New method for the synthesis of β-bromostyrenes

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A new stereoselective method was developed for the synthesis of β-bromostyrenes ($E/Z > 5/1$) starting from hydrazones of aromatic aldehydes and bromoform in the presence of CuCl.

Key words: catalysis, copper salts, bromostyrenes, hydrazones, bromoform, olefination.

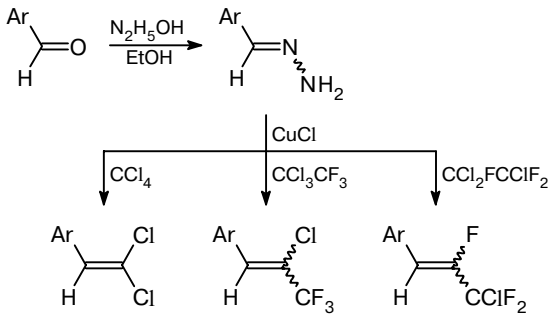
β-Bromostyrenes find wide application in the stereospecific synthesis of substituted alkenes[1—5] and as synthetic precursors of the corresponding acetylenes.[6,7] Besides, *cis*- and *trans*-bromostyrenes are extensively used in the total synthesis of natural compounds and antibiotics.[1,8]

Classical methods for the synthesis of bromostyrenes involve debromocarboxylation of dibromocinnamic acids,[6] various versions of the Hunsdiecker—Borodin reaction[9,10], and the Wittig reaction.[11,12] Generally, these reactions afford mixtures of (*E*)- and (*Z*)-bromoalkenes in ratios from 1 : 1 to 4 : 1. Pure (*E*)- and (*Z*)-bromostyrenes can be prepared by bromination of *cis*- and *trans*-alkenylsilanes[13,14] and alkenylboron compounds[15] or by stereospecific reduction of dibromostyrenes.[1,16,17]

Previously,[18] we have reported the redox reactions of *N*-unsubstituted hydrazones of aromatic aldehydes with carbon tetrachloride in the presence of catalytic amounts of copper(I) chloride. These reactions represent an essentially new method for the transformation of the C=O bond into the C=C bond (olefination of carbonyl compounds). We have demonstrated that these reactions can be used for the synthesis of a wide range of aromatic and heteroaromatic dichloroolefins.[19,20] These reactions have a general character and can involve other polyhaloalkanes along with carbon tetrachloride. Thus, we synthesized fluorine-containing olefins by treatment of hydrazones, which were prepared *in situ*, with freons CCl_3CF_3 or CCl_2FCClF_2 (the reactions proceeded stereoselectively to form predominantly the *Z* isomers) (Scheme 1).*

In the present study, we report new results of investigation on the use of the catalytic system based on copper(I) chloride for olefination of aromatic aldehydes.

Scheme 1

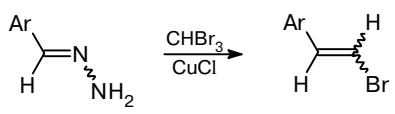


Results and Discussion

We expected that the behavior of bromoform in these reactions would be analogous to that of CCl_4 and freons and hoped that it would allow us to develop a new procedure for the preparation of the corresponding bromoalkenes. Actually, the reactions of bromoform with solutions of *N*-unsubstituted hydrazones of aromatic aldehydes in DMSO in the presence of CuCl and a base (an aqueous solution of NH_4OH) afforded bromostyrenes as the major reaction products (Table 1).

We performed the reactions with hydrazones of aromatic aldehydes containing substituents of various nature (Scheme 2).

Scheme 2



1a—m

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Table 1. Synthesis of β-bromostyrenes

Compound	Aryl	Yield (%)	*E*/*Z**
1a	4-$O_2NC_6H_4$	56	20/1
1b	2-$O_2NC_6H_4$	19	5/1
1c	4-ClC_6H_4	67	6/1
1d	2-ClC_6H_4	53	8/1
1e	4-FC_6H_4	52	10/1
1f	2-FC_6H_4	84	5/1
1g	4-BrC_6H_4	73	10/1
1h	2-BrC_6H_4	57	13/1
1i	4-MeC_6H_4	64	5/1
1j	2,6-$Cl_2C_6H_3$	31	*E*
1k	4-$CF_3C_6H_4$	29	9/1
1l	2-$CF_3C_6H_4$	84	6/1
1m	4-$CH_3OC_6H_4$	60	5/1

* The isomer ratio was determined based on the data from ^1H NMR spectroscopy; the signals were assigned to particular isomers by comparing the spin-spin coupling constants of the hydrogen atoms at the double bond ($J_{trans} \approx 14$ Hz > $J_{cis} \approx 8$ Hz).

It was found that the yields of bromoalkenes **1** depend on the nature of the substituent in the aromatic nucleus and its position. As in the case of dichlorostyrenes[19] and fluorine-containing alkenes, *ortho*-substituted alkenes were obtained in lower yields than the corresponding *para*-substituted analogs. The formation of bromostyrenes proceeded stereoselectively to give predominantly alkenes in a *trans* configuration.

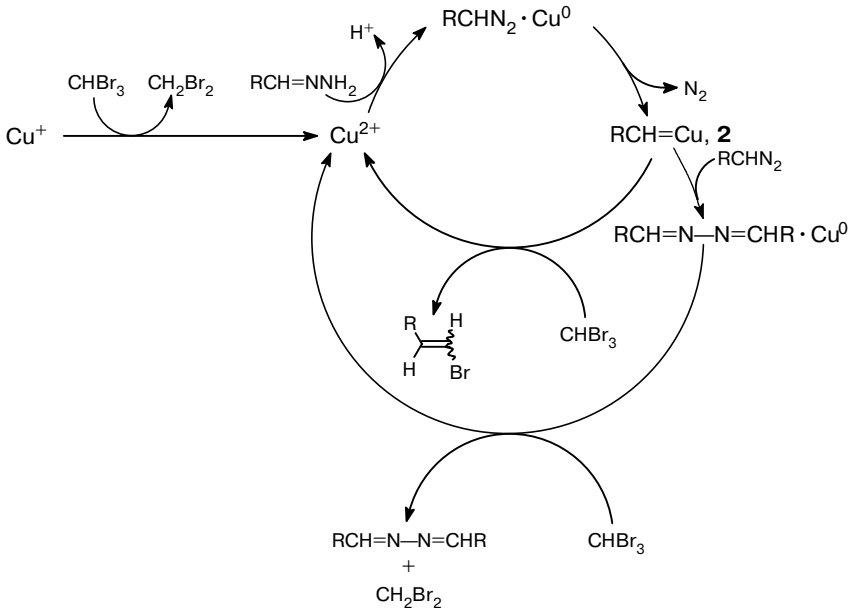
This reaction is adequately described by the catalytic cycle, which we have proposed previously.[20] The reactions involved the carbenoid copper complex as the key intermediate (Scheme 3), which is analogous to carbenoid complexes of copper and other metals described in the literature.[21—23] Since the reactions of hydrazones with bromoform gave rise to analogous products, we believe that this mechanism can be extended to the reactions of formation of bromostyrenes.

At the first stage, Cu^I was oxidized by bromoform, the latter being reduced to dibromomethane and Cu^I being converted into Cu^{II}. Earlier,[19] we have examined the effect of various salts of transition metals as olefination catalysts and demonstrated that copper monochloride is the reagent of choice because it made it possible to circumvent noncontrolled heat evolution and foaming of the reaction mixture, which were observed in the reactions involving $CuCl_2$ as the catalyst.[19] At the subsequent stage, Cu^{II} reacted with hydrazone to form carbenoid copper complex **2** (through intermediate formation of the corresponding diazoalkane). The reaction of complex **2** with $CHBr_3$ afforded the corresponding bromostyrene accompanied by regeneration of Cu^{II} and gave rise to a new catalytic cycle. Simultaneously, the carbenoid complex reacted with diazoalkane to yield symmetrical azine (the side reaction).[19,24]

The major and side reactions afforded the common key intermediate (complex **2**), both reactions being catalytic (completion of both cycles resulted in regeneration of Cu^{II}).

We studied the reaction of 4-methylbenzaldehyde hydrazone with bromoform by ^1H NMR spectroscopy. It appeared that the reaction mixture consisted of bromostyrene, azine, CH_2Br_2, and an unconsumed excess of bromoform (Fig. 1). Consequently, under the reaction conditions, hydrazone was converted into bromostyrene and azine, while bromoform was converted into bromostyrene and CH_2Br_2.

Scheme 3



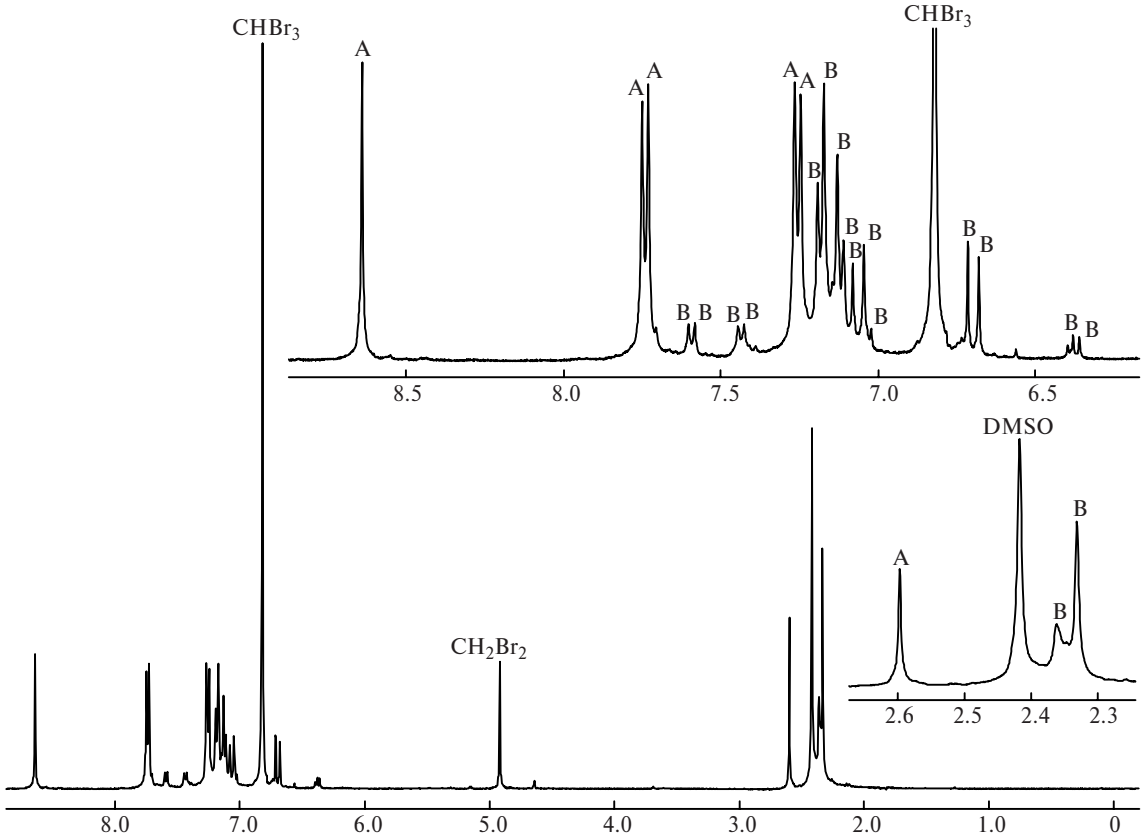


Fig. 1. ^{1}H NMR spectrum of the reaction mixture formed in the reaction of 4-methylbenzaldehyde hydrazone with bromoform (A, signals of *symm*-azine; B, signals of the *E* and *Z* isomers of bromostyrene).

To summarize, we developed a new stereoselective method for the synthesis of bromostyrenes. This method is characterized by simplicity of the reaction procedure and isolation of the products, involves readily accessible and inexpensive reagents, requires mild conditions, and is applicable to a wide range of substrates.

Experimental

The IR spectra were recorded on a UR-20 spectrophotometer in thin layers (liquids) and Nujol mulls (solids). The ^{1}H and ^{13}C NMR spectra were measured on a Varian VXR-400 spectrometer (400 and 100 MHz, respectively) in $CDCl_3$ with Me_4Si as the internal standard. The course of the reaction was monitored by TLC on Merck $60F_{254}$ plates. Column chromatography was carried out with the use of silica gel (63—200 mesh) purchased from Merck.

Hydrazones of aromatic aldehydes were prepared from commercial aldehydes according to a procedure reported previously.[19]

Synthesis of bromostyrenes (general procedure). A solution of NH_4OH (1.2 mL) and CuCl (50 mg, 0.5 mmol, 10 mol.%) was added to a solution of hydrazone (5 mmol) in DMSO (5 mL). Then a solution of $CHBr_3$ (1.34 mL, 15 mmol) in DMSO (10 mL) was added dropwise at 0 °C for 10 min, vigorous gas evolution being observed. The reaction mixture was stirred for 24 h and then decomposed with a 0.1 *M* HCl solution (300 mL). The reaction products were extracted with CH_2Cl_2 (3 × 50 mL), the extracts were dried over Na_2SO_4, and CH_2Cl_2 was evaporated. Products **1a—m** were isolated by column chromatography (SiO_2, hexane). Attempts to isolate the *E* and *Z* isomers by column chromatography failed.

The spectral characteristics of compounds **1a—c** and **1f—m** agree with the published data.[1,6,25—28]

1-[2-Bromovinyl]-4-nitrobenzene (1a):[6,25] a 20/1 mixture of *E*—*Z* isomers was obtained. M.p. 136—137 °C. R_f 0.10 (hexane). ^{1}H NMR, δ, *E* isomer: 7.02 (d, 1 H, =CH(Br), J = 14.2 Hz); 7.17 (d, 1 H, =CH—Ar, J = 14.2 Hz); 7.44 (d, 2 H, Ar, J = 8.8 Hz); 8.18 (d, 2 H, Ar, J = 8.8 Hz); *Z* isomer: 6.67 (d, 1 H, =CH(Br), J = 8.2 Hz); 7.69 (d, 2 H, Ar, J = 8.8 Hz); 7.81 (d, 2 H, Ar, J = 8.8 Hz). The remaining signals of the minor isomer overlap with the signals of the major isomer.

1-[2-Bromovinyl]-2-nitrobenzene (1b):[6] a 5/1 mixture of *E*—*Z* isomers was obtained. M.p. 56—57 °C. R_f 0.10 (hexane). ^{1}H NMR, δ, *E* isomer: 6.78 (d, 1 H, =CH(Br), J = 14.0 Hz); 7.62 (d, 1 H, =CH—Ar, J = 14.0 Hz); 7.45—7.70 (m, 3 H, Ar); 7.97 (dd, 1 H, Ar, J_1 = 9.0 Hz, J_2 = 0.8 Hz); *Z* isomer: 6.62 (d, 1 H, =CH(Br), J = 7.9 Hz); 8.10 (d, 1 H, Ar, J = 8.2 Hz). The remaining signals of the minor isomer overlap with the signals of the major isomer.

1-[2-Bromovinyl]-4-chlorobenzene (1c):[1,27] a 6/1 mixture of *E*—*Z* isomers was obtained (colorless oil). R_f 0.60 (hexane). ^{1}H NMR, δ, *E* isomer: 6.76 (d, 1 H, =CH(Br), J = 14.1 Hz); 7.04 (d, 1 H, =CH—Ar, J = 14.1 Hz); 7.22 (d, 2 H, Ar, J = 8.5 Hz); 7.28 (d, 2 H, Ar, J = 8.5 Hz); *Z* isomer: 6.44 (d, 1 H, =CH(Br), J = 8.2 Hz); 7.01 (d, 1 H, =CH—Ar,

J = 8.2 Hz); 7.33 (d, 2 H, Ar, J = 8.4 Hz); 7.62 (d, 2 H, Ar, J = 8.4 Hz).

1-[2-Bromovinyl]-2-chlorobenzene (1d): a 8/1 mixture of *E*—*Z* isomers was obtained (colorless oil). R_f 0.60 (hexane). IR, ν/cm^{-1}: 1610 (C=C). Found (%): C, 44.34; H, 2.56. C_8H_6BrCl. Calculated (%): C, 44.18; H, 2.78. ^{1}H NMR, δ, *E* isomer: 6.76 (d, 1 H, =CH(Br), J = 13.9 Hz); 7.15—7.21 (m, 2 H, Ar); 7.31—7.37 (m, 2 H, Ar); 7.43 (d, 1 H, =CH(Ar), J = 13.9 Hz); *Z* isomer: 6.56 (d, 1 H, =CH(Br), J = 8.0 Hz); 7.21—7.26 (m, 3 H, Ar, =CH(Ar)); 7.37—7.39 (m, 1 H, Ar); 7.77—7.81 (m, 1 H, Ar). ^{13}C NMR, δ, *E* isomer: 109.1 (=CBr); 126.7 (Ar); 126.9 (Ar); 129.2 (Ar); 129.3 ($\underline{C}_{Ar}$—C); 129.8 (Ar); 133.5 (=CH—); 133.9 (C_{Ar}—Cl); *Z* isomer: 109.3 (=CBr); 126.1 (Ar); 129.3 (Ar); 130.1 (Ar); 132.3 (=CH—).

1-[2-Bromovinyl]-4-fluorobenzene (1e): a 10/1 mixture of *E*—*Z* isomers was obtained (colorless oil). R_f 0.65 (hexane). IR, ν/cm^{-1}: 1600 (C=C). Found (%): C, 47.60; H, 2.83. C_8H_6BrF. Calculated (%): C, 47.80; H, 3.01. ^{1}H NMR, δ, *E* isomer: 6.67 (d, 1 H, =CH(Br), J = 14.1 Hz); 7.04 (d, 1 H, =CH(Ar), J = 14.1 Hz); 7.00 (dd, 2 H, CH(3), CH(5), J_1 = 17.1 Hz, J_2 = 8.6 Hz); 7.24 (dd, 2 H, CH(2), CH(6), J_1 = 8.6 Hz, J_2 = 5.3 Hz); *Z* isomer: 6.39 (d, 1 H, =CH(Br), J = 8.1 Hz); 7.50 (dd, 2 H, Ar, J_1 = 9.1 Hz, J_2 = 5.3 Hz); 7.65 (dd, 2 H, Ar, J_1 = 8.6 Hz, J_2 = 5.3 Hz). The remaining signals of the minor isomer overlap with the signals of the major isomer. ^{13}C NMR, δ, *E* isomer: 106.7 (=CBr); 115.4 (C(3), C(5), J = 21.4 Hz); 128.4 (C(2), C(6), J = 7.5 Hz); 131.0 ($\underline{C}_{Ar}$—C, J = 3.5 Hz); 136.7 (=CH—); 163.5 (CF, J = 247 Hz); *Z* isomer: 106.8 (=CBr); 116.1 (C(3), C(5), J = 22.9 Hz); 131.5 (C(2), C(6), J = 7.6 Hz); 136.5 (=CH—).

1-[2-Bromovinyl]-2-fluorobenzene (1f):[6] a 5/1 mixture of *E*—*Z* isomers was obtained (colorless oil). R_f 0.65 (hexane). ^{1}H NMR, δ, *E* isomer: 6.79 (d, 1 H, =CH(Br), J = 14.2 Hz); 6.87—6.98 (m, 2 H, Ar); 7.05 (d, 1 H, =CH—Ar, J = 14.2 Hz); 7.10—7.19 (m, 2 H, Ar); *Z* isomer: 6.42 (d, 1 H, =CH(Br), J = 8.1 Hz); 7.20—7.22 (m, 2 H, Ar); 7.29—7.33 (m, 2 H, Ar). The remaining signals of the minor isomer overlap with the signals of the major isomer.

4-Bromobenzene-1-[2-bromovinyl] (1g):[6] a 10/1 mixture of *E*—*Z* isomers was obtained (colorless oil). R_f 0.65 (hexane). ^{1}H NMR, δ, *E* isomer: 6.77 (d, 1 H, =CH(Br), J = 14.2 Hz); 7.03 (d, 1 H, =CH—Ar, J = 14.2 Hz); 7.15 (d, 2 H, Ar, J = 8.2 Hz); 7.43 (d, 2 H, Ar, J = 8.2 Hz); *Z* isomer: 6.47 (d, 1 H, =CH(Br), J = 8.2 Hz); 6.98 (d, 1 H, =CH—Ar, J = 8.2 Hz); 7.48 (d, 2 H, Ar, J = 8.5 Hz); 7.54 (d, 2 H, Ar, J = 8.5 Hz).

2-Bromobenzene-1-[2-bromovinyl] (1h):[26] a 13/1 mixture of *E*—*Z* isomers was obtained (colorless oil). R_f 0.65 (hexane). ^{1}H NMR, δ, *E* isomer: 6.74 (d, 1 H, =CH(Br), J = 13.9 Hz); 7.13 (ddd, 1 H, Ar, J_1 = 7.8 Hz, J_2 = 7.5 Hz, J_3 = 1.8 Hz); 7.26 (dd, 1 H, Ar, J_1 = 7.2 Hz, J_2 = 7.2 Hz); 7.37 (dd, 1 H, Ar, J_1 = 7.5 Hz, J_2 = 1.8 Hz); 7.42 (d, 1 H, =CH—Ar, J = 13.9 Hz); 7.53 (dd, 1 H, Ar, J_1 = 7.8 Hz, J_2 = 1.5 Hz); *Z* isomer: 6.57 (d, 1 H, =CH(Br), J = 8.0 Hz); 7.18 (d, 1 H, =CH—Ar, J = 8.0 Hz); 7.32 (dd, 1 H, Ar, J_1 = 7.7 Hz, J_2 = 7.7 Hz); 7.58 (dd, 1 H, Ar, J_1 = 7.7 Hz, J_2 = 1.0 Hz); 7.76 (dd, 1 H, Ar, J_1 = 7.7 Hz, J_2 = 1.8 Hz). The remaining signals of the minor isomer overlap with the signals of the major isomer.

1-[2-Bromovinyl]-4-methylbenzene (1i):[1,27] a 5/1 mixture of *E*—*Z* isomers was obtained (colorless oil). R_f 0.70 (hexane). ^{1}H NMR, δ, *E* isomer: 2.30 (s, 3 H, Me); 6.67 (d, 1 H, =CH(Br), J = 14.0 Hz); 7.03 (d, 1 H, =CH—Ar, J = 14.0 Hz); 7.09 (d, 2 H, Ar, J = 8.2 Hz); 7.15 (d, 2 H, Ar, J = 8.2 Hz); *Z* isomer: 2.33 (s, 3 H, Me); 6.33 (d, 1 H, =CH(Br), J = 8.2 Hz); 6.98 (d, 1 H, =CH—Ar, J = 8.2 Hz); 7.42 (d, 2 H, Ar, J = 8.2 Hz); 7.57 (d, 2 H, Ar, J = 8.2 Hz).

1-[(*E*)-2-Bromovinyl]-2,6-dichlorobenzene (1j): was obtained as a colorless oil. R_f 0.50 (hexane). IR, ν/cm^{-1}: 1610 (C=C). ^{1}H NMR, δ: 6.96 (d, 1 H, =CH(Br), J = 14.4 Hz); 7.12 (t, 1 H, CH(4), J = 8.0 Hz); 7.17 (d, 1 H, =CH(Ar), J = 14.4 Hz); 7.31 (d, 2 H, CH(3), CH(5), J = 8.0 Hz). ^{13}C NMR, δ: 115.4 (=CBr); 129.3 (Ar); 129.6 (Ar); 131.3 (=CH—); 133.5 ($\underline{C}_{Ar}$—C); 134.8 (C_{Ar}—Cl). Found (%): C, 38.03; H, 2.07. $C_8H_5BrCl_2$. Calculated (%): C, 38.14; H, 2.00.

1-[2-Bromovinyl]-4-trifluoromethylbenzene (1k):[25] a 9/1 mixture of *E*—*Z* isomers was obtained (colorless oil). R_f 0.70 (hexane). ^{1}H NMR, δ, *E* isomer: 6.88 (d, 1 H, =CH(Br), J = 14.2 Hz); 7.13 (d, 1 H, =CH—Ar, J = 14.2 Hz); 7.37 (d, 2 H, Ar, J = 8.5 Hz); 7.55 (d, 2 H, Ar, J = 8.5 Hz); *Z* isomer: 6.55 (d, 1 H, =CH(Br), J = 8.3 Hz); 7.08 (d, 1 H, =CH—Ar, J = 8.3 Hz); 7.62 (d, 2 H, Ar, J = 8.5 Hz); 7.74 (d, 2 H, Ar, J = 8.5 Hz).

1-[2-Bromovinyl]-2-trifluoromethylbenzene (1l):[28] a 6/1 mixture of *E*—*Z* isomers was obtained (colorless oil). R_f 0.70 (hexane). ^{1}H NMR, δ, *E* isomer: 6.77 (d, 1 H, =CH(Br), J = 13.9 Hz); 7.36—7.51 (m, 4 H, Ar, =CH—Ar); 7.63 (d, 1 H, Ar, J = 7.9 Hz); *Z* isomer: 6.88 (d, 1 H, =CH(Br), J = 8.2 Hz); 7.13 (d, 1 H, =CH—Ar, J = 8.2 Hz). The remaining signals of the minor isomer overlap with the signals of the major isomer.

1-[2-Bromovinyl]-4-methoxybenzene (1m):[1,6,25,27] a 5/1 mixture of *E*—*Z* isomers was obtained (colorless oil). R_f 0.20 (hexane). ^{1}H NMR, δ, *E* isomer: 3.78 (s, 3 H, Me); 6.59 (d, 1 H, =CH(Br), J = 13.9 Hz); 6.83 (d, 2 H, Ar, J = 8.5 Hz); 7.02 (d, 1 H, =CH(Ar), J = 13.9 Hz); 7.21 (d, 2 H, Ar, J = 8.5 Hz); *Z* isomer: 3.80 (s, 3 H, Me); 6.28 (d, 1 H, =CH(Br), J = 8.0 Hz); 6.97 (d, 1 H, =CH(Ar), J = 8.0 Hz); 7.49 (d, 2 H, Ar, J = 9.0 Hz); 7.65 (d, 2 H, Ar, J = 9.0 Hz).

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