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Reactions of Bisdiazonium Salts Derived from Monosubstituted *m*-Phenylenediamines with Amides and Nitriles of Unsaturated Acids under Anionarylation Conditions

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Abstract—Reactions of 5-carboxy and 4-methylphenylene-1,3-bisdiazonium tetrafluoroborates with amides and nitriles of acrylic and methacrylic acids in the presence of chloride, bromide, and thiocyanate anions proceed as anionarylation at one of the diazo groups and nucleophilic substitution at another one. With 4-methylphenylene-1,3-bisdiazonium tetrafluoroborate as the arylating agent, the anionarylation and the Sandmeyer reaction occur involving *para*- and *ortho*-positioned diazo groups, respectively.

Keywords: anionarylation, Sandmeyer reaction, phenylenebisdiazonium tetrafluoroborate, unsaturated acid amide, unsaturated acid nitrile

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It has been earlier shown that *m*-phenylenebisdiazonium chlorides afford the products of chloroarylation of esters and nitriles of acrylic and methacrylic acids at a single diazo group under the Meerwein reaction conditions, probably, due to electronic and steric effects [1]. Similar regioselectivity has been observed in the case of thiocyanatoarylation of acrylamide and methacrylamide with *p*- and *m*-phenylenebisdiazonium tetrafluoroborates [2].

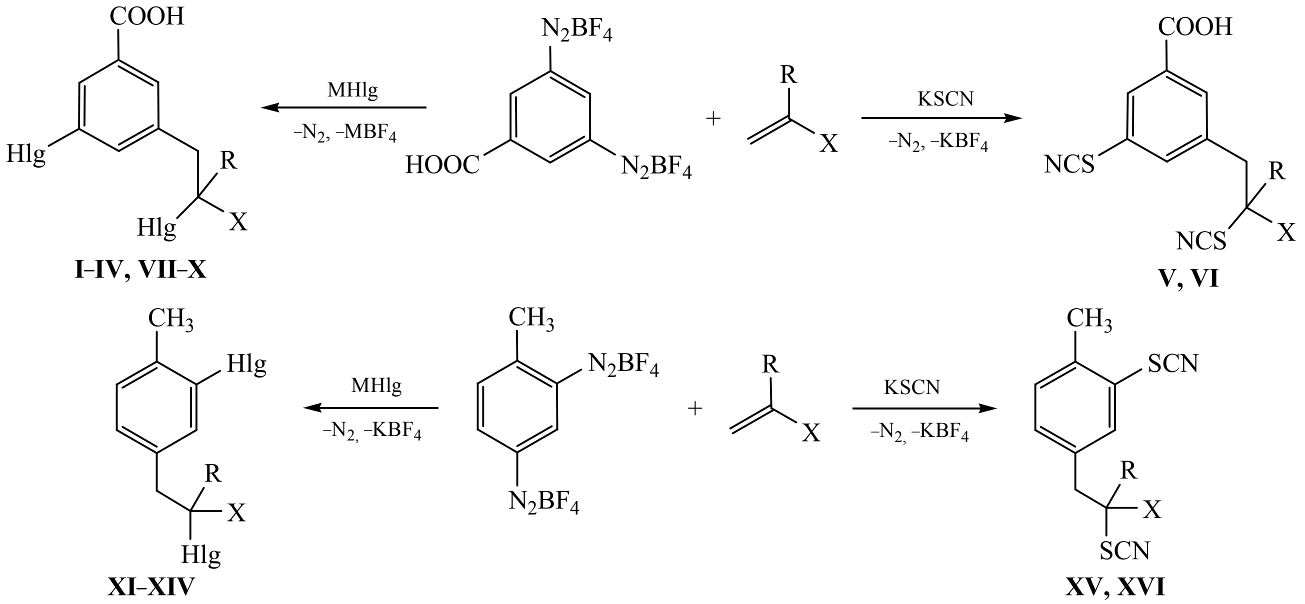
In order to extend the knowledge on the anionarylation and broaden its synthetic applications, we studied the reaction involving bisdiazonium salts derived from monosubstituted *m*-phenylenediamines: 5-carboxyphenylene-1,3-bisdiazonium and 4-methylphenylene-1,3-bisdiazonium tetrafluoroborates [3–5].

We found that the interaction of 5-carboxyphenylene-1,3-bisdiazonium tetrafluoroborate with amides and nitriles of acrylic and methacrylic acids in the presence of chloride, bromide, or thiocyanate anion afforded the corresponding substituted benzoic acids **I**–**X** via anionarylation at one of the diazo groups and simultaneous substitution of another diazo moiety with halogen or thiocyanate. Anionarylation of acrylamide and methacrylamide with 4-methylphenylene-1,3-bisdiazonium tetrafluoroborate yielded the corresponding propionamides **XI**–**XVI** (Scheme 1).

The reactions occurred in a water–acetone (1 : 2.5) medium at –25 to 10°C in the presence of copper(II) tetrafluoroborate as a catalyst. The products yield was of 33–71%; the reactions were accompanied by nucleophilic substitution of the diazo group to give the corresponding products in 10–30% yield with respect to the diazonium salt.

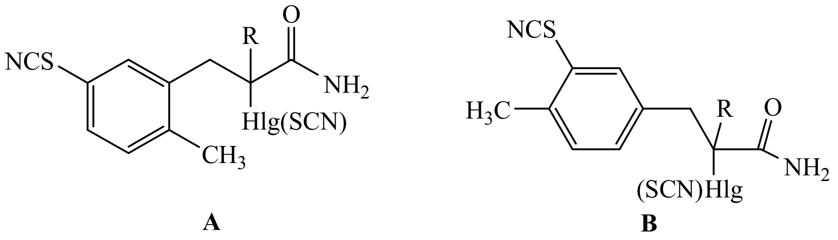
The attempts to perform anionarylation of acrylic and methacrylic acids nitriles with 4-methylphenylene-1,3-bisdiazonium tetrafluoroborate or thiocyanatoarylation of the nitriles with 5-carboxyphenylene-1,3-bisdiazonium tetrafluoroborate failed. The major reaction products were 4-methyl-1,3-dichloro(bromo, thiocyanato)benzene and 3,5-dithiocyanatobenzoic acid. Probably, the presence of a strong nucleophile (thiocyanate anion) and/or an active arylating agent induced the Sandmeyer reaction, normally occurring at higher temperature than anionarylation.

Scheme 1.



X = C(O)NH$_2$ (**I**–**VI**, **IX**–**XVI**), CN (**VII**–**X**); Hlg = Cl (**I**, **II**, **VII**, **VIII**, **IX**, **XII**), Br (**III**, **IV**, **IX**, **X**, **XIII**, **XIV**); R = H (**I**, **III**, **V**, **VII**, **IX**, **XI**, **XIII**, **XV**), CH$_3$ (**II**, **IV**, **VI**, **VIII**, **X**, **XII**, **XIV**, **XVI**); M = Na, K.

Scheme 2.



Yields and ^{1}H NMR data of the obtained compounds **I–XVI** are collected in Table 1.

IR spectra of compounds **I–VI** and **IX–XVI** contained the absorption bands of the carbonyl and amide groups at 1660–1688 and 3382–3404 cm^{-1}, respectively. Absorption band of the nitrile group of compounds **VII–X** was observed at 2232–2244 cm^{-1}. Spectra of thiocyanatoamides **V**, **VI**, **XV**, and **XVI** additionally contained the absorption band of thiocyanate group at 2152–2164 cm^{-1}.

^{1}H NMR spectra of compounds **1–XVI** contained the signals of the aromatic protons at 8.07–7.28 ppm. In the cases of acrylic and methacrylic acids derivatives, the signals of protons of methylene moieties adjacent to the aromatic rings were observed as two doublets of doublets (3.56–3.29 and 3.47–3.15 ppm) and two doublets (3.55–3.41 and 3.49–3.13 ppm), respectively. The signals of protons of the amide NH$_2$ group (compounds **I–VI** and **XI–XVI**) were observed at 8.19–7.52 ppm. In the spectra of compounds **I**, **III**, **V**, **VI**, **IX**, **XI**, **XIII**, and **XV**, the methine protons resonated at 5.52–4.27 ppm. The broadened signals of carboxyl group of compounds **I–X** were observed in weaker field (about 13.4–13.2 ppm). The ratio of the signals integral intensity indicated the presence of a single propionylamide (nitrile) moiety in the structure of compounds **I–XVI**, thus confirming that anionarylation involved only one of the diazo groups.

Since anionarylation could involve the both *ortho*- and *para*-positioned diazo groups, ^{1}H NMR data did not ambiguously reveal the structure of amides **XI–XVI**: the possible structural isomers of **XI–XVI** were expected to reveal similar spectral characteristics (Scheme 2).

In order to elucidate the structure of thiocyanatoamide **XVI,** we took advantage of 2D NMR spectral

Table 1. Yields, melting points, and NMR spectral data for compounds **I–XVI**

Comp. no.	Yield, %	mp, °C[a]	δ_H, ppm (*J*, Hz)
I	40	165	13.27 br.s (1H, HOOC), 7.72 s and 7.51 s (2H, NH_2); 7.83 s, 7.80 s and 7.62 s (3H, C_6H_3), 4.57 t [1H, CH(Cl), *J* 12.4], 3.52 d.d and 3.33 d.d [2H, $\underline{CH_2}C_6H_3$, *J* 13.7]
II	45	139	13.19 br.s (1H, HOOC), 7.70 s and 7.52 s (2H, NH_2); 7.91 s, 7.89 s and 7.70 s (3H, C_6H_3), 3.55 d and 3.49 d [2H, $\underline{CH_2}C_6H_3$, *J* 14.1], 1.83 s (3H, CH_3)
III	58	174	13.41 br.s (1H, HOOC), 7.66 c and 7.59 s (2H, NH_2); 7.89 s, 7.82 s and 7.69 s (3H, C_6H_3), 4.49 t [1H, CH(Br), *J* 11.8], 3.46 d.d and 3.27 d.d [2H, $\underline{CH_2}C_6H_3$, *J* 13.9]
IV	51	162	13.34 br.s (1H, HOOC), 7.63 s and 7.55 s (2H, NH_2); 7.93 s, 7.88 s and 7.73 s (3H, C_6H_3), 3.52 d and 3.45 d [2H, $\underline{CH_2}C_6H_3$, *J* 14.1], 1.76 s (3H, CH_3)
V	63	197	13.45 br.s (1H, HOOC), 7.77 s and 7.52 s (2H, NH_2); 8.04 s, 7.96 s and 7.80 s (3H, C_6H_3), 4.30 t [1H, CH(SCN), *J* 12.4], 3.42 d.d and 3.21 d.d [2H, $\underline{CH_2}C_6H_3$, *J* 13.7]
VI	71	191	13.27 br.s (1H, HOOC), 8.19 s and 8.00 s (2H, NH_2); 8.07 s, 7.92 s and 7.70 s (3H, C_6H_3), 3.55 d and 3.23 d [2H, $\underline{CH_2}C_6H_3$, *J* 14.0], 1.87 s (3H, CH_3)
VII	33	121	13.30 br.s (1H, HOOC); 8.03 s, 7.99 s and 7.74 s (3H, C_6H_3), 5.52 t [1H, CH(Cl), *J* 11.8], 3.50 d.d and 3.41 d.d [2H, $\underline{CH_2}C_6H_3$, *J* 13.7]
VIII	38	148	13.18 br.s (1H, HOOC); 7.99 s, 7.96 s and 7.72 s (3H, C_6H_3), 3.60 d and 3.47 d [2H, $\underline{CH_2}C_6H_3$, *J* 13.4]), 1.97 s (3H, CH_3)
IX	50	149	13.42 br.s (1H, HOOC); 7.98 s, 7.96 s and 7.87 s (3H, C_6H_3), 5.43 t [1H, CH(Br), *J* 12.2], 3.56 d.d and 3.47 d.d [2H, $\underline{CH_2}C_6H_3$, *J* 13.4]
X	53	155	13.38 br.s (1H, HOOC); 8.02 s, 7.99 s and 7.91 s (3H, C_6H_3), 3.53 d and 3.44 d [2H, $\underline{CH_2}C_6H_3$, *J* 13.1], 1.82 s (3H, CH_3)
XI	36	116	8.03 s and 7.80 s (2H, NH_2); 7.45 s, 7.30 s and 7.22 s (3H, C_6H_3), 4.52 t [1H, CH(Cl), *J* 11.6], 3.38 d.d and 3.25 d.d [2H, $\underline{CH_2}C_6H_3$, *J* 13.8], 2.42 s (3H, $\underline{CH_3}C_6H_3$)
XII	40	134	8.06 s and 7.88 s (2H, NH_2); 7.48 s, 7.34 s and 7.25 s (3H, C_6H_3), 3.41 d and 3.22 d [2H, $\underline{CH_2}C_6H_3$, *J* 13.6], 2.44 s (3H, $\underline{CH_3}C_6H_3$), 1.80 s (3H, CH_3)
XIII	44	129	8.10 s and 7.95 s (2H, NH_2); 7.51 s, 7.40 s and 7.32 s (3H, C_6H_3), 4.46 t [1H, CH(Br), *J* 12.0], 3.36 d.d and 3.19 d.d [2H, $\underline{CH_2}C_6H_3$, *J* 13.4], 2.41 s (3H, $\underline{CH_3}C_6H_3$)
XIV	53	144	8.14 s and 7.98 s (2H, NH_2); 7.55 s, 7.44 s and 7.32 s (3H, C_6H_3), 3.42 d and 3.18 d [2H, $\underline{CH_2}C_6H_3$, *J* 13.5], 2.40 s (3H, $\underline{CH_3}C_6H_3$), 1.84 s (3H, CH_3)
XV	59	169	8.17 s and 7.91 s (2H, NH_2); 7.50 s, 7.36 s and 7.28 s (3H, C_6H_3), 4.27 t [1H, CH(SCN), *J* 12.0], 3.29 d.d and 3.15 d.d [2H, $\underline{CH_2}C_6H_3$, *J* 13.4], 2.44 s (3H, $\underline{CH_3}C_6H_3$)
XVI	65	164	8.17 s and 7.94 s (2H, NH_2); 7.53 s, 7.40 s and 7.29 s (3H, C_6H_3), 3.47 d and 3.13 d [2H, $\underline{CH_2}C_6H_3$, *J* 13.4], 2.42 s (3H, $\underline{CH_3}C_6H_3$), 1.83 s (3H, CH_3)

[a] The substances were recrystallized from methanol.

analysis (NOESY, COSY, HSQC, and HMBC); its results are shown in the Figure and in Table 2.

The cross-peaks in the NOESY spectrum of compound **XVI** (3.13↔7.29, 3.13↔7.53, 3.47↔7.29, 3.47↔7.53, and 2.42↔7.40), as well as in the HMBC spectrum (2.42↔123.75, 2.42↔131.71, 3.13↔132.30, 3.13↔133.67, 3.47↔132.30, and 3.47↔133.67) confirmed that the questionable structure corresponded to 3-(4-methyl-3-thiocyanatophenyl)-2-methyl-2-thiocyanatopropionamide. It should be noted that no correlations between the signals at 113.92 and 111.34 ppm was found in the HMBC spectrum, so assignment of those signals was performed accounting to the general views on the electron density distribution.

In summary, when using 4-methylphenylene-1,3-bisdiazonium tetrafluoroborate as arylating reagent, the

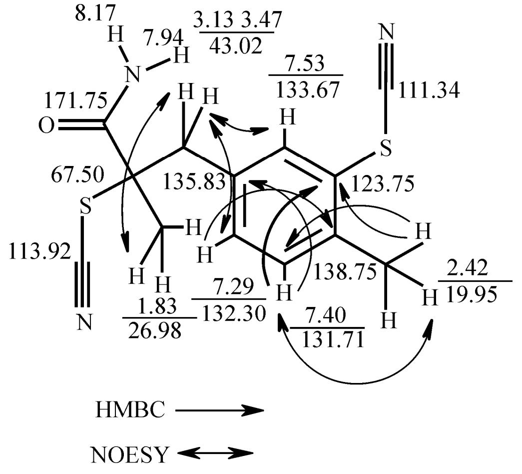
Table 2. Cross-peaks (δ, ppm) in the COSY, NOESY, HSQC, and HMBC spectra of compound **XVI**

^{1}H	COSY	NOESY	HSQC	HMBC
1.83	–	3.13, 3.47, 7.29, 7.53, 7.94, 8.17	26.98	43.02, 171.75
2.42	7.40	7.40	19.95	123.75, 138.75
3.13	3.47	1.83, 3.47, 7.29, 7.53	43.02	67.50, 171.75, 135.83, 132.30, 133.67
3.47	3.13	1.83, 3.13, 7.29, 7.53, 7.94, 8.17	43.02	67.50, 171.75, 135.83, 132.30, 133.67
7.29	7.53, 7.40	1.83, 3.13, 3.47, 7.40, 7.53, 7.94, 8.17	132.30	133.67, 138.75
7.40	7.29, 2.42	2.42, 7.29	131.71	123.75, 135.83
7.53	7.29	1.83, 3.13, 3.47, 7.29, 7.94, 8.17	133.67	138.75, 132.30
7.94	–	1.83, 3.47, 7.53, 7.29	–	67.50
8.17	–	1.83, 3.47, 7.53, 7.29	–	–

thiocyanatoarylation and the Sandmeyer reactions occurred at the *para*- and *ortho*-positioned diazo groups, respectively. Interaction of 5-carboxy- and 4-methylphenylene-1,3-bisdiazonium tetrafluoroborates with amides and nitriles of acrylic and methacrylic acids in the presence of halide or thiocyanate anions yielded monoanionarylated derivatives. Such chemoselectivity was probably due to the high reactivity of the arylating agents and the nucleophilic anions, in agreement with the data presented in [1, 2].

EXPERIMENTAL

IR spectra (paraffin oil) were recorded using a SPECORD M80 instrument. ^{1}H NMR spectra (DMSO-d_6 or $CDCl_3$) were registered with a Varian Mercury (400 MHz) and a Bruker Avance DRX-500 (500 MHz) spectrometers relative to the internal TMS reference.



Main correlations in the HMBC and NOESY spectra of compound **XVI**.

Purity of the products was confirmed by TLC performed on Silufol UV-254 plates (eluents: benzene–methanol, 4 : 1 or methanol–benzene–acetone, 1 : 3 : 1).

3-(3-Amino-2-chloro-3-oxopropyl)-5-chlorobenzoic acid (I). 5-Carboxyphenylene-1,3-bisdiazonium tetrafluoroborate (7.6 g, 0.022 mol) was added to a mixture of 1.7 g (0.024 mol) of acrylamide, 0.8 g (0.0023 mol) of copper(II) tetrafluorborate hexahydrate, and 2.8 g (0.048 mol) of sodium chloride in 150 mL of a water–acetone (1 : 2.5) mixture over 30 min. After nitrogen evolution had ceased (60 min), 30 mL of water was added, and the mixture was extracted with 50 mL of methylene chloride. The organic layer was separated, washed with water, dried over anhydrous calcium chloride, and evaporated. The residue was incubated at –20°C till complete crystallization and then recrystallized from methanol to yield 2.3 g (40%) of compound **I** and 0.9 g (21%) of 3,5-dichlorobenzoic acid melting at 183°C (methanol) (mp 181°C [7]).

Amides **II**, **XI**, and **XII** and nitriles **VII** and **VIII** were prepared similarly.

3-(3-Amino-2-bromo-3-oxopropyl)-5-bromobenzoic acid (III). 5-Carboxyphenylene-1,3-bisdiazonium tetrafluoroborate (7.6 g, 0.022 mol) was added to a mixture of 1.9 g (0.026 mol) of acrylamide, 0.9 g (0.0025 mol) of copper(II) tetrafluorborate hexahydrate, and 6.3 g (0.053 mol) of potassium bromide in 150 mL of a water–acetone (1 : 2.5) mixture over 60 min. After nitrogen evolution had ceased (60 min), the reaction mixture was treated as described above for compound **I**. 4.4 g (58%) of compound **3** and 1.0 g (16%) of 3,5-dibromobenzoic acid melting at 218°C (methanol) (mp 219–220°C [8]) were obtained.

Amides **IV**, **XIII**, and **XIV**, and nitriles **IX** and **X** were prepared similarly.

3-(3-Amino-2-thiocyanato-3-oxopropyl)-5-thiocyanatobenzoic acid (V). 5-Carboxyphenylene-1,3-bisdiazonium tetrafluoroborate (6.4 g, 0.018 mol) was added to a mixture of 1.4 g (0.02 mol) of acrylamide, 0.7 g (0.002 mol) of copper(II) tetrafluorborate hexahydrate, and 3.9 g (0.04 mol) of potassium thiocyanate in 120 mL of a water–acetone (1 : 2.5) mixture over 60 min. After nitrogen evolution had ceased (60 min), the reaction mixture was treated as described above for compound **I**. 3.5 g (63%) of compound **V** and 0.8 g (19%) of 3,5-dithiocyanatobenzoic acid melting at 202°C (methanol) were obtained.

Amides **VI**, **XV**, and **XVI** were obtained similarly.

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