

# Chloroarylation and Thiocyanatoarylation of Itaconic Acid

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Received October 11, 2011

**Abstract**—Under conditions of Meerwein reaction and anionarylation the aryldiazonium salts and itaconic acid form 2-chloro(thiocyanato)-2-benzylbutanedioic acids as the chloro- and thiocyanatoarylation products. The reaction is not accompanied by the decarboxylation process and other transformations affecting the carboxy groups of itaconic acid.

**DOI:** 10.1134/S1070363213020151

At present, a significant number of acrylic and methacrylic acids derivatives has been investigated in the anionarylation and Meerwein reaction conditions. The preparative methods of obtaining the anionarylation and arylation products starting from unsaturated compounds are developed. Some approaches to the synthesis of heterocycles based on these processes are described [1–5].

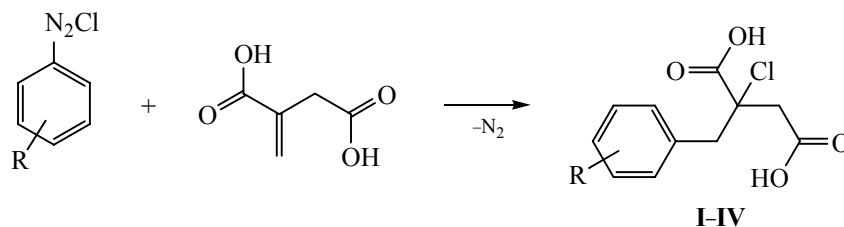
A considerable interest in the synthetic and theoretical terms is the anionarylation of the unsaturated dicarboxylic acids and their derivatives, which were investigated only sporadically in the Meerwein reaction [3].

The reactions of aryl diazonium chlorides with itaconic and aconitic acids are known to afford  $\alpha$ -

benzylacrylic and arylitaconic acids in yields of ~20% [6].

In continuation of the study on the derivatives of  $\alpha,\beta$ -unsaturated carboxylic acids [7–9] we examined for the first time 2-methylenebutandioic (itaconic) acid in the conditions of Meerwein reaction and anionarylation.

Aryldiazonium chlorides were found to react readily with itaconic acid in a water–acetone medium (1:2) at 20–25°C in the presence of copper(II) chloride as a catalyst to form 2-chloro-2-benzylbutanedioic acids **I–IV**. The reaction proceeds with the nitrogen release and the addition of an aryl group and chlorine atom at the place of the double bond rupture.



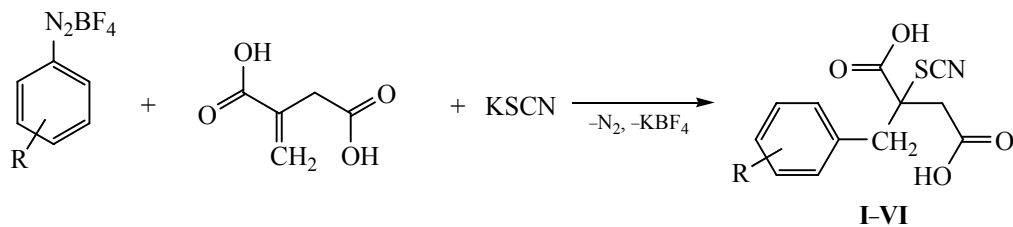
R = 2-CH<sub>3</sub> (**I**), 4-CH<sub>3</sub> (**II**), 4-CH<sub>3</sub>O (**III**), 4-Br (**IV**).

Aryldiazonium tetrafluoroborates react with itaconic acid in the presence of potassium thiocyanate and copper(II) tetrafluoroborate as a catalyst at –15 to –10°C to form 2-thiocyanato-2-benzylbutanedioic acids **V–X**.

The optimal ratio aromatic diazonium salt–itaconic acid–potassium thiocyanate–catalyst is 1.1:1:1.2:0.11.

The yields of the products **I–X** are 54–75%. The yields, melting points, and elemental analysis data of the synthesized compounds **I–X** are presented in Table 1.

The chloroarylation and thiocyanatoarylation of itaconic acid are also accompanied by a side formation of chloroarenes (20–25%) and a mixture of thio- (3–5%) and isothiocyanatoarenes (15–20%), respectively.



R = H (V), 2-CH<sub>3</sub> (VI), 3-CH<sub>3</sub> (VII), 4-CH<sub>3</sub> (VIII), 4-CH<sub>3</sub>O (IX), 4-Br (X).

Under the investigated conditions the chloroarylation and thiocyanatoarylation reactions were not accompanied with the release of hydrogen chloride or thiocyanate and decarboxylation of one COOH group, which is consistent with the data of elemental analysis, IR and mass spectroscopy of compounds I–X.

The structure of the synthesized compounds was confirmed by the IR and <sup>1</sup>H NMR spectroscopy. The IR spectra of compounds I–X contain the characteristic absorption bands of carboxy (1696–1716 cm<sup>-1</sup>) and thiocyanate groups (2148–2164 cm<sup>-1</sup>). In the <sup>1</sup>H NMR spectra there are the signals of aromatic protons at 7.55–6.99 ppm. The protons of the methylene groups associated with the aromatic rings, along with the protons of the methylene groups of succinic acid fragment are observed as the doublets of doublets in the region of 3.34–2.89 ppm. The spectral data of compounds I–X are presented in Table 2.

Thus, under the Meerwein reaction conditions the itaconic acid gives exclusively the chloroarylation products. The results presented in [5] concerning the structure of the final products may be due to the fact that the chloroarylated itaconic acid derivatives are thermally unstable compounds, which during the vacuum distillation can relatively easily eliminate hydrogen chloride or undergo other destructive changes.

The presence of two carboxy groups in the structure of the unsaturated compounds does not affect the regioselectivity of the chloro- and thiocyanatoarylation and proves a sufficiently high activation of the multiple carbon–carbon bond.

## EXPERIMENTAL

The IR spectra were recorded on a Specord M80 instrument from the samples in mineral oil. The <sup>1</sup>H

**Table 1.** Yields, melting points, and elemental analysis data of 2-chloro(thiocyanato)-2-benzylbutandioic acids I–X

Comp. no.	Yield, %	mp, °C <sup>a</sup>	Found, %			Formula	Calculated, %		
			Cl	N	S		Cl	N	S
I	58	170	13.88	–	–	C <sub>12</sub> H <sub>13</sub> O <sub>4</sub> Cl	13.81	–	–
II	56	199	13.90	–	–	C <sub>12</sub> H <sub>13</sub> O <sub>4</sub> Cl	13.81	–	–
III	54	192	13.09	–	–	C <sub>12</sub> H <sub>13</sub> O <sub>5</sub> Cl	13.00	–	–
IV	62	182	11.11	–	–	C <sub>11</sub> H <sub>10</sub> BrO <sub>4</sub> Cl	11.03	–	–
V	67	125	–	5.19	12.15	C <sub>12</sub> H <sub>11</sub> NO <sub>4</sub> S	–	5.28	12.09
VI	61	171	–	4.96	11.51	C <sub>13</sub> H <sub>13</sub> NO <sub>4</sub> S	–	5.01	11.48
VII	55	118	–	5.14	11.55	C <sub>13</sub> H <sub>13</sub> NO <sub>4</sub> S	–	5.01	11.48
VIII	70	128	–	5.06	11.53	C <sub>13</sub> H <sub>13</sub> NO <sub>4</sub> S	–	5.01	11.48
IX	75	127	–	4.83	10.97	C <sub>13</sub> H <sub>13</sub> NO <sub>5</sub> S	–	4.74	10.86
X	58	156	–	4.00	9.29	C <sub>12</sub> H <sub>10</sub> BrNO <sub>4</sub> S	–	4.07	9.32

<sup>a</sup> Compounds I–IV were recrystallized from ethanol, compounds V–X, from methanol.

**Table 2.** Parameters of IR and  $^1\text{H}$  NMR spectra of 2-chloro(thiocyanato)-2-benzylbutandioic acids **I–X**

Comp. no.	IR spectrum, $\nu$ , $\text{cm}^{-1}$		$^1\text{H}$ NMR spectrum, $\delta$ , ppm
	C–Cl (SCN)	C=O	
<b>I</b>	672	1712	12.79 br.s (2H, COOH), 7.29–7.13 m (4H, $\text{C}_6\text{H}_4$ ), 3.29 d.d [2H, $\text{CH}_2\text{C}(\text{O})\text{O}$ ], 2.89 d.d (2H, $\text{CH}_2\text{C}_6\text{H}_4$ ), 2.29 s (3H, $\text{CH}_3$ )
<b>II</b>	668	1704	12.77 br.s (2H, COOH), 7.12 s (4H, $\text{C}_6\text{H}_4$ ), 3.30 d.d [2H, $\text{CH}_2\text{C}(\text{O})\text{O}$ ], 2.92 d.d (2H, $\text{CH}_2\text{C}_6\text{H}_4$ ), 2.27 s (3H, $\text{CH}_3$ )
<b>III</b>	676	1700	12.80 br.s (2H, COOH), 7.50 and 7.14 two d (4H, $\text{C}_6\text{H}_4$ ), 3.78 s (3H, $\text{CH}_3\text{O}$ ), 3.32 d.d [2H, $\text{CH}_2\text{C}(\text{O})\text{O}$ ], 2.94 d.d (2H, $\text{CH}_2\text{C}_6\text{H}_4$ )
<b>IV</b>	684	1708	12.88 br.s (2H, COOH), 7.53 and 7.18 two d (4H, $\text{C}_6\text{H}_4$ ), 3.34 d.d [2H, $\text{CH}_2\text{C}(\text{O})\text{O}$ ], 2.91 d.d (2H, $\text{CH}_2\text{C}_6\text{H}_4$ )
<b>VI</b>	2152	1712	12.64 br.s (2H, COOH), 7.25–7.08 m (4H, $\text{C}_6\text{H}_4$ ), 3.20 d.d [2H, $\text{CH}_2\text{C}(\text{O})\text{O}$ ], 3.01 d.d (2H, $\text{CH}_2\text{C}_6\text{H}_4$ ), 2.30 s (3H, $\text{CH}_3$ )
<b>VII</b>	2156	1704	12.75 br.s (2H, COOH), 7.20–6.99 m (4H, $\text{C}_6\text{H}_4$ ), 3.14 d.d [2H, $\text{CH}_2\text{C}(\text{O})\text{O}$ ], 2.98 d.d (2H, $\text{CH}_2\text{C}_6\text{H}_4$ ), 2.29 s (3H, $\text{CH}_3$ )
<b>VIII</b>	2160	1700	12.82 br.s (2H, COOH), 7.08 s (4H, $\text{C}_6\text{H}_4$ ), 3.11 d.d [2H, $\text{CH}_2\text{C}(\text{O})\text{O}$ ], 2.95 d.d (2H, $\text{CH}_2\text{C}_6\text{H}_4$ ), 2.26 s (3H, $\text{CH}_3$ )
<b>IX</b>	2156	1704	12.71 br.s (2H, COOH), 7.54 and 7.10 two d (4H, $\text{C}_6\text{H}_4$ ), 3.82 s (3H, $\text{CH}_3\text{O}$ ), 3.17 d.d [2H, $\text{CH}_2\text{C}(\text{O})\text{O}$ ], 2.96 d.d (2H, $\text{CH}_2\text{C}_6\text{H}_4$ )
<b>X</b>	2148	1708	12.84 br.s (2H, COOH), 7.51 and 7.15 two d (4H, $\text{C}_6\text{H}_4$ ), 3.19 d.d [2H, $\text{CH}_2\text{C}(\text{O})\text{O}$ ], 2.99 d.d (2H, $\text{CH}_2\text{C}_6\text{H}_4$ )

NMR spectra were obtained on a Varian Mercury instrument (400 MHz) relative to internal TMS from  $\text{DMSO}-d_6$  solutions. The mass spectra were registered on an Agilent 6850/5973 N GC-mass spectrometer. The individuality of the synthesized compounds was established by TLC on Silufol UV-254 plates eluting with a chloroform–methanol (ethanol)–acetone mixture (2:1:1).

#### 2-Chloro-2-(2-methylbenzyl)butanedioic acid (**I**).

To a mixture of 9.2 g (0.07 mol) of itaconic acid and 1.3 g (0.0077 mol) of copper(II) chloride dihydrate in 120 ml of a water–acetone (1:2) mixture was added a solution of 11.9 g (0.077 mol) of *o*-tolyl diazonium chloride within 30 min. The nitrogen release was observed at 25°C for 2 h. After the nitrogen release completed the reaction mixture was diluted with 100 ml of water and extracted with 150 ml of diethyl ether. The extract was washed with water, dried with anhydrous calcium chloride, and concentrated. The solid residue was eluted with benzene and recrystallized from ethanol. Yield 11.1 g (58%). Mass spectrum:  $m/z$  246 [ $M$ ] $^+$ .

Compounds **II–IV** were obtained similarly.

**2-Thiocyanato-2-benzylbutanedioic acid (**V**).** To a mixture of 4.2 g (0.032 mol) of itaconic acid, 1.4 g

(0.004 mol) of copper(II) tetrafluoroborate hexahydrate, and 3.9 g (0.04 mol) of potassium thiocyanate in 150 ml of a water–acetone (1:2.5) mixture was added 6.8 g (0.035 mol) of phenyldiazonium tetrafluoroborate within 1 h. The nitrogen release was observed at  $-10^\circ\text{C}$  for 1.5 h. After the nitrogen release completed the reaction mixture was diluted with 100 ml of water, and extracted with 100 ml of diethyl ether. The extract was washed with water, dried with anhydrous calcium chloride, concentrated, and cooled to  $-20^\circ\text{C}$ . The colorless crystals formed were recrystallized from methanol. Yield 5.7 g (67%). Mass spectrum:  $m/z$  255 [ $M$ ] $^+$ .

Compounds **VI–X** were obtained similarly.

#### ACKNOWLEDGMENTS

This work was financially supported by the Ministry of Science and Education of Ukraine.

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