UDC 547.539.04

INVESTIGATION OF PREPARATIVE POSSIBILITIES OF IODINATING SYSTEMS ON THE BASIS OF N-IODOACETAMIDE

V.K. Chaykovskiy, A.A. Funk, O.A. Martynyuk, V.D. Filimonov, T.S. Kets*

Tomsk Polytechnic University
E-mail: clg@mail.ru
*Tomsk State Pedagogical University

N-iodoacetamide in organic solvents with H_2SO_4 iodinates successfully alkylbenzenes, aromatic amines and phenol ether. Electrophilic iodine activity is controlled by medium acidity. Super electrophilic iodine formed at N-iodoacetamide dissolution in sulfuric acid reacts easily with electron-deficient arenes at 0...20 °C forming iodinated products.

Iodating properties of N-iodamides and N-iodimides are known for a long time but earlier their application in iodating reactions was restricted by interaction with a rather small range of aromatic substrate substantially aryl amines and phenol ethers. And only for the last 10–15 years iodating possibilities of some compounds with bonds N-I are managed to be expanded. First of all it refers to such substances as N-iodine succimide [1–4] and N,N,N,N-tetraiodglicoluryl [4–6]. N-iodoacetamide (**NIA**) is not entered into this row yet.

The aim of the given investigation was to study in details preparative possibilities of iodating systems on the basis of N-iodoacetamide in the medium of organic solvents and sulfuric acid.

1,2,4,5-tetramethylbenzene (durene) and nitrobenzene were selected as model compounds for studying iodating processes as well as in earlier works [2, 3, 5]. By their example the efficiency of applying NIA for iodating aromatic compounds with electron-donor and electron-acceptor groups was studied. Durene (**1a**) was iodated in different organic solvents (Table 1). As NIA is low-activity in neutral and subacid medium then the reactions were carried out with small quantities of sulfuric acid. We suppose that the role of H_2SO_4 in this case came to acidolysis of N-iodoacetamide to acetamide and formation of compound of hypo iodated character probably iodine bisulfate(Diagram 1).

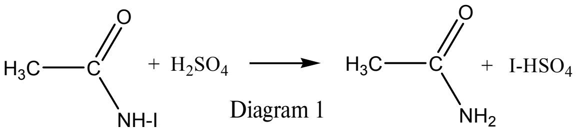

Diagram 1

In support to the given Diagram there is a fact that after NIA dissolution in H_2SO_4 in spectra NMR ^{13}C of the obtained solution there is only a signal of carbonyl group of unsubstituted protonated acetamide at 181,5 m.u. which is completely identical to the corresponding signal of etalon acetamide spectrum in H_2SO_4. That results in conclusion that electrophilic iodine of N- iodoacetamide firstly transfers into sulfuric acid and only then the formed intermediate iodates substrate (Diagram 2).

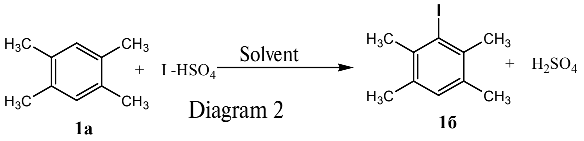

Diagram 2

The efficiency of solvent action at iodating arene turned out to be different **1a** (Table 1).

Table 1 *Iodating durene with the systems of NIA-organic solvent-sulfiric acid*

Solvent	Reaction time, min	Product yield (**1б**), %	Melting t of techn. product (**1б**), °C
Acetic acid	30	84	77...78
Ethanol	30	75	76...77
Methanol	30	74	75...77
Dioxane	10	47	71...73
Acetone	20	42	62...64
Dimethyl formamide	20	36	63...65

Satisfactory results were obtained in acetic acid, ethanol and menthol. But monoioddurene **(1б)** of better quality with melting point 77...78 °C was extracted while using acetic acid (literary melting point of the compound **1б** 78...79 °C).

In acetic acid, ethanol and methanol after NIA loading the monoiodine sediment **1б** starts precipitating almost immediately but arene complete conversion **1a** into iodated product **1б** takes 25...30 min. Considerably worth results are obtained in dioxane, acetone and DMFA. In these solvents product **1б** precipitated from reaction mass only being diluted with water and had melting point rather lower than reference one. Besides, it was noted that acetone in this process may partially interact with NIA forming lacrimatory α-iodine acetone.

Carrying out synthesis the preliminary dissolution of substrate in acetic acid with sulfuric acid and then achieving required temperature NIA addition in parts is necessary. Adding substrate **1a** to reaction mass last of all the yield of the product **1б** decveases at the average by 10...12 %, as in the mixture NIA-CH_3COOH-H_2SO_4 prepared preliminarily the NIA decomposition with extraction of inactive metal iodine is observed.

By the given technique diioddurene (**1в**) was obtained except monoioddurene **1б** from durene **1a** and monoiodine- (**2б**) and diodine- (**2в**) mesitylene were obtained from mesitylene (**2a**). Fluorene (**3a**), diphenyl (**4a**) and 4-nitroaniline (**5a**) were iodated to the corresponding diiodine derivatives (**3б**, **4б**, **5б**) (Table 2).

Iodating arenes containing amides (**5a, 6a**) and phenol ethers (**7a, 8a**) system NIA – EtOH – H_2SO_4 turned out to be the most efficient. Obtaining diiodine derivatives it is ne-

Table 2. *Iodating activate arenas with the system NIA-CH_3COOH (EtOH)-H_2SO_4 at 20 °C*

Substrate	Solvent	Reaction time, min	Product	Yield, %	Melting point, °C. (solv.)
Durene **(1a)**	AcOH	30	Ioddurene **(1б)**	84	77...78 (EtOH)
Durene **(1a)**	AcOH	40	Diioddurene **(1в)**	58	161...162 (EtOH)
Mesitylene **(2a)**	AcOH	30	Iodine mesitylene **(2б)**	50	29...30 (MeOH)
Mesitylene **(2a)**	AcOH	40	Diiodine mesitylene **(2в)**	86	74...75 (EtOH)
Fluorene **(3a)**	AcOH	60	2,7-Diiodine fluorene **(3б)**	72	208...209 (toluene)
Diphenyl **(4a)**	AcOH	60	4,4′-Diiod diphenyl **(4б)**	53	203...204 (AcOH)
4-Nitroanilin **(5a)**	EtOH	30	2,5-Diiodine-4-nitroaniline **(5б)**	89	249...251 (PrOH)
Acetanilide **(6a)**	EtOH	30	4-Iodacetanilide **(6б)**	83	183...184 (EtOH)
Anisole **(7a)**	EtOH	30	4-Iodanisole **(7б)**	69	50...52 (MeOH)
Diphenyl ether **(8a)**	EtOH	30	4,4′-Diiodine diphenyl ether **(8б)**	83	138...139 (EtOH)

Table 3. *Iodating arenes containing decontaminating groups with agent on the basis of NIA в H_2SO_4 at 0...3 °C*

Substrate	Reaction time, min	Product	Yield, %	Melting point, °C. (solv.)
Nitrobenzene **(9a)**	60	3-iodine-nitrobenzene **(9б)**	75	35...36 (MeOH)
2-Nitrotoluene **(10a)**	60	4-Iodine-2-nitrotoluene **(10б)**	40	59...60 (MeOH)
Benzoic acid **(11a)**	60	3-Iodine-benzoic acid **(11б)**	88	185...187 (PrOH)
4-Fluorine-benzoic acid **(12a)**	90	3-Iodine-4-fluorine-benzoic acid **(12б)**	78	173...174 (PrOH)
Benzaldehyde **(13a)**	30	3-Iodine-benzaldehyde **(13б)**	65	55...56 (EtOH)
Benzophenone **(14a)**	30	3,3′-Diiodine-benzophenone **(14б)**	63	145...147 (EtOH)
Phluorenone **(15a)**	60	2,7-Diiodine-phluorenone **(15б)**	67	204...205 (бензол)
Benzyl **(16a)**	30	3,3′-Diiodine-benzyl **(16б)**	80	127...128 (EtOH)

cessary to increase medium acidity adding multiple sulfuric acid at introduction of each additional iodine atom into substrate. Having excluded completely the organic solvent and carrying out synthesis in H_2SO_4 iodating system activity with NIA could be increased manifold (Table 3).

For example the agent obtained by dissolving NIA in H_2SO_4 with density 1,828 g/cm^3 iodates easily nitrobenzene (**9a**), 2-nitrotoluene (**10a**), benzoic (**11a**) and fluorine-benzoic (**12a**) acids, benzaldehyde (**13a**), benzophenone (**14a**), phluorenone (**15a**), benzyl (**16a**) forming relative iodine-derivatives (**9б-16б**). Reaction courses at 0...3 °C during 30...60 min (Table 3). Optimization of obtaining iodine-nitrobenzene (**9б**) showed that in comparison with arene iodation with electron-donor groups in organic solvents where equimolar ratios of substrate – N-iodacetamide are used; in solution H_2SO_4 twofold molar excess of NIA is required for introduction of one atom of iodine into nitroarene **9a.** The same ratios are also observed at iodine introduction into decontaminated substrates (**10a-16a**). It was mentioned before that at arene iodation in sulfuric acid the twofold excess of agent was also required while using N-iodine-succinimide [2] and N,N,N,N-tetraiodglicoluryl [5]. Similar stoichiometry of the process may be explained by formation and presence of electrophilic triodine-cation (I_3^+) in solutions H_2SO_4 [7], but this requires further studying and experimental confirmation.

Experimental part

Chromatographic control of reaction and purity of obtained substances was carried out by the method of TLC at plates Sorbfil at the development with UV light. Spectra NMR ^{13}C were recorded at spectrometer Bruker AS-300, external standard – D_2O. Structure of iodation products was determined on the basis of their spectral characteristics, analytical results and comparison with authentic samples. Tests of mixing the obtained compounds with known samples do not give melting temperature depression. N-iodacetamide was obtained by the technique [8].

General iodating technique in organic solvents. 5 millimole of substrate (**1a-8a**) was solved in 15 ml of acetic acid (or EtOH) and while cooling 1 ml of sulfuric acid (1,828 g/cm^3) was added. Then at mixing and ~20 °C 0,93 g (5 millimole) of N-iodacetamide was added. The mixture was stirred during 30...60 min. Reaction mass was poured into water. Sediments were filtered and dried and recrystallized if it was necessary. Soft products were extracted with dichloromethane, dried by $CaCl_2$, the solvent was distilled off. Obtaining diiodine-derivatives substarte loading was decreased twice.

Ioddurene (1б). 0,67 g (5 millimole) of durene (**1a**) was solved in 15 ml of acetic acid and while cooling 1 ml (1,828 g/cm^3) of sulfuric acid was added. Then at stirring and room temperature 0,93 g (5 millimole) of N-iodacetamide was added. The mixture was stirred for 30 min. Reaction mass was poured into water, sediment was filtered and dried. Ioddurene yield (**1б**) was 0,96 g (74 %). Melting point 77...78 °C

4-Iodacetanilide (6б). 0,68 g (5 millimole) of acetanilide (**6a**) was solved in 15 ml ethanoland while cooling 1 ml (1,828 g/cm^3) of sulfuric acid was added. Then at mixing and ~20 °C 0,93 g (5 millimole) of N-iodacetamide was added. The mixture was stirred during 30 min. Reaction mass was poured into water; the sediment was filtered and dried. Yield of 4-iodacetanilide (**6б**) was 1,08 g (83 %). Melting point 183...184 °C.

Preparation of agent on the basis of NIA in sulfuric acid. 20 ml of 93 % (1,828 g/cm^3) H_2SO_4 was put into a bulb and cooled to the temperature ~0 °C then 0,93 g (5 millimole) of N-iodacetamide was gradually added while mixing and continued stirring at room temperature (~20 °C) during 15...20 min up to the complete NIA dissolving and obtaining homogeneous solution of dark brown color.

General technique of iodation with agent on the basis of NIA in sulfuric acid. 2,5 millimole of aromatic substrate (**9a-13a**) was added to the prepared agent and stirred during 30...60 min at temperature 0...3 °C. To obtain diiodine-derivatives (**14б-16б**) substrates loading (**14a-16б**) was twice decreased. At the end of synthesis the reaction mass was poured into water and washed with 5 % solution of sodium sulfite. The sediments were filtered, dried, recrystallized if necessary.

3-Iodnitrobenzene (9б). 0,31 g (2,5 millimole) of nitrobenzene was added to the prepared agent and mixed during 60 min at temperature 0...3 °C. At the end of synthesis the reaction mass was poured into water and washed with 5 % solution of sodium sulfite. Product **9б** was extracted with chloride methylene, dried by $CaCl_2$, the solvent was distilled off. Yield of 3-iodnitrobenzene was 0,47 g (75 %). Melting point 35...36 °C.

REFERENCES

1. Olah G.A., Wang Qi, Sandford G., Prakash G.K.S. Iodination of Deactivated Aromatics with N-Iodosuccinimide in Trifluoromethanesulfonic Acid (NIS – CF_3SO_3H) via in Situ Generated Superelectrophilic Iodine (I) Trifluoromethanesulfonate // J. Org. Chem. – 1993. – V. 58. – P. 3194–3195.
2. Chaikovski V.K., Filimonov V.D., Skorokhodov V.I. Synthesis and use of N-iodine sucimide in H_2SO_4 as the efficient agent for iodation of decontaminated aromatic compounds. // Zhurnal Organicheskoy Khimii. – 2001. – V. 37. – Issue 20. – № 10. – P. 1572–1573.
3. Chaikovski V.K., Filimonov V.D., Skorokhodov V.I. Iodation of aromatic compounds of N-iodine sucimide in organic solvents with H_2SO_4 // Izvestiya Vuzov. Khimiya i Khimicheskaya Tekhnologiya. – 2002. – V. 43. – Issue 3. – P. 48–51.
4. Chaikovski V.K., Filimonov V.D., Skorokhodov V.I., Sarycheva T.A., Kharlova T.S. Iodation of aromatic α-diketons with new super electrophilic agents // Izvestiya Vuzov. Khimiya i Khimicheskaya Tekhnologiya. – 2002. – V. 43. – Issue 3. – P. 45–47.
5. Chaikovski V.K., Filimonov V.D., Yagovkin A.Y., Kharlova T.S. 2,4,6,8-Tetraiodoglykoluril in sulfuric acid as a new available and powerful reagent for iodination of deactivated arenes // Tetrahedron Lett. – 2000. – V. 41. – № 47. – P. 9101–9104.
6. Chaikovski V.K., Filimonov V.D., Yagovkin A.Y., Ogorodnikov V.D. 2,4,6,8-Tetraiod-2,4,6,8-tetraasabi-cyclo[3.3.0]oktan-3,7-dion as universal and soft agent for aromatic compound iodation // Bulletin of RAS. Chemical series. – 2001. – V. 50. – № 12. – P. 2302–2306.
7. Filimonov V.D., Krasnokutskaya E.A., Poleshuk O.Kh., Lesina Yu.A., Chaikovski V.K. Studying electron structure and reactivity of iodating agents in gaseous phase and solutions by the method of density functional // Bulletin of RAS. Chemical series. – 2006. – № 8. – P. 1280–1288.
8. Gottardi W. Uber die Reaktion von N-Bromoverbindungen mit Jod: eine einfache Synthesemethode fur N-Jodverbindungen // Monatsh. Chem. – 1975. – Bd. 106. – № 4. – S. 1019–1025.

Received on 6.12.2006