

Generation of Electrophilic Iodine from Iodine Monochloride in Neutral Media. Iodination and Protodeiodination of Carbazole

V. D. Filimonov, E. A. Krasnokutskaya, and Yu. A. Lesina

Tomsk Polytechnic University, Tomsk, 634050 Russia

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Abstract—In reaction of iodine monochloride with CF_3COOAg , CH_3COONa or $(\text{CH}_3\text{COO})_2\text{Pb}$ in acetonitrile and acetic acid the chloride is bonded by metal cations, and electrophilic iodine is generated able to easily iodinate anthracene and carbazole. However at the iodination of anthracene in the presence of oxygen the prevailing process is anthracene oxidation to anthraquinone. In the presence of sulfuric acid protodeiodination of 3-iodocarbazole was found to occur resulting in rearranged products.

A direct iodination of aromatic and heterocyclic compounds proceeds difficultly both at the use of deactivated and many among activated substrates. Whereas in the former case the difficulty is obviously caused by relatively low electrophilicity of iodine and it can be sharply raised using strong acids as media (trifluoromethanesulfonic or sulfuric acids [1, 2]), the negative results of iodination of highly active arenes and π -excessive heterocycles are poorly understood.

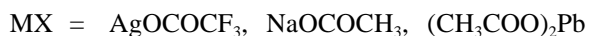
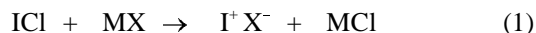
For instance, phenanthrene fluorene did not undergo direct iodination, and iodination of anthracene succeeded only using iodine in the presence of copper sulfate adsorbed on Al_2O_3 [3], or by *N,N,N,N*-tetraiodoglycoluril in the presence of trifluoroacetic acid [4]. Therefore the efficient synthesis procedure for 9-iododerivatives of anthracene and phenanthrene is based on substitution with iodide ion of bromine in the respective bromoderivatives [5].

The inertness of polycyclic arenes toward iodination is commonly rationalized as formation of strong charge-transfer complexes with iodine [6]. Treating anthracene and phenanthrene with iodine monochloride in acetonitrile resulted in chlorination of substrates and not in iodination [7]. This unexpected behavior was also ascribed to formation of the charge-transfer complexes with ICl which decomposed into cation-radicals that reacting with Cl^- furnished the chlorinated products [7].

If the above iodination problems are really caused by concurrent formation of inactive complexes then one possible way to overcome the difficulty would be the application of compounds of electrophilic iodine which do not form with substrates similar complexes. The method of the electrophilic iodine I^+ generation

that was formerly advanced consisted in reacting iodine monochloride with silver sulfate in sulfuric acid [2]. However this reagent is not applicable to iodination of activated substrates since in sulfuric acid would occur numerous side processes (sulfation, tarring, etc.).

The target of this study was a search for new methods of electrophilic iodine generation in neutral or weakly acid media and the application of these methods to iodination of anthracene (**I**) and carbazole (**II**) as typical π -excessive heterocycle. To this end we used reaction of ICl with salts containing cations that were able to a certain extent capture chloride and to remove it from the reaction zone liberating the electrophilic iodine: silver trifluoroacetate in acetonitrile, and lead and sodium acetates in acetonitrile containing 14 vol% of acetic acid.



On mixing the components the corresponding chlorides precipitated in the following amounts: AgCl , 100–110%; PbCl_2 , 90–110%; NaCl , 35–40% with respect to the initial iodine monochloride. Therewith formed stable brown solutions. The amounts of AgCl and PbCl_2 exceeding 100% evidently arise from partial formation of complex salts AgICl^+ , AgI_2^+ and compounds of lead(IV).

To the solutions obtained corresponds absorption in the region 459 nm; besides with reagents based on acetate salts a maximum appears at λ_{max} 340 nm originating from the absorption of the residual iodine monochloride. Thus sodium and lead acetates in contrast to CF_3COOAg do not capture completely

chlorine anions, i.e. the reaction (1) is to a certain extent reversible. This observation is in agreement with better solubility of sodium and lead chlorides than those of silver.

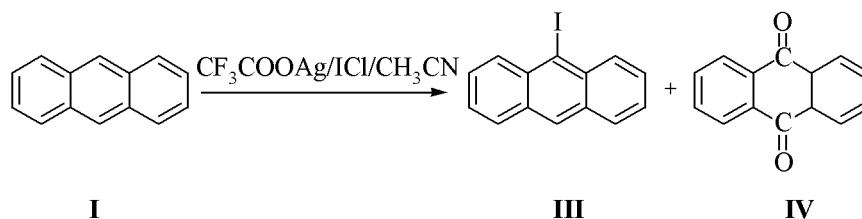
It should be noted that electron absorption spectra of solutions in sulfuric acid of "superelectrophilic iodine" ($\text{Ag}_2\text{SO}_4\text{-ICl-H}_2\text{SO}_4$ system) [2], tetraiodoglycoluril [4], and *N*-iodosuccinimide have similar spectral characteristics: in all cases absorption was observed in the region 452, 450, and 451 nm respectively.

The iodine proper has absorption in the region of 360–520 nm (478 nm in acetic acid, 502 nm in sulfuric acid, 360 nm in acetone [9]). In the solutions under study the iodine absorption was lacking.

A detailed investigation of the structure of the iodinating reagents obtained $\text{I}^+ \text{X}^-$ should be an object of a special research, but within the framework of the present study we can state the following. It is often assumed that in iodine solutions in acetic or trifluoroacetic acids under the action of oxidants arise the corresponding acyl hypoiodites RCOOI which are

the real iodinating agents (see, e.g., reviews [10, 11]). It might be assumed *a priori* that in the systems we are investigating the obtained active iodine-containing species are acyl hypoiodites. However these compounds same as hypoiodic acid should not have absorption bands in the visible region. Moreover as has been already mentioned the spectral characteristics of the solutions obtained from ICl and the salts in question are quite similar and resemble those of the iodinating agents where no acyl hypoiodite cannot be present at all. It is also known that in the region 460 nm in sulfuric acid absorbs such form of electrophilic iodine as I_3^+ , and solution of iodine cation I^+ are blue with λ_{max} 410, 500 and 640 nm [12]. Thus our preliminary results suggest that the solutions under study contain certain amount of I_3^+ probably alongside acyl hypoiodites.

The solution prepared from silver trifluoroacetate and iodine monochloride in acetonitrile readily reacts with anthracene (**I**) affording 9-iodoanthracene (**III**) and unexpectedly 9,10-anthraquinone (**IV**) that forms as prevailing product in the presence of oxygen.



The iodination proceeded at room temperature. However at equimolar amount or at double excess of the iodinating reagent with respect to substrate (**I**) the conversion of the latter was incomplete. Only at the

Table 1. Anthracene (**I**) iodination effected by $\text{CF}_3\text{COOAg-ICl}$ in acetonitrile at 20°C (ratio $\text{CF}_3\text{COOAg-ICl}$ 1.5 : 1, substrate–reagent, 1 : 4)

Run no.	Reaction time, h	Yield, %	
		III	IV
1		17	60
2 ^a	1	12	8
3 ^b	2.5	15	58
4	4	–	93
5 ^c	0.5	Traces	83

^a Under nitrogen.

^b DMSO was used as solvent.

^c Reaction at 0°C.

use of 4 equiv of the iodinating reagent per substrate (**I**) resulted in complete consumption of the latter within 1 h (Table 1). In reaction prolonged to 4 h nearly quantitative yield of anthraquinone **IV** was obtained. The application of DMSO instead of acetonitrile did not affect the result of the process.

It was established that at 0°C the rate of anthraquinone formation sharply increased (Table 1) apparently due to a higher oxygen concentration in solution at lower temperature. In reaction carried out under nitrogen atmosphere the amount of anthraquinone **IV** sharply decreased (8%), but the yield of iododerivative **III** did not grow. The initial compound was lacking in the reaction mixture, and it was contaminated with tar.

It is not yet clear whether iodoanthracene **III** is an intermediate in this oxidation process. However it was found that at storage in solution (in hexane, chloroform) iodoanthracene **III** in some time was

Table 2. Characteristics of mass spectra of products obtained by carbazole iodination at 20°C within 90 min

Reagent (substrate- reagent ratio, mmol)	Reaction product	Reten- tion time, min	Data of mass spectra, m/z (I_{rel} , %)	Content in mixture, %	
CH ₃ COONa-ICl (1:1.5)	Carbazole	18.05	168 (13), 167 [M] ⁺ (100), 166 (21), 140 (7), 139 (10), 83 (12), 82 (2), 71 (3), 70 (4)	2.2	
	1-Iodocarbazole	21.02	294(12), 293 [M] ⁺ (100), 167(4), 166(27), 165(7), 164(7), 146 (10), 140 (7), 139 (21), 138(5), 137(4), 83 (6), 69(8)	3.7	
	3-Iodocarbazole	22.88	294(12), 293 [M] ⁺ (100), 167(3), 166(37), 165(4), 164 (6), 146 (9), 140 (4), 139 (17), 138 (3), 83 (5), 69 (6)	70.5	
	3,6-Diiodo- carbazole	27.54	420(12), 419 [M] ⁺ (100), 293(2), 292(21), 265(2), 209(9), 165 (12), 164 (17), 146 (8), 138 (6), 137 (4), 82 (9), 69 (3)	19.6	
	1,6-Diiodo- carbazole	25.33	420(12), 419 [M] ⁺ (100), 293(2), 292(22), 265(2), 209(10), 165 (15), 164 (19), 146 (8), 138 (6), 137 (6), 82 (8), 69 (3)	3.3	
	Products of unidentified structure		23.79	308 (12), 307 [M] ⁺ (100), 181 (6), 180 (60), 179 (12), 178 (10), 153 (8), 152 (10), 151 (7), 128 (6), 127 (6), 90 (21), 89 (8), 77 (8), 76 (11), 75 (6), 63 (5)	0.2
			25.10	420(14), 419 [M] ⁺ (100), 293(2), 292 (8), 209(9), 165(48), 164 (17), 146 (8), 138 (4), 137 (4), 82 (9), 69 (2)	0.3
		29.01	434 (12), 433 [M] ⁺ (100), 306(20), 305(4), 216(4), 180(8), 150 (6), 179 (17), 178 (12), 177 (8), 153 (17), 152 (6), 151 (8), 133 (5), 90 (5), 89 (12), 76 (9), 57 (5), 32 (4)	0.2	
(CH ₃ COO) ₂ Pb- ICl (1:1.5)	carbazole	18.08	168 (12), 167 [M] ⁺ (100), 166(21), 140(8), 139(10), 83(12), 82 (2), 70 (3)	61.2	
	1-Iodocarbazole	21.02	294 (12), 293 [M] ⁺ (100), 167(4), 166(27), 165(8), 164(8), 146 (10), 140 (6), 139 (17), 138 (3), 137 (2), 82 (4), 69 (4)	1.3	
	3-Iodocarbazole	22.81	294 (12), 293 [M] ⁺ (100), 167(4), 166(32), 165(6), 164(8), 146 (12), 140 (6), 139 (21), 138 (4), 83 (6), 69 (8)	36.5	
	3,6-Diiodo- carbazole	27.5	420(10), 419 [M] ⁺ (100), 293(4), 292(25), 265(4), 209(15), 165(12), 164(17), 146(10), 139(4), 138(8), 137(6), 83(8), 69 (4), 32 (6)	0.6	
	Product of unidentified structure	23.79	308 (14), 307 [M] ⁺ (100), 181 (8), 180 (50), 179 (12), 178 (15), 153 (8), 152 (13), 151 (7), 90 (19), 89 (8), 77 (9), 76 (11)	0.5	
ICl (1:1.5)	carbazole	18.07	169 (12), 167 [M] ⁺ (100), 166 (21), 140 (8), 139 (10), 83 (10), 82 (2), 71 (3), 70 (4)	28.9	
	1-Iodocarbazole	21.02	294 (12), 293 [M] ⁺ (100), 167 (6), 166 (31), 165 (7), 164 (7), 146 (10), 140 (7), 139 (21), 138 (5), 137 (4), 83 (6), 69 (8)	1.5	
	3-Iodocarbazole	22.81	294 (12), 293 [M] ⁺ (100), 167 (4), 166 (33), 165 (6), 164 (8), 146 (12), 140 (6), 139 (21), 138 (4), 83 (7), 69 (9)	62.7	
	3,6-Diiodo- carbazole	27.49	420 (12), 419 [M] ⁺ (100), 293 (5), 292 (12), 265 (3), 209 (11), 165 (14), 164 (21), 146 (12), 138 (8), 137 (4), 82(6), 69 (3)	6.6	
	Product of unidentified structure	23.80	308 (14), 307 [M] ⁺ (100), 306 (8), 293 (2), 208 (4), 207 (18), 181 (8), 180 (35), 179 (6), 178 (5), 152 (7), 151 (8), 127 (6), 96 (3), 91 (4), 90 (10), 89 (4), 77 (6), 76 (6), 32 (4)	0.3	

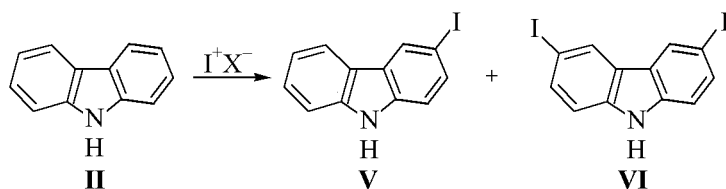
transformed into anthraquinone. On the other hand, anthracene (**I**) proper is not oxidized into quinone **IV** at heating its solutions in acetonitrile in the presence of the double molar excess of CF₃COOAg or tri-

fluoroacetic acid but without iodine monochloride. The above facts are an indirect indication that just 9-iodoanthracene (**III**) is involved into the side transformation into quinone **IV**.

The reaction of solutions prepared from ICl and sodium or lead acetates with anthracene (at the ratio iodinating agent–substrate 1.5:1) proceeds sufficiently fast (20°C, 30 min), but the only product is a mixture of 9- and 9,10-chloroderivatives of anthracene (TLC data). Thus the reagents prepared from ICl and sodium and lead acetates provide virtually the same products as iodine monochloride proper [7]. This is understandable since as shown above the chloride ion

is not completely removed by these salts. However low yield of iodoanthracene **III** in the absence of free ICl (at the use of the system CF₃COOAg–ICl) indicates that the problems in anthracene iodination are due not only to its complexing with ICl or iodine [6–8].

In contrast to anthracene carbazole (**II**) successfully underwent iodination with all three reagents.



At a double excess of CF₃COOAg–ICl reagent in acetonitrile at room temperature within 1 h 3-iodocarbazole (**V**) was obtained in 82% yield, and four-fold excess of the reagent afforded in 98% yield 3,6-diiodocarbazole (**VI**). The obtained yields of compounds **V**, **VI** are significantly higher than at the use of ICl in acetic acid (39 and 19% respectively) [13]. The above yields are also higher than those obtained in iodination of carbazole (**II**) by the following reagents: I₂/NaIO₄/H₂SO₄/EtOH, KI/NaIO₄/H₂SO₄/EtOH, I₂/NaIO₄/AcOH, I₂/NaClO/EtOH, I₂/HgO/EtOH, and N-iodosuccinimide in chloroform, its mixtures with acetic acid, or in THF [14]. The other products of carbazole (**II**) iodination, 1-iodo and 1,6-diiodocarbazoles, were present in trace amounts.

The iodinating reagents based on sodium and lead acetates turned out not only to be less active than the system CF₃COOAg–ICl but also less selective. Therefore the composition of products obtained at room temperature in 1.5 h in a mixture acetonitrile–acetic acid (14 vol%) was determined by GC–MS method (Table 2). There are also given the results of carbazole iodination with iodine monochloride in acetonitrile. It is possible to conclude that the iodinating activity of reagents studied falls in the series CF₃COOAg–ICl > CH₃COONa–ICl > ICl > (CH₃COO)₂Pb–ICl.

It is long known that some iodoarenes in acid media suffer rearrangements, e.g., iodoanilines [15, 16] and iodoresorcinol with HCl [17, 18]. Iodonaphthols with H₂SO₄ [19]. These rearrangements were most thoroughly studied for alkyliodoarenes in sulfuric acid where deiodination was observed with subsequent repeated iodination under the experimental

conditions [20]. It should be borne in mind that this protodeiodination reaction is typical for iodides with a pronounced donor properties of the core, but we have not met studies in this respect concerning heterocyclic compounds.

We showed that iodocarbazol **V** in acetic acid and in the presence of 15-fold molar excess of sulfuric acid at 20°C within 6 h rearranged affording a number of products with 3,6-diiodocarbazole prevailing. By means of GC–MS the following products were identified: carbazole (3.0%), 1-iodocarbazole (9.8%), 3-iodocarbazole (**V**) (22.9%), 3,6-diiodocarbazole (45.5%), 1,6-diiodocarbazole (13.9%), 1,3,6-triiodocarbazole (2.6%). In the absence of sulfuric acid no rearrangement takes place: Even at prolonged (10 h) heating to 80°C in acetic acid iodocarbazole **V** remained unchanged. Thus a considerable amount of 1,6-diiodocarbazole and compound **VI** under conditions of monoiodination with reagents we studied [CH₃COONa–ICl, (CH₃COO)₂Pb–ICl, and ICl] and reagents used in [14] to a large extent originates from protodeiodination reactions.

EXPERIMENTAL

The reaction progress was monitored and products purity was checked by TLC on Sorbfil plates (eluent hexane–ether, 2:1), spots were visualized under UV irradiation. GC–MS measurements were carried out on HP 5972 and HP 5890 instruments (electron impact, 70 eV, quartz capillary column HP 5300×0.25 mm, stationary phase copolymer of 95% of dimethylsiloxane and 5% of diphenylsiloxane, film

0.25 μm thick). UV spectra were recorded on spectrometer Uvicon-943.

Compounds obtained were identified by comparison of analytical and physicochemical characteristics with those of authentic samples prepared by known methods.

Iodine monochloride and silver trifluoroacetate were prepared as in [21, 22].

Spectral and analytical results were obtained in the Analytical Center for General Use of Siberian Division, Russian Academy of Science (grant of the Russian Foundation for Basic Research no. 00-03-40135).

Anthracene iodination with $\text{CF}_3\text{COOAg-ICl}$ reagent. To a solution of iodine monochloride (0.2759 g, 1.7 mmol) in 6.5 ml of acetonitrile was added a solution of silver trifluoroacetate (0.575 g, 2.6 mmol) in 3 ml of acetonitrile. The suspension obtained was stirred for 1 h at 20°C, the precipitate of AgCl was filtered off to obtain a dark-brown solution of iodinating reagent stable for a long time. To a solution of anthracene (0.0768 g, 0.425 mmol) in 33 ml of acetonitrile was added at stirring within 20 min the prepared reagent solution. The reaction mixture was maintained for 1 h at 20°C and then poured into 50 ml of 10% sodium sulfite solution. The reaction products were extracted into chloroform, dried with Na_2SO_4 , the solvent was distilled off to give 0.13 g of a mixture of 9-iodoanthracene and 9,10-anthraquinone. The mixture was separated by column chromatography on silica gel L 40/100, eluent hexane, column 15 \times 1 cm. We obtained 0.22 g (17%) of 9-iodoanthracene (**III**), yellow crystals, mp 80–82°C (82–83°C [5]), and 0.053 g (60%) of 9,10-anthraquinone, yellow crystals, mp 283–286°C (286°C [23]).

3-Iodocarbazole (V). To a solution of carbazole (0.0724 g, 0.434 mmol) in 10 ml of acetonitrile within 25 min was added at stirring 4.9 ml of iodinating reagent prepared as described under the previous experiment. The reaction mixture was maintained for 1.5 h at 20°C and then poured into 50 ml of 10% sodium sulfite solution, the separated precipitate was filtered off, washed with 10% sodium carbonate solution, and dried. We obtained 0.104 g (82%) of compound **V**, colorless crystals, mp 193–195°C (from AcOH); 195–196°C (from hexane) [14].

3,6-Diiodocarbazole (VI). To a solution of carbazole (0.081 g, 0.48 mmol) in 15 ml of acetonitrile within 30 min was added at stirring 10.6 ml of

iodinating reagent prepared as described above. The reaction mixture was maintained for 1.5 h at 20°C and then poured into 50 ml of 10% sodium sulfite solution, the separated precipitate was filtered off, washed with 10% sodium carbonate solution, and dried. We obtained 0.197 g (98%) of compound **VI**, colorless crystals, mp 199–200°C (from AcOH); 204–205°C (from hexane) [14].

Protodeiodination of 3-iodocarbazole (V). A solution of 3-iodocarbazole (0.293 g, 1 mmol) in 10 ml of acetic acid and 0.44 ml (15 mmol) of 96% sulfuric acid was stirred for 6 h at 20°C. Then the reaction mixture was poured into 50 ml of 10% sodium sulfite solution, the solid precipitate was filtered off, washed with 10% sodium carbonate solution till neutral washings, and dried. The obtained solid according to GC-MS data was a mixture of carbazole (3.0%), 1-iodocarbazole (9.8%), 3-iodocarbazole (**V**) (22.9%), 3,6-diiodocarbazole (45.5%), 1,6-diiodocarbazole (13.9%), 1,3,6-triiodocarbazole (2.6%).

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