Synthesis and Isolation of Iodocarbazoles. Direct Iodination of Carbazoles by *N*-Iodosuccinimide and *N*-Iodosuccinimide-silica Gel System.

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Carbazole (**1**) undergoes electrophilic aromatic substitution with various iodinating reagents. Although, 3-iodocarbazole (**1b**) and 3,6-diiodocarbazole (**1d**) obtained by iodination of carbazole were isolated and characterized sometime ago, 1-iodocarbazole (**1a**), 1,6-diiodocarbazole (**1c**) and 1,3,6-triiodocarbazole (**1e**) had never been isolated from the reaction mixture. The preparation and subsequent isolation and characterization of **1a**, **1b**, **1c**, **1d** and **1e** are reported (mp, t_r, R_f, ^{1}H-nmr, ^{13}C-nmr and ms). As iodinating reagents, $NaIO_4/I_2$ and $NaIO_4$/KI mixtures in (i) ethanol doped with catalytical amount of sulfuric acid and in (ii) acetic acid, and *N*-iodosuccinimide and *N*-iodosuccinimide-silica gel in dichloromethane and in chloroform have been used and their uses have been compared. The iodination reaction of different carbazole derivatives such as 2-acetoxycarbazole (**2**), 3-bromocarbazole (**3**) and 3-nitrocarbazole (**4**) was also studied and the corresponding iododerivatives, **2a**, **2b**, **2c**, **3a**, **3b**, **4a** and **4b**, are described for the first time. Semiempirical PM3 calculations have been performed in order to predict reactivity of carbazole (**1**), substituted carbazoles (**2-4**) and iodocarbazoles (**1a**-**1e**, **2a**-**2c**, **3a**-**3b**, **4a** and **4b**) (Scheme 1). Theoretical and experimental results are discussed briefly.

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In our previous publication [1] we described the synthesis of six chloroderivatives of carbazole and several new chloroderivatives of 2-acetoxy-, 2-hydroxy-, 3-bromo- and 3-nitrocarbazole. As we are interested in the study of the photochemistry of azacarbazoles [2-8], carbazoles [9,10] and *N*-acyl- and *N*-alkylcarbazoles [11-13] and specially in the photoinduced electron transfer processes in which they can be involved, we decided to go on with the study of the photophysical properties of the iodide derivatives of several C-substituted carbazoles. Thus, to begin with we now report the synthesis and characterization of several C-substituted iodocarbazoles prepared by direct iodination of carbazole (**1**) and for the first time, of 2-acetoxy- (**2**), 3-bromo- (**3**) and 3-nitrocarbazole (**4**) (Scheme 1, compounds: **2a**, **2b**, **2c**, **3a**, **3b**, **4a**, **4b**).

It is well known that polymers containing the pendant carbazolyl chromphore are good electron donors and possess outstanding electrical and photoelectrical properties [14-16]. The presence of iodine in the polymer structure is desired because it modifies their physical properties [17] but owing to the so called "heavy atom effect" [18] iodine can modify the photophysical and as a consequence the photoelectrical properties of the polymer. Thus it is of use to study first the photochemistry of the iodocarbazole moieties synthesized.

In contrast to chlorination or bromination, the iodination of aromatic compounds is a mild reaction and generally requires some activating catalyst. The main method for the synthesis of most aryliodides up to the 1950's was a multistep synthesis based on the Sandmayer reaction, but this route is often complicated by various side reactions, the principle ones being substitution of the diazo group by hydrogen and formation of azo compounds. However, studies during the last 20 years has led to the discovery of new simple methods, which have made aryliodides quite easily with available reagents [19]. One of these simple methods concern the direct iodination of aromatic compounds (benzenic and polynucleararomatic rings) with a mixture of catalytic amounts of acetic acid or sulfuric acid and sodium periodate and iodine ($NaIO_4/I_2$) at 70 - 100°. Other iodinating methods use peracetic acid, hydrogen peroxide (H_2O_2) and potassium permanganate ($KMnO_4$) as oxidizing agents to oxidize the molecular iodine in acetic acid or trifluoroacetic acid at room temperature or by warming the system at 50°. Heavy metal ions such as Ag^+, Cu(II), Pb(IV) or Sb(V) are also used as oxidizing agents and no acid catalyst is required. Other iodinating agents are the combination of iodide alkaline salts with Co(III), Mn(III) and Ce(IV) in the presence of 90% trifluoroacetic acid; these have been successfully used with benzenic rings substituted with electron donating groups.

These methods give moderated-to-high yield of *para*-substituted iodinated products and in all cases the presence of organic or mineral acid is required as catalyst to activate the oxidation of the iodine towards the iodinating agent (I^+). The presence of an acid catalyst in the iodinating reagent causes this method to fail as a general method because aromatic compounds with acid labile substituent groups such as ester, acetoxy, benzoyloxy and amide, are easily hydrolized. Also, amines become protonated forming a cation that is not reactive towards the iodinating agent. In order to develope a method which does not require acid as catalyst we took recourse to *N*-iodosuccinimide and *N*-iodosuccinimide - silica gel as a convenient new and mild reagent systems for the high yield iodination

Table I

Iodination of Carbazole by Using Different Methods
Products (% yield) [a]

Experiment	Method [b]	Carbazole:Iodo (molar ratio) [c]	Time (minutes)	Conversion (%)	Temperature (°C)	**1a**	**1b**	**1c**	**1d**	**1e**
a	(i)	1:1	60	90	65	5	75	0.5	8	-
b	(i)	1:2	60	100	65	-	14	13	67	-
c	(i)	1:3	80	100	65	-	-	-	25	75
d	(i)	1:4	85	100	65	-	-	-	10	90
e	(i)	2:1	120	56	22	10	42	-	4	-
f	(i)	2:1	85	72	40	6	55	0.5	10	-
g	(i)	1:1	110	83	22	5	65	1	12	-
h	(i)	1:1	70	90	40	5	70	5	10	-
i	(i)	2:3	75	100	22	-	33	10	47	-
j	(i)	2:3	65	100	40	-	29	15	54	-
k	(ii)	1:1	120	85	65	11	59	2	12	-
l	(ii)	2:3	80	100	65	15	30	15	28	-
m	(ii)	1:2	73	100	65	-	14	15	72	-
n	(iii)	2:1	120	77	65	25	52	-	-	-
o	(iii)	1:1	120	90	65	22	56	-	19	-
p	(iii)	1:2	20	100	65	-	-	36	61	-
q	(iv)	1:1	60	85	65	25	50	1	8	-
r	(v)	1:1	180	100	25	0.5	1	26	62	-
s	(v)	1:2	180	100	25	-	-	10	35	52
t	(vi)	1:1	200	50	25	1	44	-	-	-

[a] Quantitative gc (HP-17) analysis. [b] Methods: (i) $NaIO_4/I_2/H_2SO_4$ (cat)/EtOH; (ii) $NaIO_4/KI/H_2SO_4$ (cat)/EtOH; (iii) $NaIO_4/I_2$/AcOH; (iv) $NaIO_4$/KI/AcOH; (v) NaClO/I_2/EtOH; (vi) HgO/I_2/EtOH. [c] Carbazole to iodo molar ratio.

of carbazoles to prepare mono-, di- and poly-iodinated products depending on the stoichiometry ratio used. According to our knowledge, potassium periodate and potassium iodide (KIO_3/KI) in glacial acetic acid reagent was used for the synthesis of 3-iodocarbazole (**1b**) and 3,6-diodocarbazole (**1d**) which were only characterized by melting point and spectroscopic methods (^{1}H-nmr and ir) but no spectroscopical data were published [20,22]; in this paper only the yield of the former is reported (34-41%). In 1978 Pielichowski described 3-iodocarbazole (**1b**) and 3,6-diodocarbazole (**1d**) obtained by reaction of iodo-9-vinylcarbazole with methyl alcohol in the presence of iron (III) nitrate nonahydrate ($Fe(III)(NO_3)_3.9H_2O$); mp, ms (only m/z for molecualar ions) and ^{1}H nmr (**1b**: 10.50 (s, 1H), 8.30-7.00 (m, 7H); **1d**: 10.50 (s, 1H), 8.30-7.20 (m, 6H)) data are provided [23]. Recently, Shukla [24] reported the synthesis of 3-iodocarbazole (**1b**) by using a mixture of KIO_3/KI (molar ratio 1:1) in glacial acetic acid at 50°. After recrystallization of the faintly brown residue from ethanol, 3-iodocarbazole (compound **1b**) was obtained in 44.3% yield; this compound was characterized by melting point, elemental analysis, ir and ^{1}H-nmr. It is interesting to point out that in this paper the authors have not correctly assigned the hydrogen chemical shifts of the 3-iodocarbazole moiety. Specifically, attention must be taken into account with the missassignment of the 5-H and N-H chemical shift. As far as we know the direct iodination of 2-acetoxycarbazole (**2**), 3-bromocarbazole (**3**) and 3-nitrocarbazole (**4**) has not been described. Furthermore, the corresponding iododerivatives of these carbazoles have not been previously described, as well as the iodocarbazoles **1a**, **1c** and **1e**.

This study reports the preparation of iodo derivatives from carbazoles (Scheme 1, carbazole (**1**), 2-acetoxycarbazole (**2**), 3-bromocarbazole (**3**) and 3-nitrocarbazole (**4**)) using different iodinating reagents providing for the first time iodocarbazoles **1a**, **1c**, **1e**, **2a**, **2b**, **2c**, **3a**, **3b**, **4a** and **4b** (Scheme 1). We also describe the use of several chromatographic methods (tlc, hplc and column chromatography) in order to (i) follow the iodination reaction, (ii) determine the yields of the reactions and (iii) isolate for complete characterization (elemental analysis, R_f, t_R, mp, uv, ^{1}H-nmr, ^{13}C-nmr and ms) of the iododerivatives obtained.

Additionally, computational chemistry has been used to calculate the atomic charge density values. Those for the more relevant atoms are collected in Table VI and they are of use to discuss the reactivity of carbazoles **1**-**4**.

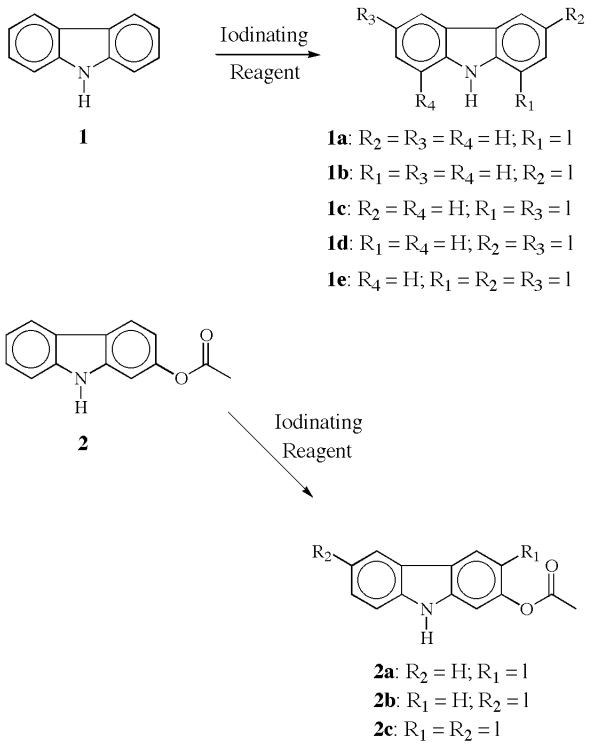
Results and discussion.

Iodination of Carbazole (**1**).

(a) Iodinating Reagents with Acid Catalysis.

In order to prepare iodocarbazoles we decided to use first the clasical method, a mixture of $NaIO_4$ and I_2 in the presence of catalytical amounts of mineral acid (concentrated sulfuric acid) in ethanol at 65° [20] to obtain **1a**, **1b**,

Scheme 1



1c, **1d** and **1e** whose relative yields depend on the stoichiometry used (see Table I, entries a-d). Thus, when the iodinating agent to carbazole molar ratio is 1:1, 3-iodocarbazole (**1b**) and 3,6-diiodocarbazole (**1d**) are formed in 75% and 8% yield, respectively. Also in the reaction mixture 1-iodocarbazole (**1a**) and 1,6-diiodocarbazole (**1c**) are detected as the minor products. In our hands, this reaction provides a product distribution which is quite different than that previously reported [20]. This author only describes the isolation and characterization of 3-iodocarbazole (**1b**). Taking into account the results mentioned above we decided to carry out the reaction in the presence of two, three and four equivalents of iodinating agent.

When two equivalents of iodinating agent were used (1:2 molar ratio), 3,6-diiodocarbazole (**1d**) was obtained as the main product, also compounds **1b** and **1c** were formed in a significant amount (see Table I, entry b). Production of 1,3,6-triiodocarbazole (**1e**) was fairly clean when four equivalent of iodinating agent were used, while when three equivalents were used a mixture of 3,6-diiodocarbazole and 1,3,6-triiodocarbazole was formed, being the latter the major product obtained (see Table I, entries d and c, respectively). No 1,3,6,8-tetraiodocarbazole was formed when an excess of iodinating agent (six equivalents) was used (results not shown).

In order to improve some selectivity in the mono-iodination of carbazole, we carried out the iodination reaction at different temperatures and varied simultaneously the amount of iodinating agent. Comparatively, we carried out the reaction at three different temperatures, *i.e.*, 22, 40 and 65° and at each temperature we have used a molecular carbazole to iodine molar ratio equal to: 2:1, 1:1 and 2:3, respectively. In all the cases an excess of $NaIO_4$ was used. The results obtained are shown in Table I. As can be seen in this table, at a given temperature polyiodination occurs as the iodine to carbazole molar ratio is increased (Table I, entries a-d, e-j). Instead, monoiodination was preferentially obtained when the carbazole to iodine molar ratio is 1:2 and the temperature is lowered, for example 22°

Table II

Iodination of Carbazole by Using *N*-Iodosuccinimide (NIS)
Products (% yield) [a]

Experiment	Solvent	Carbazole:NIS (molar ratio) [b]	Time (minutes)	Conversion (%)	Temperature (°C)	**1a**	**1b**	**1c**	**1d**	**1e**
a	$CHCl_3$	1:1	120	85	25	6	64	1	10	-
b	$CHCl_3$	1:2	120	100	25	-	-	15	70	-
c	$CHCl_3$	1:3	120	100	25	-	-	-	22	77
d	THF	1:4	120	80	25	5	60	1	8	-
e	$CHCl_3$/AcOH (3:1)	2:1	60	84	25	22	57	2	3	-
f	$CHCl_3/SiO_2$	1:1	120	70	25	4	60	0.5	6	-
g	$CHCl_3/SiO_2$	1:2	120	81	25	-	-	10	65	-
h	$CHCl_3$	1:1	120	60	-18	1.3	47	0.5	8	-
i	$CHCl_3$/AcOH (3:1)	1:2	120	100	25	-	-	35	65	-

[a] Quantitative gc (HP-17) analysis. [b] Carbazole to NIS molar ratio.

Table III

Iodination of C-Substituted Carbazoles by Using *N*-Iodosuccinimide (NIS)
Products (% yield) [a]

Experiment	Solvent	Carbazole:NIS (molar ratio) [b]	Time (minutes)	Conversion (%)	Temperature (°C)			
2-Acetoxycarbazole (**2**)								
						2a	**2b**	**2c**
a	$CHCl_3$	1:1	30	71	25	39	28	5
b	$CHCl_3$	1:2	20	92	25	10	15	67
3-Bromocarbazole (**3**)								
						3a	**3b**	
c	$CHCl_3$	1:1	75	66	25	-	65	
d	AcOH	1:1	80	70	25	12	57	
e	$CHCl_3/SiO_2$	1:1	120	62	25	-	60	
3-Nitrocarbazole (**4**)								
						4a	**4b**	
f	$CHCl_3$/EtOH (3:1)	1:1	120	92	25	-	92	
g	$CHCl_3/SiO_2$/EtOH	1:1	160	90	25	-	90	
h	AcOH	1:1	120	95	25	15	80	

[a] Quantitative gc (HP-17) analysis. [b] C-Substituted carbazole to NIS molar ratio.

(see Table I, entries e-f). These results led us to conclude that carbazole monoiodination can be obtained at low temperature in an easily and clean way, without the having to raise the reaction temperature as was previously reported [20,22].

To shed some light on the reaction mechanism and to understand what is the iodinating agent, we carried out some additional experiments. It is known that a mixture of $NaIO_4$ and KI in acidic media produces the equivalent amount of hypoiodous acid which was suggested to be the possible iodinating agent (Table I, method (ii)). We carried out the iodination reaction of carbazole in the presence of $NaIO_4$, KI and sulfuric acid (catalytic amount) in ethanol at 70°. Under these experimental conditions, compounds **1a-1d** were obtained, where **1a, 1b** and **1d** are the main products formed (see Table I, entry k). The product distribution as well as the product yields are similar to those obtained when the iodinating mixture used was $NaIO_4$, I_2 and sulfuric acid. Thus, 3-iodocarbazole and 3,6-diiodocarbazole were the main products and compounds **1a** and **1c** were also detected in the reaction medium when a reagents molar ratio 3:2 was employed (see Table I, entry l) when two equivalents of iodinating agent was used 3,6-diiodocarbazole (**1d**) is formed as the main product together with significant amount of compounds **1b** and **1c**.

Also, we have performed the iodination reaction of carbazole by using hypoiodous acid as a direct iodinating agent (Table I, methods (v) and (vi)). This reagent was synthetised *in situ* by two different methods, according to literature procedures [25,26]. One of these methods uses mercury (II) oxide as the oxidizing agent and is added to an ethanolic solution of carbazole and iodine. The other method uses aqueous sodium hypochlorite solution as the oxidizing agent which is added dropwise to a solution of carbazole and iodine in chloroform.

When mercury (II) oxide was used the main product obtained is 3-iodocarbazole (**1b,** Table I entry t), while when sodium hypochlorite was used the main product is **1d** and 1-iodocarbazole (**1a**), 3-iodocarbazole (**1b**) and 1,6-diiodocarbazole (**1c**) were also detected (Table I, entry r). By using an excess of the latter oxidizing agent, the iodination reaction gives a mixture of the di and triiodocarbazoles **1c**, **1d** and **1e** (see Table I, entry s).

Thus, these results suggest that hypoiodous acid, generated *in situ*, is the iodinating agent. Furthermore, we also conclude that when the mixtures of $NaIO_4/I_2$ or $NaIO_4$/KI are used as the iodinating agent (Table I, methods (i) and (ii)), the hypoiodous acid is the reactive species which react with the carbazole to give the iodocarbazole derivatives. However, as was pointed out in the literature [26], there may be other iodinating species derived from hypoiodous acid such as H_2IO^+, I_2O or I^+, which are indistinguishable at the present. Additionally, the former iodinating species (H_2IO^+) may be operative when the iodination reaction of carbazole is carried out with mixtures such as $NaIO_4/I_2$ or $NaIO_4$/KI in the presence of catalytic amounts of concentrated sulfuric acid (H_o = -1.87).

When acetic acid is used both as solvent and acid catalyst in the iodination reaction ($NaIO_4/I_2$ or $NaIO_4$/KI, Table I, methods (iii) and (iv)) instead of sulfuric acid, a significant change in the chemical yield and product distribution is observed. By using one equivalent of the

Table IV
Iodination of 3-Bomocarbazole (**3**) by Using Different Methods
Products (% yield) [a]

Experiment	Method [b]	Solvent	Carbazole:Iodo (molar ratio)	Time (minutes)	Conversion (%)	Temperature (°C)	**3a**	**3b**
a	(i)	EtOH	1:1[c]	180	90	70	-	89
b	(i)	AcOH	1:1[c]	180	95	70	10	85
c	(ii)	$CHCl_3$	1:1[d]	75	66	25	-	65
d	(ii)	AcOH	1:1[d]	80	70	25	12	57
e	(ii)	$CHCl_3/SiO_2$	1:1[d]	120	62	25	-	60

[a] Quantitative gc (HP-17) analysis. [b] Methods: (i) $NaIO_4/I_2/H_2SO_4$ (cat)/EtOH; (ii) NIS. [c] Carbazole to iodo molar ratio. [d] Carbazole to NIS molar ratio.

iodinating agent in acetic acid, monoiodination occurs preferentially and 1-iodocarbazole (**1a**) and 3-iodocarbazole (**1b**) are obtained as main products (Table I, compare entries a, o and q). Also, in these experiments 3,6-diiodocarbazole was formed.

It is necessary to take into account that in the presence of acetic acid one possible attacking agent present in the reaction mixture is the acetylhypoiodite (CH_3COOI) yielded according to the equilibrium:

$$CH_3COOH + HIO \longrightarrow CH_3COOI + H_2O \quad (1)$$

Although, there seems to be no decisive evidence to distinguish between hypoiodous acid and acetylhypoiodite, the tendency to give an electrophilic agent should be greater in the latter because of the stability of the acetate ion as compared with the hydroxide ion. Hence, CH_3COOI is more probable than HIO when acetic acid is used as solvent. It is noteworthy to mention that in acetic acid the reaction is slower than in ethanol-sulfuric acid mixture, and a shift to a red solution color was observed while only monoiodination occurs.

Taking into account the results discussed above, there is no evidence of the formation of *N*-iodocarbazole as a reaction intermediate. Furthermore, if an intermediate like a *N*-halocarbazole is formed during the iodination reaction, it would be easily identified by tlc. However, in our experimental conditions this kind of intermediate was not detected. Also, the product distribution observed during the iodination reaction of carbazole does not resemble what we observed when the chlorination reaction of carbazole was carried out with sodium hypochlorite (or *N*-chlorobenzotriazole) where a reaction intermediate like a *N*-halocarbazole was proposed [1,27].

(b) *N*-Iodosuccinimide Iodinating Regent.

(b-1) Neutral Conditions.

Taking into account that the iodinating agents presented above are of use for reactions with organic compounds stable in acidic media, we decided to study the use of *N*-iodosuccinimide and *N*-iodosuccinimide - silica gel systems as general reagents for the iodination of carbazoles.

Thus, carbazole in chloroform with *N*-iodosuccinimide (1:1 molar ratio) was treated in the absence and in the presence of silica gel, at room temperature, and the yields of the products were determined by hplc (Table II, entries a and f). Simultaneously, similar experiments were run using carbazole to *N*-iodosuccinimide in molar ratio 1:2 in the presence and in the absence of silica gel, at room temperature (see Table II, entries b and g). The reactions were monitored (hplc) every five minutes to obtain additional information about the rates of formation of iodocarbazole derivatives. As can be seen in Table II (entries a and f) this reaction provided a simple synthesis of 3-iodocarbazole (**1b**) (reagents molar ratio 1:1) together with significant amount of 1-iodocarbazole (**1a**) and 3,6-diiodocarbazole (**1d**). Similar product distributions were observed when the reaction was performed in THF (see Table II, entry d). Production of 3,6-diiodocarbazole (**1d**) was fairly clean when two equivalent of *N*-iodosuccinimide were used but a significant amount of **1c** was also obtained (see Table II, entries b and g). When the iodination reaction of carbazole was carried out at -18° using one equivalent of NIS no improvement of the product yield was observed. Thus, 3-iodocarbazole (**1b**) was formed in 47% as the main product together with **1a**, **1c** and **1d** (see table II, entry h).

The results obtained when the iodination reactions of carbazole were carried out in the presence of silica gel (see Table II, enties f and g) show that a considerable lowering of the product yields occurs even when three or four equivalents of NIS were used. In this experimental condition a noticeable decomposition of the iodinating agent was observed; as a consequence, polyiodination of carbazole is not possible by using this method.

(b-2) Acid Conditions.

It is noteworthy to mention that when the iodination reaction of carbazole is carried out in chloroform doped with glacial acetic acid or directly in glacial acetic acid the product distribution is quite different. When one equivalent of *N*-iodosuccinimide was used monoiodination occurs. Thus, 1-iodocarbazole (**1a**) and 3-iodocarbazole (**1b**) were obtained as the main products and a noticeable increase in the 1-iodocarbazole chemical yield was

Table V

Iodination of 3-Nitrocarbazole (**4**) by Using Different Methods
Products (% yield) [a]

Experiment	Method [b]	Solvent	Carbazole:Iodo (molar ratio)	Time (minutes)	Conversion (%)	Temperature (°C)	**4a**	**4b**
a	(i)	EtOH	1:1[c]	200	90	70	2	89
b	(i)	AcOH	1:1[c]	240	85	70	10	74
c	(ii)	$CHCl_3$/EtOH (3:1)	1:1[d]	120	92	25	-	92
d	(ii)	$CHCl_3$/EtOH (3:1)	1:1[d]	160	90	25	-	90
e	(ii)	AcOH	1:1[d]	120	95	25	15	80

[a] Quantitative gc (HP-17) analysis. [b] Methods: (i) $NaIO_4/I_2/H_2SO_4$ (cat)/EtOH; (ii) NIS. [c] Carbazole to iodo molar ratio. [d] Carbazole to NIS molar ratio.

observed (see Table II, entry e). When carbazole (**1**) was treated with two equivalents of *N*-iodosuccinimide diiodination occurs and **1c** and **1d** were formed (see Table II, entry i). Also, under this experimental condition, an increase in the 1,6-diiodocarbazole yield was observed.

Probably, under this acidic conditions, particularly using acetic acid, the iodinating agent would be the acetylhypoiodite [26] according to the following equation:

$$CH_3COOH + NIS \longrightarrow CH_3COOI + NHS \quad (2)$$

We arrived to this conclusion taking into account that the product distribution obtained under this experimental condition is similar to the results obtained when $NaIO_4/I_2$ or $NaIO_4$/KI systems were used in glacial acetic acid. Although, the iodination reaction of carbazole (**1**) performed using the latter systems showed a slightly lower yield of formation of 1-iodocarbazole (**1a**).

Iodination of Substituted Carbazoles **2**-**4**.

In order to shed some light on the mechanism of iodination reaction of carbazole we decided to apply some iodination reagents to substituted carbazoles whose reactivity was modified by the introduction of different substituents in one of the benzene rings of the carbazole moiety. The compounds selected for this study were 2-acetoxycarbazole (**2**), 3-bromocarbazole (**3**) and 3-nitrocarbazole (**4**) (see Scheme 1).

Iodination of 2-Acetoxycarbazole (**2**).

When 2-acetoxycarbazole (**2**) reacted with the iodinating agent (NIS) in a molar ratio 1:1 at room temperature, two main products were obtained: 3-iodo-2-acetoxycarbazole (**2a**) and 6-iodo-2-acetoxycarbazole (**2b**), together with 3,6-diiodo-2-acetoxycarbazole (**2c**) (Table III). Production of 3,6-diiodo-2-acetoxycarbazole (**2c**) was fairly clean when two equivalents of NIS were used. Also, compounds **2a** and **2b** were detected in the reaction mixture.

Iodination of 3-Bromocarbazole (**3**).

The iodination reaction of 3-bromocarbazole (**3**) was carried out with one equivalent of a mixture of $NaIO_4/I_2$ in ethanol at 70° during 180 minutes. This reaction was selective and 3-bromo-6-iodocarbazole (**3b**) was obtained as the only product. Lowering the iodination reaction temperature a longer period of reaction time was required and the reaction did not go to completion even after 300 minutes.

When the iodination reaction of **3** with a mixture of $NaIO_4/I_2$ in glacial acetic acid was carried out at 70°, the reaction mixture was quite different. Thus, compound **3a** was obtained in significant amount together with compound **3b**, the latter being the main product obtained (see Table IV). As previously discussed, the use of glacial acetic acid in the presence of the iodinating mixture (for example $NaIO_4/I_2$) would provide as iodinating reagent the acetylhypoiodite species (equation 2), which is responsible for causing iodination to favor the *ortho* positions in the carbazole moiety.

We also studied the iodination reaction of 3-bromocarbazole (**3**) with one equivalent of *N*-iodosuccinimide in chloroform and in glacial acetic acid at room temperature (Table III). When the iodination reaction was carried out in chloroform with one equivalent of NIS, 6-iodo-3-bromocarbazole (**3b**) was formed in 65% yield. Addition of silicagel to the reaction mixture does not improve the formation of compound **3b**, requiring a longer period of time in order to react (see Table III, entries c and e). Again, this reaction is selective for the formation of 6-iodo-3-bromocarbazole, which is obtained as the only product. When the same reaction was carried out in glacial acetic acid at room temperature, a significant change in the product distribution was observed. Thus, 1-iodo-3-bromocarbazole (**3a**) was formed in a significant amount together with compound **3b**, the latter being the main product formed.

Iodination of 3-Nitrocarbazole (**4**).

We also studied the iodination reaction of 3-nitrocarbazole (**4**) by using one and two equivalent of iodinating agent ($NaIO_4/I_2$) in the presence of catalytic amounts

Table VI

Static Charge Distribution for Carbazole (**1**), 2-Acetoxycarbazole (**2**), 3-Bromocarbazole (**3**) and 3-Nitrocarbazole (**4**) [a]

	Atom number								
	1-C	2-C	3-C	4-C	5-C	6-C	7-C	8-C	9 (NH)
Compounds									
1	-0.107	-0.082	-0.126	-0.049					+0.194
1a	-0.140	-0.061	-0.124	-0.045	-0.047	-0.126	-0.079	-0.107	+0.219
1b	-0.103	-0.060	-0.151	-0.026	-0.046	-0.125	-0.079	-0.107	+0.199
1c	-0.142	-0.058	-0.123	-0.042	-0.023	-0.152	-0.058	-0.103	+0.224
1d	-0.102	-0.058	-0.152	-0.023					+0.204
1e	-0.146	-0.034	-0.158	-0.018	-0.021	-0.154	-0.055	-0.102	+0.228
2	-0.120	+0.060	-0.151	-0.033	-0.048	-0.123	-0.079	-0.105	+0.200
2a	-0.189	+0.107	-0.191	-0.015	-0.049	-0.123	-0.079	-0.104	+0.220
2b	-0.153	+0.099	-0.192	-0.007	-0.047	-0.121	-0.078	-0.104	+0.196
2c	-0.153	+0.102	-0.194	-0.003	-0.024	-0.152	-0.057	-0.100	+0.201
3	-0.102	-0.064	-0.131	-0.029	-0.046	-0.125	-0.078	-0.107	+0.200
3b	-0.101	-0.062	-0.132	-0.026	-0.022	-0.153	-0.057	-0.102	+0.205
4	-0.137	+0.010	-0.447	+0.056	-0.045	-0.116	-0.076	-0.101	+0.222
4a	-0.136	+0.011	-0.445	+0.058	-0.021	-0.153	-0.054	-0.097	+0.226

[a] Calculations were performed using PM3 method [28].

of concentrated sulfuric acid and glacial acetic acid, respectively. In both experiments 6-iodo-3-nitrocarbazole (**4b**) was obtained as the main product in 89% yield (see Table V, entries a and b). Also, 8-iodo-3-nitrocarbazole (**4a**) was obtained in *ca*. 2% when sulfuric acid was used. When the iodination reaction was carried out in the presence of glacial acetic acid the production of **4a** was improved. Nevertheless, the chemical yield of **4a** was not high even working in the presence of acetic acid (see Table V). It is noteworthy to mention that the iodination reaction of **4** with the system $NaIO_4/I_2$ or $NaIO_4$/KI require an increase in both the reaction temperature and reaction time. This particular behavior, shown by **4** in comparison with other substituted carbazoles and carbazole itself, may be rationalized by taking into account its lower reactivity towards the iodinating agent because of the presence of a withdrawing substituent in the carbazole moiety.

The iodination reaction of **4** with *N*-iodosuccinimide were carried out with a mixture of chloroform-ethanol (3:1) owing to the low solubility of **4** in neat chloroform. When 3-nitrocarbazole (**4**) was reacted with *N*-iodosuccinimide (molar ratio 1:1) at room temperature, 6-iodo-3-nitrocarbazole (**4b**) was formed as the only product. The iodination reaction of **4** with *N*-iodosuccinimide was also performed in the presence of silica gel. Again, under our experimental conditions, the presence of silica gel in the reaction medium was not beneficial due to a lowering of the product chemical yields and the long period of reaction time required (see Table III).

Also, the product distribution changed significantly in the iodination reaction of **4** with *N*-iodosuccinimide (molar ratio 1:1) in glacial acetic acid at room temperature. Thus, compund **4b** was again the main product and the formation of 8-iodo-3-nitrocarbazole (**4a**) has been improved to a 15% of yield (Table III). As was pointed out before, the change in product distribution observed when glacial acetic acid was used, could be explained by the formation of the acetylhypoiodite. Similar results were obtained when $NaIO_4/I_2$ or $NaIO_4$/KI in acetic acid were used (Table V).

Semiempirical calculations

As known, the high reactivity of the aromatic ring of carbazole in electrophilic substitution makes it highly probable that these reactions reflect the proven I^+ activity of the different iodinating systems. Also, the experimental results obtained in the iodination reaction of carbazoles show a preferential substitution pattern which is the 3-C and/or 6-C *para*-substitution in the carbazole moiety. A further piece of evidence in favor of the above statement was provided by the net atomic charge values calculated by using the semiempirical PM3 method, as implemented in the version of the HyperChem 5.1 program [28] to obtain the optimized geometry of carbazoles **1**-**4** and iodocarbazoles. The charge distributions are frequently used for interpreting and predicting chemical reactivity, and that the static charge distribution should indicate sites of kinetic attack by incoming reagents.

The static charge distribution of carbazoles and iodocarbazole derivatives are collected in Table VI. As can be seen in this Table, the static charge values pattern of carbazole and carbazole derivatives show the preferential electrophilic substituition postions which are in agrement with the experimental results obtained.

It is interesting to mention that, even though the highest negative charge density values are localized at 1-C, 3-C and also at 6-C, 8-C, the experimental results obtained show a dramatically *para*-substitution pattern on the

carbazole moiety. These results can be explained by taking into account the large volume of the iodine cation which makes it difficult for the iodine cation to approach the *ortho*-position of the carbazole moiety. In conclusion, it seems certain that electrophilic attack of carbazole under a wide variety of conditions occurs preferentially at the carbon atoms with charge values higher than -0.095.

To gain further insight into the mechanism of the above processes a series of experiments on different carbazole derivatives are in progress in our laboratory.

EXPERIMENTAL

Thin layer chromatography (tlc) analysis was performed with aluminium silica gel sheets (0.2 layer thickness, silica-gel 60 F254). Gas chromatography (gc) analysis was conducted with a HP-17 column (Crosslinked 50% Phenyl Methyl Silicone; 10m x 0.53mm x 2.0 μm film; Magabor column) and an Ultra 2 column (Crosslinked 5% Phenyl Silicone; 25 m x 0.2 mm x 0.33 μm; Capillary column). Mass spectra (ms) were obtained under electron impact (70 eV). The ratios m/z and the relative intensities are reported. Gas chromatography-mass spectrometry (gc-ms) analysis was conducted with the Ultra 2 column. Products were isolated by preparative thick layer chromatography and column chromatography which was carried out using silica gel 200-400 mesh 60A and hexane and hexane-ethyl acetate as eluent. Melting points are uncorrected. ^{1}H- and ^{13}C-nmr spectra were run in dimethylsulfoxide-d_6 at 200 MHz. Chemical shifts are reported in ppm values, using tetramethylsilane as internal standard. ^{13}C-nmr resonance assignments were made using DEPT experiment.

Dichloromethane, chloroform, acetic acid, ethanol, hexane, ethyl acetate and other reagents used were analytical grade. Solvents were freshly distilled and dried before using. Carbazole and *N*-iodosuccinimide were purchased from Aldrich. 2-Hydroxycarbazole was purchased from Aldrich and was recrystallized from ethanol before it was used. 2-Acetoxycarbazole [29], 3-bromocarbazole [30] and 3-nitrocarbazole [10] were prepared according to procedures described in the literature.

Iodination Reaction of Carbazole (**1**) with Sodium Periodate/-Iodine/Catalytic Acid and Sodium Periodate/Potassium Iodide/Catalytic Acid Systems.

To a stirred solution of carbazole (**1**) (100 mg, 0.60 mmol) in ethanol (20 ml) solid sodium periodate (0.15 to 0.60 mmol depending on the stoichiometry used) and molecular iodine previously ground (0.30 to 0.90 mmol depending on the stoichiometry used) were added. Then concentrated sulfuric acid (42 μl to 1.68 ml depending on the stoichiometry used, δ: 1.85 g/ml) was added gently. The reaction was stirred for an appropriate time in the absence of light at controlled temperature (0°, 25°, 40° and 70°) until the tlc and gc indicated that the reaction was completed. All of these reaction were carried out under normal (air) atmosphere. The reaction mixture was neutralized with sodium hydroxide, extracted with dichloromethane (3 x 15 ml) and washed with water (3 x 20 ml). The combined extracts were dried over sodium sulfate, filtered off and evaporated *in vacuo* to give a brownish solid residue. The residue was separated by column chromatography (silica gel-hexane-ethyl acetate mixtures) to give (**1a)**, (**1b)**, (**1c**), (**1d**) and (**1e**). According to the experimental conditions used the percentage yield of the products obtained are different as can be seen in Table I. This set of reactions were also performed with $NaIO_4$/KI/sulfuric acid system according to the procedure described above. In these cases solid sodium periodate (0.15 to 0.90 mmol depending on the stoichiometry used) and solid potassium iodide (0.15 to 0.60 mmol depending on the stoichiometry used) were added to an ethanolic solution of carbazole (100 mg, 0.60 mmol). Then concentrated sulfuric acid (42 μl to 1.68 ml depending on the stoichiometry used, δ: 1.85 gr/ml) was added gently.

This set of reactions were also performed in glacial acetic acid which works as solvent and acid catalysis simultaneously.

1-Iodocarbazole (**1a**).

This compound was obtained as white needles (hexane), mp 128-130°; ir (potassium bromide): 3410 (NH), 1118, 1052 (Ar-I) cm^{-1}; ^{1}H-nmr (dimethylsulfoxide-d_6): δ 11.8 (s, 1H, NH), 8.13 (d, 1H, 4-H, J = 7.7 Hz), 8.09 (d, 1H, 5-H, J = 7.0 Hz), 7.77 (d, 1H, 2-H, J = 7.6 Hz), 7.61 (d, 1H, 8-H, J = 8.0 Hz), 7.43 (dd, 1H, 7-H, J = 7.1 and 8.0 Hz), 7.20 (dd, 1H, 6-H, J = 7.0 and 7.1 Hz), 6.98 ppm (dd, 1H, 3-H, J = 7.6 and 7.7 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 141.4, 139.5, 134.0, 126.1, 123.0, 122.6, 120.6, 120.4, 120.0, 119.2, 111.7, 72.5 ppm; ms: m/z 294 (13), 293 ($M^{+\cdot}$, 100), 166 (47), 165 (11), 164 (15), 139 (37), 138 (9).

Anal. Calcd. for $C_{12}H_8NI$: C, 49.18; H, 2.73; N, 4.78; I, 43.31. Found: C, 49.21; H, 2.72; N, 4.77.

3-Iodocarbazole (**1b**).

This compound was obtained as white needles (hexane), mp 195-196°; ir (potassium bromide): 3412 (NH), 1110, 1053 (Ar-I) cm^{-1} ^{1}H-nmr (dimethylsulfoxide-d_6): δ 11.40 (s, 1H, NH), 8.51 (d, 1H, 4-H, J = 1.6 Hz), 8.15 (d, 1H, 5-H, J = 7.8 Hz), 7.65 (dd, 1H, 2-H, J = 1.6, 8.4 Hz), 7.52 (d, 1H, 8-H, J = 8.0 Hz), 7.43 (m, 1H, 7-H, J = 1.1, 6.9 and 8.0 Hz), 7.37 (d, 1H, 1-H, J = 8.4 Hz), 7.18 ppm (m, 1H, 6-H, J = 1.1, 6.9 and 7.8 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 139.7, 138.7, 133.3, 128.6, 126.2, 125.1, 121.1, 120.5, 118.9, 113.3, 111.0, 81.2 ppm; ms: m/z 294 (13), 293 ($M^{+\cdot}$, 100), 166 (58), 165 (11), 164 (17), 140 (17), 139 (48), 138 (11), 83 (19), 69 (30).

1,6-Diiodocarbazole (**1c**).

This compound was obtained as white needles (hexane), mp 167-169°; ir (potassium bromide): 3376 (NH), 1040, 1023 (Ar-I) cm^{-1} ^{1}H-nmr (dimethylsulfoxide-d_6): δ 11.3 (s, 1H, NH), 8.5 (s, 1H, 5-H), 8.18 (d, 1H, 4-H, J = 7.8 Hz), 7.80 (d, 1 H, 2-H, J = 7.5 Hz), 7.69 (d, 1H, 7-H, J = 8.0 Hz), 7.45 (d, 1H, 8-H, J = 8.0 Hz), 6.99 ppm (dd, 1H, 3-H, J = 7.5 and 7.8 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 138.8, 138.6, 134.8, 134.0, 129.1, 125.5, 121.7, 120.8, 120.5, 114.1, 82.2, 73.0 ppm; ms: m/z 420 (3), 419 ($M^{+\cdot}$,24), 294 (12), 193 (88), 166 (45), 165 (22),139 (32), 138 (11).

Anal. Calcd. for $C_{12}H_7NI_2$: C, 34.41; H, 1.67; N, 3.34; I, 60.58. Found: C, 34.42; H, 1.68; N, 3.37.

3,6-Diiodocarbazole (**1d**).

This compound was obtained as white needles (hexane), mp 204-206°; ir (potassium bromide): 3423 (NH), 1073, 1058, 1016 (Ar-I) cm^{-1} ^{1}H-nmr (dimethylsulfoxide-d_6): δ 11.53 (s, 1H, NH), 8.57 (s, 2H, 4-H, 5-H), 7.67 (dd, 2H, 2-H, 7-H,

J = 1.4, 8.6 Hz), 7.36 ppm (d, 2H, 1-H, 8-H, J = 8.6 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 138.8, 134.0, 129.1, 123.8, 113.5, 81.7 ppm; ms: m/z 420 (13), 419 ($M^{+\cdot}$,100), 293 (12), 292 (38), 166 (9), 165 (38), 164 (43), 139 (9), 138 (22), 137 (15), 82 (25).

1,3,6-Triiodocarbazole (**1e**).

This compound was obtained as white needles (hexane), mp 236-238°; ir (potassium bromide): 3422 (NH), 1110, 1077, 1058, 1020 (Ar-I) cm^{-1} ^{1}H-nmr (dimethylsulfoxide-d_6): δ 11.43 (s, 1H, NH), 8.57 (s, 1H, 4-H), 8.55 (s, 1H, 5-H), 8.02 (s, 1H, 2-H), 7.70 (d, 1H, 7-H, J = 8.5 Hz), 7.43 ppm (d, 1H, 8-H, J = 8.5 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 140.9, 140.0, 138.7, 134.7, 129.6, 128.9, 124.2, 123.8, 114.2, 82.7, 82.0, 77.9 ppm; ms: m/z 546 (13), 545 ($M^{+\cdot}$, 100), 419 (11), 418 (11), 292 (3), 291 (22), 165 (3), 164 (24), 163 (12).

Anal. Calcd. for $C_{12}H_6NI_3$: C, 26.45; H, 1.10; N, 2.57; I, 69.88. Found: C, 26.43; H, 1.11; N, 2.58.

Iodination Reaction of Carbazole (**1**) with I-Iodosuccinimide.

To a stirred solution of carbazole (**1**) (100 mg, 0.60 mmol) in dichloromethane (10 ml) containing silica gel (6 g) (or not depending on the chlorination method used), a solution of *N*-iodosuccinimide (0.60 mmol to 2.40 mmol depending on the stoichiometry used) in dichloromethane (10 ml) was added dropwise. The reaction was stirred for an appropriate time in the absence of light at controlled temperature (- 18°, 0° and 25°) until the tlc and gc indicated the reaction was complete. All reaction were carried out under normal (air) atmosphere. The reaction mixture was then filtered and the silica-gel washed with dichloromethane (3 x 15 ml). The combined extracts were washed with water (100 ml) and the organic layer was dried over sodium sulfate, filtered off and was evaporated *in vacuo* to give a brownish solid residue. The residue was separated by column chromatography (silica gel-hexane-ethyl acetate mixtures) to give (**1a**), (**1b**), (**1c**), (**1d**) and (**1e**). According to the experimental conditions used the percentage yield of the products obtained are different as can be seen in Table II. This set of reactions were also performed in ethanol, in glacial acetic acid and in chloroform doped with glacial acetic acid.

Iodination Reaction of Carbazole (**1**) with Mercury (II) Oxide/Iodine/Sulfuric acid System.

To a stirred solution of carbazole (**1**) (154 mg, 0.92 mmol) in ethanol (20 ml) solid mercury (II) oxide (100 mg, 0.46 mmol) and molecular iodine previously ground (235 mg, 0.92 mmol) were added. Then concentrated sulfuric acid (100 µl, δ: 1.85 g/ml) was added gently. The reaction was stirred for an appropriate time in the absence of light at room temperature until the tlc and gc indicated that the reaction was complete. All reactions were carried out under normal (air) atmosphere. The reaction mixture was neutralized with sodium hydroxide, extracted with dichloromethane (3 x 15 ml) and washed with water (3 x 20 ml). The combined extracts were dried over sodium sulfate, filtered off evaporated *in vacuo* to give a brownish solid residue. The residue was separated by column chromatography (silica gel-hexane-ethyl acetate mixtures) to give (**1a**) and (**1b**). According to the experimental conditions used the percentage yield of the products obtained are different as can be seen in Table I.

Iodination Reaction of Carbazole (**1**) with Sodium Hypochlorite/Iodine System.

To a vigorously stirred solution of carbazole (**1**) (100 mg, 0.40 mmol) in chloroform (20 ml) solid molecular iodine previously ground (304.2 mg, 0.12 mmol) were added. Then, an aqueous solution of NaClO (0.74 *M*, 5 ml) was added dropwise. The reaction was stirred for an appropriate time in the absence of light at room temperature until gc indicated the reaction was complete. The reaction mixture was neutralized with hydrochloride acid, extracted with chloroform (2 x 20 ml) and washed with water (2 x 15 ml). the combined extracts were dried over sodium sulfate, filtered off and evaporated *in vacuo* to give a brownish residue. The residue was separated by column chromatography (silica gel, hexane-ethyl acetate mixtures) to give **1a**, **1b**, **1c** and **1d**. The percent yield of the products obtained are reported in Table I.

General Procedure for the Iodination Reaction of Carbazoles **2** - **4** with *N*-Iodosuccinimide.

To a stirred solution of 2-acetoxycarbazole (**2**) (100 mg, 0.44 mmol) in dichloromethane (10 ml) a solution of *N*-iodosuccinimide (0.44 mmol to 1.78 mmol depending on the stoichiometry used) in dichloromethane (10 ml) was added dropwise. The reaction was stirred for an appropriate time in the absence of light at room temperature until the tlc and hplc indicated the reaction was complete. Reactions were carried out under normal (air) atmosphere. The workup was conducted in a similar manner as described above. The violet solid residue was separated by column chromatography (silica gel-hexane-ethyl acetate mixtures) to give **2a**, **2b** and **2c**. According to the experimental conditions used the percent yield of the products obtained are different as can be seen in Table IV (see Result and Discussion). These set of reactions were also performed in glacial acetic acid and in chloroform doped with glacial acetic acid.

3-Iodo-2-acetoxycarbazole (**2a**).

This compound was obtained as white needles (hexane), mp 146-147°; ir (potassium bromide): 3422 (NH), 1760, 1134 (C=O), 1131, 1017 (Ar-I) cm^{-1}; ^{1}H-nmr (dimethylsulfoxide-d_6): δ 11.8 (s, 1H, NH), 8.13 (s, 1H, 4-H), 8.06 (dd, 1H, 5-H, J =1.7, 8.3 Hz), 7.35-7.25 (m, 3H, 6-H, 7-H and 8-H), 6.87 (s, 1H, 1-H), 2.32 ppm (s, 3H, CH_3CO); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 169.4, 158.2, 139.4, 139.2, 139.0, 131.0, 124.9, 123.7, 120.0, 118.6, 111.0, 107.0, 80.0, 21.2 ppm; ms: m/z 51 (M+, 10), 309 (70), 183 (100), 154 (26), 126 (22).

Anal. Calcd. for $C_{14}H_{11}NO_2I$: C, 47.76; H, 3.12; N, 3.98; O, 9.09; I, 36.05. Found: C, 47.79; H, 3.13; N, 4.01.

6-Iodo-2-acetoxycarbazole (**2b**).

This compound was obtained as white needles (hexane), mp 164-166°; ir (potassium bromide): 3418 (NH), 1763, 1136 (C=O), 1130, 1010 (Ar-I) cm^{-1}; ^{1}H-nmr (dimethylsulfoxide-d_6): δ 8.14 (s, 1H, NH), 8.21 (d, 1H, 5-H, J = 1.7 Hz), 7.79 (d, 1H, 4-H, J = 8.5 Hz), 7.63 (dd, 1H, 7-H, J = 1.7, 8.5 Hz), 7.11 (d, 1H, 8-H, J = 8.5 Hz), 7.08 (d, 1H, 1-H, J = 2.0 Hz), 6.91 (dd, 1H, 3-H, J = 2.0, 8.5 Hz), 2.38 ppm (s, 3H, CH_3CO); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 168.4, 148.3, 139.4, 138.8, 134.0, 129.4, 123.8, 121.4, 120.1, 112.8, 111.8, 105.0, 82.0, 21.3 ppm; ms: m/z 351 (M+, 14), 309 (100), 182 (12), 154 (14), 126 (10).

Anal. Calcd. for $C_{14}H_{11}NO_2I$: C, 47.76; H, 3.12; N, 3.98; O, 9.09; I, 36.05. Found: C, 47.78; H, 3.13; N, 4.0.

3,6-Diiodo-2-acetoxycarbazole (**2c**).

This compound was obtained as white needles (hexane), mp 192-193°; ir (potassium bromide): 3426 (NH), 1762, 1135 (C=O), 1073, 1055, 1017 (Ar-I) cm^{-1}; ^{1}H-nmr (dimethylsulfoxide-d_6): δ 8.24 (s, 1H, NH), 8.03 (d, 1H, 5-H, J = 1.4 Hz), 7.98 (s, 1H, 4-H), 7.67 (dd, 1H, 7-H, J = 1.7, 8.5 Hz), 7.10 (d, 1H, 8-H, J = 8.4 Hz), 7.02 (s, 1H, 1-H), 2.47 ppm (s, 3H, CH_3CO); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 107.1, 157.9, 138.9, 138.7, 134.2, 131.0, 129.1, 124.0, 123.5, 113.1, 107.2, 82.0, 79.7, 21.2 ppm; ms: m/z 77 (M+, 13), 435 (16), 308 (100), 182 (9), 164 (4), 154 (13), 126 (12).

Anal. Calcd. for $C_{14}H_{10}NO_2I_2$: C, 35.18; H, 2.09; N, 2.93; O, 6.69; I, 53.11. Found: C, 35.21; H, 2.10; N, 2.94.

General Procedure for the Iodination Reaction of Carbazoles **3 - 4** with Sodium Periodate/Iodine /Catalytic Acid and Sodium Periodate /Potassium Iodide/Catalytic Acid Systems.

To a stirred solution of 3-bromocarbazole (**3**) (100 mg, 0.41 mmol) in ethanol (20 ml) solid sodium periodate (0.10 to 0.41 mmol depending on the stoichiometry used) and molecular iodine previously ground (0.20 to 0.62 mmol depending on the stoichiometry used) were added. Then concentrated sulfuric acid (42 µl to 1.68 ml depending on the stoichiometry used, δ: 1.85 g/ml) was added gently. The reaction was stirred for an appropriate time in the absence of light at controlled temperature (70°) until tlc and hplc analysis indicated the reaction was complete. The workup was conducted in a similar manner as described above. The brownish residue was separated by column chromatography (silica gel-hexane-ethyl acetate mixtures) to give **3a** and **3b**. The percentage yield of the products obtained are presented in Tables III and IV. Also, this set of reactions were performed in glacial acetic acid, which works as solvent and acid catalysis simultaneously. The percentage yield of the products obtained are presented in Tables III and IV.

Iodination Reaction of 3-Bromocarbazole (**3**) with *N*-Iodosuccinimide.

The iodination reaction of 3-bromocarbazole (**3**) was performed according to the general procedure described above. These reactions were conducted at room temperature. The brownish solid residue was separated by column chromatography (silica gel-hexane-ethyl acetate mixtures) to give two crystalline products **3a** and **3b**. The percentage yield of the products obtained are presented in Table IV (see Result and Discussion). These set of reactions were also performed in glacial acetic acid.

3-Bromo-6-iodocarbazole (**3b**).

This compound was obtained as white needles (hexane, ethyl acetate), mp 203-204°; ir (potassium bromide): 3422 (NH), 1084, 1065, 1032 (Ar-Br and Ar-I) cm^{-1} ; ^{1}H-nmr (dimethylsulfoxide-d_6): δ 11.52 (s, 1H, NH), 8.56 (d, 1H, 5-H, J = 1.6 Hz), 8.39 (d, 1H, 4-H, J = 1.7 Hz), 7.67 (dd, 1H, 7-H, J = 1.6 and 8.5 Hz), 7.53 (dd, 1H, 2-H, J = 1.7, 8.7 Hz), 7.46 (d, 1H, 1-H, J = 8.7 Hz), 7.37 ppm (d, 1H, 8-H, J = 8.5 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 139.1, 138.4, 134.1, 129.1, 128.6, 124.1, 123.1, 123.0, 113.6, 113.2, 110.9, 81.7 ppm; ms: m/z 373 ($M^{+\cdot}$, 100), 371 (91), 246 (20), 244 (22), 166 (5), 165 (44), 164 (40), 138 (21), 137 (17), 82 (36).

Anal. Calcd. for $C_{12}H_7NBrI$: C, 38.75; H, 1.88; N, 3.77; O, 21.48; I, 34.12. Found: C, 38.79; H, 1.88; N, 3.79.

3-Bromo-1-iodocarbazole (**3a**).

This compound was obtained as white needles (hexane, ethyl acetate), mp 91-92°; ir (potassium bromide): 3420 (NH), 1080, 1058, 1030 (Ar-Br and Ar-I) cm^{-1} ;^{1}H-nmr (dimethylsulfoxide-d_6): δ 11.1 (s, 1H, NH); 8.38 (s, 1H, 4-H), 8.13 (d, 1H, 5-H, J = 7.8 Hz), 7.74 (s, 1H, 2-H), 7.60-7.46 (m, 2H, 6-H and 7-H, J = 1.2, 7.8 Hz), 7.16 ppm (d, 1H, 8-H, J = 7.8 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 80.7, 138.5, 111.0, 118.4, 119.4, 118.4, 125.3, 110.8, 132.3, 139.4, 124.6, 138.7 ppm; ms: m/z 373 ($M^{+\cdot}$, 100), 371 (91), 246 (20), 244 (22), 166 (5), 165 (44), 164 (40), 138 (21), 137 (17), 82 (36).

Anal. Calcd. for $C_{12}H_7NBrI$: C, 38.75; H, 1.88; N, 3.77; O, 21.48; I, 34.12. Found: C, 38.80; H, 1.89; N, 3.78.

Iodination Reaction of 3-Nitrocarbazole (**4**) with *N*-Iodosuccinimide.

The iodination reaction of 3-nitrocarbazole (**4**) was performed according to the general procedure described above. These reactions were conducted at room temperature. The yellowish solid residue was separated by column chromatography (silica gel-hexane-ethyl acetate mixtures) to give two crystalline products **4a** and **4b**. The percentage yield of the products obtained are presented in Table V (see Result and Discussion). These set of reactions were also performed in glacial acetic.

6-Iodo-3-nitrocarbazole (**4a**).

This compound was obtained as white needles (hexane-ethyl acetate), mp 256-257°; ir (potassium bromide): 3331 (NH), 1313 (NO_2); 1090, 1045 (Ar-I) cm^{-1} ; ^{1}H-nmr (dimethylsulfoxide-d_6): δ 11.56 (s, NH), 8.74 (d, 1H, 4-H, J = 1 Hz), 8.27 (m, 2H, 2-H, 5-H, J = 2.2, 8.5 Hz), 7.74 (dd, 1H, 7-H, J = 1.6, 8.5 Hz), 7.60 (d, 1H, 1-H, J = 9.0 Hz), 7.42 ppm (d, 1H, 8-H, J = 8.5 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 143.1, 140.1, 140.0, 135.1, 129.8, 125.0, 121.6, 120.9, 117.8, 114.1, 111.2, 83.3 ppm; ms: m/z 339 (14), 338 ($M^{+\cdot}$, 100), 308 (16), 293 (4), 292 (32), 211 (5), 165 (34), 164 (44), 139 (7), 138 (22).

Anal. Calcd. for $C_{12}H_7N_2O_2I$: C, 42.64; H, 2.07; N, 8.29; O, 9.47; I, 37.53. Found: C, 42.68; H, 2.06; N, 8.31.

8-Iodo-3-nitrocarbazole (**4b**).

This compound was obtained as white needles (hexane-ethyl acetate), mp 253-254°; ir (potassium bromide): 3331 (NH), 1315 (NO_2); 1089, 1040 (Ar-I) cm^{-1} ; ^{1}H-nmr (dimethylsulfoxide-d_6): δ 11.56 (s, NH), 8.74 (d, 1H, 4-H, J = 2.2 Hz), 8.27 (dd, 1H, 2-H, J = 2.2, 9.0 Hz), 8.18 (d, 1H, 5-H, J = 8.5 Hz), 7.74 (dd, 1H, 7-H, J = 1.6, 8.5 Hz), 7.60 (d, 1H, 1-H, J = 9.0 Hz), 6.98 ppm (dd, 1H, 6-H, J = 8.5 Hz); ^{13}C-nmr (dimethylsulfoxide-d_6): δ 140.0, 139.0, 138.5, 135.7, 125.0, 122.0, 121.0, 120.9, 120.5, 117.0, 114.1, 72.0 ppm; ms: m/z 339 (14), 338 ($M^{+\cdot}$, 100), 308 (16), 293 (4), 292 (32), 211 (5), 165 (34), 164 (44), 139 (7), 138 (22).

Anal. Calcd. for $C_{12}H_7N_2O_2I$: C, 42.64; H, 2.07; N, 8.29; O, 9.47; I, 37.53. Found: C, 42.67; H, 2.08; N, 8.30.

Iodination Reaction of 3-Nitrocarbazole **4** with Sodium Periodate/Iodine /Catalytic Acid.

The iodination reaction of 3-nitrocarbazole was performed according to the general procedure described above. The reaction was conducted at 70°. The yellowish residue was separated by column chromatography (silica gel-hexane-ethyl acetate

mixtures) to give **4a** and **4b**. The percentage yield of the products obtained are presented in Table V. Also, this set of reactions were performed in glacial acetic acid, which works as solvent and acid catalysis simultaneously.

Calculations.

The ground-state geometry and heat of formation, static charge distribution for predicting chemical reactivity of carbazoles **1** - **4**, iodocarbazoles and possible reaction intermediates were calculated by using the semiempirical parametrized PM3 method as implemented in version of the HyperChem program [28], which has proven to be effective in studies of molecules containing heteroatoms, compared with other methods such as MINDO/3 or MNDO.

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