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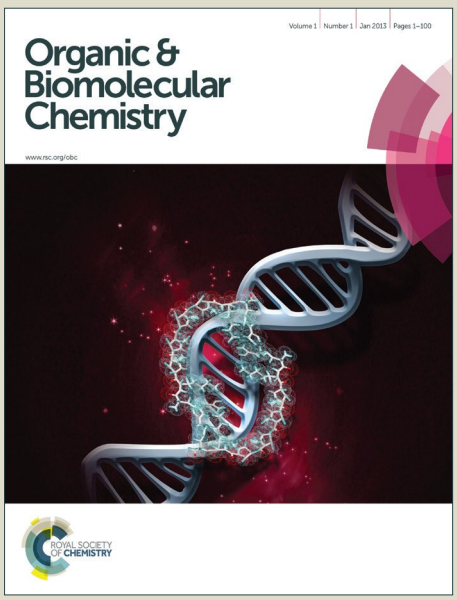

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ARTICLE

New electron-donor and –acceptor architectures from benzofurazans and sym-triaminobenzenes: intermediates, products and unusual nitro group shift

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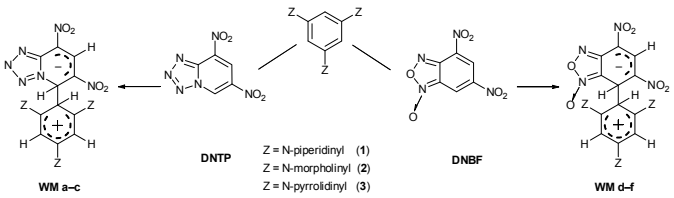
New all-conjugated C–C coupling products bearing both an electron-poor and an electron-rich aromatic moiety have been obtained from the reaction between *sym*-triaminobenzene derivatives and a series of isomeric chloro-nitrobenzofurazans. The reactions occur under mild conditions and in some cases a different behaviour dependent by the presence, or not, of triethylamine, was observed. From 1,3,5-tris(*N*-morpholinyl)benzene and 5-chloro-4-nitrobenzofurazan in the presence of triethylamine an unexpected product derived from the shift of the nitro group from C-4 to C-5 of the electrophile and bearing the nucleophile in position 4 was obtained. Moreover, from the coupling between 1,3,5-tris(*N*-pyrrolidinyl)benzene and 4-chloro-7-nitrobenzofurazan a highly stable Wheland intermediate was isolated.

Introduction

2,1,3-Benzoxadiazoles and related 1-oxides, commonly indicated as benzofurazans and benzofuroxans, are compounds widely studied in many fields of chemistry.[1] The annulation of the benzene ring by the electron-withdrawing five-membered heterocyclic moiety results in 10π electron-deficient ring systems exhibiting high S_NAr reactivity[2-4] that is strongly enhanced when one, or more, electron-withdrawing substituents are introduced on the carbocyclic ring. For example, 4-chloro-7-nitrobenzofurazan shows the same S_NAr reactivity of picryl chloride towards different reagents[5] and is widely used, as well as 4-fluoro-7-nitrobenzofurazan, as fluorogenic reagent for the detection and quantification of amino and thiol groups on proteins and biologically active molecules.[6,7] Nitrobenzofurazans and nitrobenzofuroxans are versatile compounds in pharmaceutical[8,9] optoelectronic, agrochemical, and material fields,[10,11] and long since they have been privileged reagents to study σ-anionic intermediates (Meisenheimer complexes) of the S_NAr reaction.[2] Moreover, when two nitro groups are located on the homocyclic ring, these neutral heterocycles, such as 4,6-dinitrobenzoxadiazole (**DNBF**) show a reactivity that allowed them to be ranked as 'superelectrophilic heteroaromatics'.[12,13] This feature prompted us to combine **DNBF** and 4,6-dinitrotetrazolopyridine (**DNTP**), whose electrophilicity parameters, calculated according to Mayr's equation[14-16] are –5.06 and –4.67, respectively, with strongly activated aromatic nucleophiles such as 1,3,5-triaminobenzene derivatives **1-3**.[17] This allowed to obtain the first evidence of Wheland-Meisenheimer intermediates (**WM a-f**, Scheme 1) of the aromatic substitution reaction,[18] and some of them were also theoretically studied.[19] The ability of the moiety deriving from aminobenzene to stabilize the positive charge played a key role in the succeeding of the detection and characterization of this kind of intermediates.



Scheme 1. Zwitterionic intermediates of the aromatic substitution reaction between 1,3,5-tris(*N*,*N*-dialkylamino)benzenes and carbon neutral aromatic superelectrophiles.

In the above reaction, as well as in the Michael-type addition to 1,2-diazabuta-1,3-dienes,[20] and in azo coupling with diazonium salts,[21-23] *sym*-triaminobenzenes **1–3** behave as carbon nucleophiles. On the contrary, with electrophiles such as proton[24,25] and alkyl halides[26-28] they undergo attack on both, the aromatic carbon atom and the nitrogen atom of the amino substituent, in a relative extent dependent on the experimental conditions. It has been reported[29] that the reaction between **1–3** and halo-nitrobenzene derivatives gives, mainly under drastic conditions, the corresponding biphenyls

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but, to the best of our knowledge, no literature report involving heteroaryl halides has appeared so far. On the other hand, chloro-nitrobenzofurazans have been widely employed as electrophiles in S_NAr reactions with nitrogen-,[30,31] sulfur-,[32,33] and oxygen-nucleophiles,[34-38] but only in a few cases[39-41] with carbon nucleophiles.

This prompted us to study the reaction between compounds **1-3** and a series of chloro-nitrobenzofurazans to gain information on this S_NAr/S_EAr combination between carbon neutral aromatic substrates. Moreover, the products derived from this reaction are highly conjugated and bear both an electron-withdrawing and an electron-donor moiety on the same unit. Given that heteroaromatics with electron-donor and -acceptor architectures are receiving growing interest in diverse applicative fields, such as solar energy conversion[42] and optoelectronic devices,[43] the products formed in this study may be of interest in material chemistry. Herein we report the results we have obtained.

Results and discussion

The S_EAr/S_NAr coupling between 1,3,5-tris(*N*,*N*-dialkylamino)benzenes **1–3** and the series of chloro-nitrobenzofurazans **4–7** (hereafter indicated also with acronyms shown in Fig. 1) was carried out in different experimental conditions.

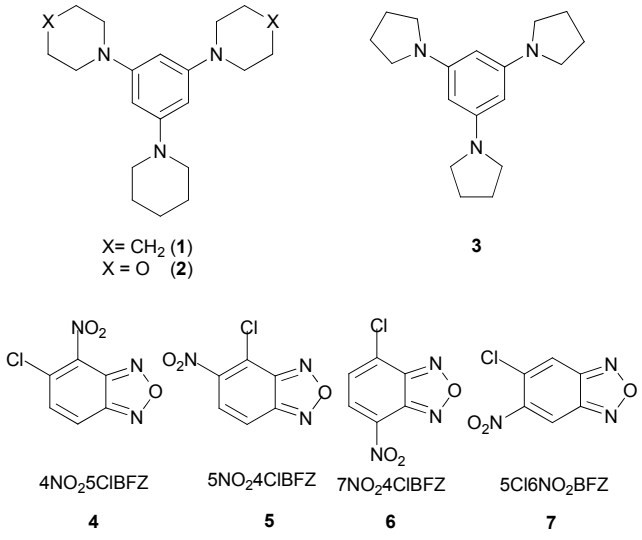
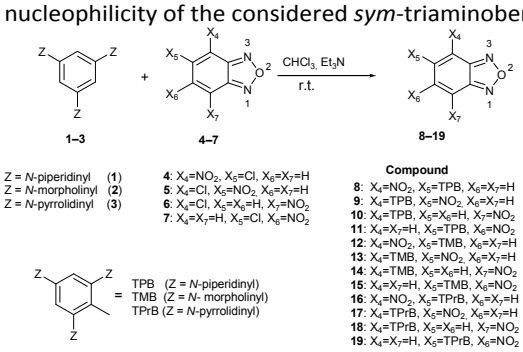


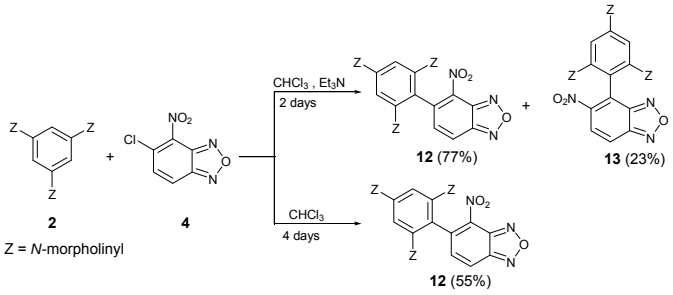
Figure 1. Neutral aromatic nucleophiles **1-3** and electrophiles **4-7**.

First, the reactions were carried out in chloroform at room temperature with equimolar amount of reagents and in the presence of triethylamine to neutralize the acid produced during the reaction (Scheme 2). The reaction progress was monitored by TLC and the products were purified by chromatography on silica gel and fully characterized. From yields shown in Scheme 2 emerges that the reaction between benzofurazans **4**, **5** or **6** and 1,3,5-tris(*N*-piperidinyl)benzene (**1**) or 1,3,5-tris(*N*-pyrrolidinyl)benzene (**3**) occurs almost quantitatively after about 2 h giving the C–C coupling products **8–10** and **16–18**, respectively, whereas the reactions with 1,3,5-tris(*N*-morpholinyl)benzene (**2**) required at least 24 h to give the product in moderate yield due to low conversion: this can be considered a consequence of the different nucleophilicity of the considered *sym*-triaminobenzenes.



Scheme 2. Reactions between triaminobenzene and benzofurazan derivatives.

An unexpected behaviour emerged when, in order to improve the yield of the product **12**, reagents **4** and **2** were left for long time in the presence of triethylamine. After 2 days, the ^1H NMR spectrum of the crude reaction mixture showed absence of the starting benzofurazan **4** and presence of signals compatible with those of two new benzofurazan derivatives in 77/23 relative % ratio. After separation by FC, their NMR and MS spectra agreed with those of two isomeric structures, corresponding to products **12** and **13** (Scheme 3, up).



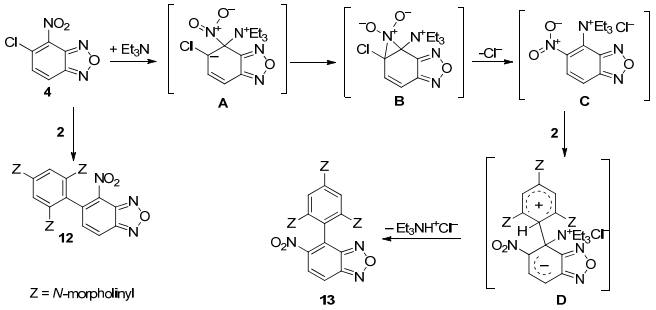
Scheme 3. Reaction products from **2** and **4** in the presence, or not, of Et_3N.

The formation of the minor isomer **13** was totally unexpected and its identification was ascertained by comparison with an authentic sample obtained by reaction of **2** with **4Cl5NO$_2$BFZ**. Even more interesting, when the reaction between **2** and **4** was carried out without triethylamine only **12** was produced (Scheme 3, bottom). Moreover, the reactions of **4** with **1** or **3**, as well as those of **2** with **5** or **6** produced only the expected product of *ipso*-substitution of chlorine coming from the classical S_NAr reaction.

It is noteworthy that the formation of **13** from **4** represents, to the best of our knowledge, the first instance of a nitro group shift in benzofurazan series and one of the few examples reported so far. To this regard, two cases, in particular, seem akin to the transformation herein: *i*) the reaction of 3-bromo-2-nitrobenzo-[b]thiophene with some amines that gives

mixtures of *N*-substituted 3-amino-2-nitrobenzo[b]-thiophenes and *N*-substituted 2-amino-3-nitrobenzo[b]thiophenes;[44] *ii*) the base-catalyzed 1,2-nitro group shift in some conjugated nitroalkenes.[45] In both cases, a mechanisms involving the formation of a three-membered nitrogen ring as intermediate was advanced.

In current case, we attempted a possible explanation for the formation of the compound **13** from **2** and **4** in the presence of triethylamine by hypothesizing the reaction pathway shown in Scheme **4**.



Scheme 4. Tentative pathway to explain the behaviour of the reaction between **2** and **4** in the presence of triethylamine.

In the presence of 1,3,5-tris(*N*-morpholinyl)benzene (**2**) that, among those currently used, is the less nucleophilic reagent, triethylamine might attack, even if in low extent, the C-4 carbon atom producing a sigma-anionic intermediate like **A**. Indeed, the C-4 carbon atom is made highly electrophilic by the bond with the nitro group and by the presence of the adjacent fused furazan ring: in these conditions, it cannot be excluded that triethylamine can behave as nucleophile.[46,47] Then, a further intermediate (**B**), characterized by a three membered ring involving the nitro group can be formed (formation of **B** might also derive directly from **4**). The departure of the chloride ion from **B** produces the species **C** in which the nitro migration is realized. Finally, **C** might undergo nucleophilic attack of **2** on the C-4 producing the Wheland Meisenheimer intermediate **D** that, after the departure of the neutral triethylamine from the benzofurazan moiety and of the proton from the triaminobenzene moiety, re-aromatizes to the product **13**. An indication of the plausibility of the reaction pathway hypothesized was obtained by some experiments carried out directly in the NMR spectroscopy tube: 1) equimolar amounts of compound **4** and *N*-methylpyrrolidine (more nucleophilic than triethylamine)[46] were dissolved in $CDCl_3$ and after 5 h an equimolar amount of **2** was added; the ^{1}H NMR spectrum of the reaction mixture showed, after 5 min, presence of **12** and **13** in 66/34 relative % yield; 2) to an equimolar mixture of **4** and triethylamine kept for 5 h in $CDCl_3$ an equimolar amount of 1,3,5-tris(*N*-piperidinyl)benzene (**1**) was added: after about 4 h the ^{1}H NMR spectrum showed presence of both, the classic coupling compound **8** and that with the nitro group shifted in position 5 (**9**): this was also confirmed by comparison, through TLC analysis, with authentic samples. The reason for which the nitro group shift was observed only with **5Cl4NO$_2$BFZ** and not with **4Cl5NO$_2$BFZ** might be related to the relative minor reactivity of the first.[48] No product was obtained from the reaction between **1** or **2** and **5Cl6NO$_2$BFZ** (Scheme 1). This might be explained by considering that in benzofurazans derivatives there is a high degree of double-bond fixation in the 4,5- and 6,7-position;[36] in the case of **5Cl6NO$_2$BFZ** isomer (**7**) the chloro- and the nitro-group are connected by a C5–C6 bond with a single bond character thus the nitro group cannot exert important electronic effects on the adjacent position and this limits the possibility of occurrence of a S_NAr in position 5 of reagent **7**.[35,36]

Once the products formed in the reaction between *sym*-triaminobenzene derivatives **1–3** and benzofurazans **4–6** were isolated and characterized, an investigation on the reaction course in the absence of Et_3N was started. For this purpose, equimolar amount of each electrophile/nucleophile couple, dissolved in $CDCl_3$, was added directly in the NMR spectroscopy tube and the reaction was monitored with time. In Table 1 are reported the results obtained from NMR measurements.

Table 1. Reactions between equimolar amount of **1-3** and **4–6** in $CDCl_3$ at room temperature without triethylamine.[a]

Entry	Reagents[b]		Product	Yield[c] 15 min	Yield[c] 60 min	Yield[c] 22 h	Yield[c] 96 h
1	**4NO$_2$5ClBFZ (4)**	**1**	**8**	50	56	66	70
2	**5NO$_2$4ClBFZ (5)**	**1**	**9**	58	64	73[d]	n.d.
3	**7NO$_2$4ClBFZ (6)**	**1**	**10**	31	42	53	60
4	**4NO$_2$5ClBFZ (4)**	**2**	**12**	0	7	37	55
5	**5NO$_2$4ClBFZ (5)**	**2**	**1**[e]	9	26	45	58
6	**7NO$_2$4ClBFZ (6)**	**2**	**14**	0	1	6	18[f]
7	**4NO$_2$5ClBFZ (4)**	**3**	**16**[g]	53	55	58	n.d.
8	**5NO$_2$4ClBFZ (5)**	**3**	**17**[g]	62[d]	71[d]	86	n.d.
9	**7NO$_2$4ClBFZ (6)**	**3**	**18+20**	89[h]	96[i]	n.d.	n.d.

[a] Reactions carried out in the NMR spectroscopy tube and monitored by ^{1}H NMR. [b] After 9 h reactions between **1** (or **2**) and **7** did not occur while with **3** a complex mixture of signals belonging to unidentified compounds was observed after about 4 h. [c] Calculated from ^{1}H NMR spectrum of the crude reaction mixture (that showed only signals of starting reagents and of the coupling product) with respect to the signals of the starting electrophile; n.d. means not determined. [d] Approximate yield due to the difficult integration of broad and not well separated signals. [e] Yield reached 72% after 24 h from the addition of a further equivalent of **2**. [f] 27% after 118 h. [g] Spectrum showed presence of the Wheland intermediate **E3** formed by C-protonation of **3**. [h] Starting compound **6** was present in 11% and the

remaining 89% was constituted by a mixture of **18**/**20** in a 13/87 relative ratio. [i] Compound **6** was present in 4% and the relative ratio **18**/**20** was 5/95.

Data of Table 1 show that all the reactions between triaminobenzenes **1–3** and benzofurazans **4–6**, except that of entry 6, gave conversion to coupling product higher than 50%.
By considering that the reactions were carried out between equimolar amount of reagents and in the absence of triethylamine, the expected conversion to substitution product was no higher than 50% because of the possibile attack of the proton, released in the re-aromatization step, on the starting triaminobenzene. In this regard, it is known[25] that the protonation of triaminobenzenes can occur both at the carbon atom and/or at the nitrogen atom of the amino substituents, producing the CH salt (Wheland intermediates **E1–3** in Fig. 2) and/or the ammonium salt (structures **F1–3** in Fig. 2). In the latter case, the structure **F** shown in Fig. 2, bearing the proton bound to a precise nitrogen atom, is a limited representation of the real situation since previous studies on the protonation of the *sym*-triaminobenzenes **1–3** reported that in solution the proton is not located onto a definite nitrogen atom but is involved in a sort of proton dance that produces equivalence of the aromatic protons.[25]

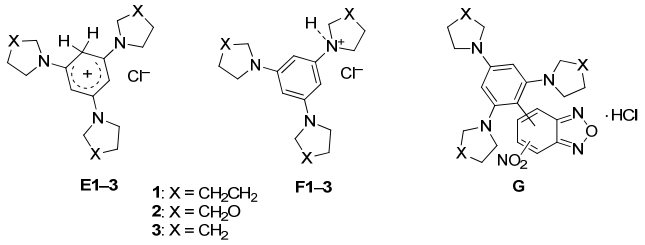
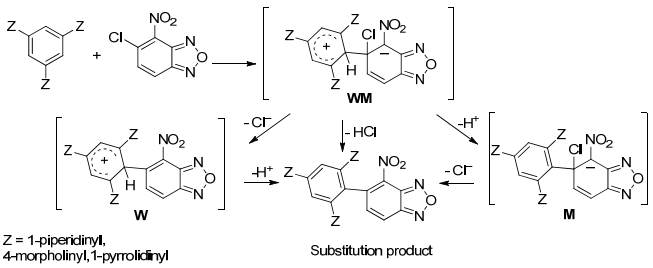


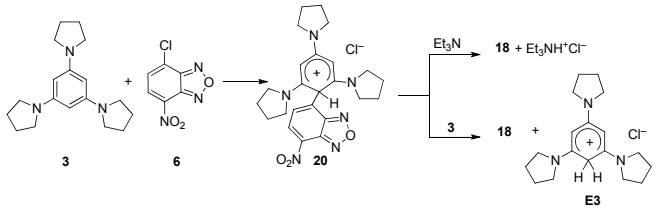
Figure 2. Possible products obtained from the attack of the proton on the sym-triaminobenzenes **1–3** or on the C–C coupling product.

According to this, in cases involving nucleophiles **1** and **2** (Table 1, entries 1–6), the ^{1}H NMR spectra showed a remarkable broadening of signals belonging to the yet unreacted triaminobenzene and the equivalence of his aromatic protons indicates the occurrence of the protonation at the nitrogen atom of **1** and 2.
In the case of the reactions between 1,3,5-tris(*N*-pyrrolidinyl)benzene (**3**) and 5Cl4NO$_2$BFZ (**4**) and 4Cl5NO$_2$BFZ (**5**) (Table 1, entries 7 and 8) the ^{1}H NMR spectra showed, besides the signals of the starting benzofurazan and of the product derived from the S_NAr reaction, signals ascribable to the C-protonated form of **3** (Wheland intermediate **E3** in Figure 2). The formation of **E3** was inferred by the presence in the spectrum of two sharp singlets of equal area at 4.72 and 3.93 ppm, corresponding to the aromatic protons and to those bound to the sp^3 hybridized carbon atom, respectively, as confirmed by *g*-HSQC experiments. When a second equivalent of **3** was added to the crude reaction mixture, the conversion became complete and an increasing of the signals belonging to both, **16** (or **17**) and **E3**, was observed (see spectra in Fig. SI-30). This agrees with the already reported propensity of **3** to give preferentially C-protonated forms instead of *N*-protonated ones.[17,25]
Moreover, in many cases the substitution product was formed in yields higher than 50% and in those cases the ^{1}H NMR spectrum showed a gradual broadening of the signal of the aromatic protons belonging to the triaminobenzene moiety of the product (Table 1, entries 1, 2, 3, 7, 8) thus indicating the protonation of the reaction product (form **G** of Fig. 2) and his involvement in a dynamic phenomenon similar to that previously observed for the *N*-protonation of **1** and **2**. When the reactions were carried out in the presence of an excess of triethylamine in the NMR spectroscopy tube, or with two equivalents of triaminobenzene, the conversion increased and all the signals of the product in the ^{1}H NMR spectrum became sharp.
Scheme 5 shows some possible σ-intermediates of the aromatic substitution reaction currently studied related to 5Cl4NO$_2$BFZ (**4**), chosen as representative electrophile among those herein considered. Being triaminobenzenes **1–3** aromatic neutral nucleophiles, a zwitterionic intermediate, Wheland on the triaminobenzene moiety and Meisenheimer on the benzofurazan moiety (**WM** in Scheme 5), is first produced.



Scheme 5. σ-Intermediates in the aromatic substitution between 1,3,5-triaminobenzene derivatives and 5Cl4NO2BFZ (**4**).

In principle, prior to the re-aromatization step, this intermediate might lose a proton producing a Meisenheimer intermediate (**M**), or might evolve to a Wheland intermediate (**W)** by departure of the chloride ion. Among these intermediates, we observed and isolated the Wheland intermediate **20**, derived from **3** and **6** (Scheme 6). In particular, the ^{1}H HNMR spectrum recorded 30 h after the addition of **3** to **6** showed the disappearance of the starting materials and only the presence of a compound that, after removal of the solvent, was analyzed by ESI-MS (ESI$^+$ mode). The mass spectrum showed a m/z = 449 and absence of the ion indicative of the Na adduct (Fig. SI-29) thus suggesting that the analyzed specie might be positively charged in itself. Further NMR experiments (^{13}C NMR, DEPT and g-HSQC) on this residue confirmed the Wheland-like structure **20** (Scheme 6).



Scheme 6. Formation of the stable Wheland complex **20** evolving to **18** by addition of Et_3N (or **3**). The protonation of **3** gave the Wheland intermediate **E3**.

It is noteworthy that **20** represents the first instance of a Wheland intermediate involving a benzofurazan moiety. Furthermore, it showed an unusual stability: his ^{1}H NMR spectrum in deuterochloroform remained unchanged after several days at room temperature. When triethylamine (≥ 1 eq) was added to this solution, immediate disappearance of the ^{1}H NMR signals of **20** and appearance of those belonging to **18** was observed (Figure SI-31).

Moreover, when a second equivalent of 1,3,5-tris(*N*-pyrrolidinyl)benzene (**3**) was added to a solution of **20** in $CDCl_3$, the ^{1}H NMR spectrum showed only presence of signals belonging to the re-aromatized product **18** and to the Wheland complex **E3** thus indicating that **3** acts as a base on **20**, giving its own C-protonated stable species **E3** (see spectra in Fig. SI-32).

It has to be noted that in all other combinations of nucleophiles **1**–**3** with electrophiles **4**–**6** no reaction intermediates **20**-like were detected. The unusual stability of **20** might be due to the occurrence of two conditions: the high stabilization of the positive charge by the pyrrolidinyl substituents in **20**, and the position of the nitro group. Actually, in **20**, the nitro group is situated away from the reactive center (*para*), thus exerting a minor inductive effect on it and decreasing the possible interaction with the hydrogen atom bound to the sp^3 carbon atom of the Wheland form **20** with respect to the cases in which the nitro group is in *ortho* position to the carbon atom bound to the triaminobenzene moiety. In cases of electrophiles **4** and **5**, as the reaction proceeds, the unreacted fraction of compound **3** is able to extract immediately the proton from intermediates **20**-like, giving the substitution product and the protonated form **E3**; in these cases also an assistance of the nitro group in the removal of the proton from the sp^3 carbon atom of Wheland forms **20**-like might occur.[49,50]

In the past[21-23] we found that the azo-coupling reaction between **1** (or **2**) and diazonium salts is a reversible process in which the rate-determining step is the proton abstraction: the new stable Wheland intermediate **20** represents another example in which the re-aromatization step of the aromatic substitution reaction does not occur in a fast step.

From an overview focused on the behaviour showed by nucleophiles and electrophiles here studied one can draw two main considerations: *i*) the conversion of each electrophile using nucleophiles **1**, **2**, or **3** increases in the order: **3**≥**1**>**2**, in agreement with their relative nucleophilicity, *ii*) keeping constant the nucleophile, the same degree of conversion of the starting benzofurazan into the reaction product requires a different time dependent on the position of the substituents on the benzofurazan moiety (compare data of Table 1, entries 1-6). For example, the reaction of **1** (entries 1–3) with **4** and **6** requires 15 min and 22 h, respectively, to reach about 50 % of conversion, whereas the 58% of the benzofurazan **5** was converted into **9** after 15 min and 5-chloro-6-nitrobenzofuroxan (**7**), under the same experimental conditions, did not react, even after 96 h. An analogous trend was observed for reactions of **4**–**7** with **2**. From these data, the tendency of the isomeric benzofurazans **4**–**7** to react with **1** or **2** can be placed, although qualitatively, in the following order: $5NO_2$4ClBFZ (**5**) > $4NO_2$5ClBFZ (**4**) > $7NO_2$4ClBFZ (**6**) > $6NO_2$5ClBFZ (**7**). These results might be explained by the intervention of many factors (see Supporting Material), mainly steric and electronic.

Conclusions

New compounds with electron-donor and -acceptor architectures from S_EAr/S_NAr C–C coupling between benzofurazan and *sym*-triaminobenzenes have been synthesized in good yields and under mild reaction conditions. 1,3,5-Tris(*N*-piperidinyl)benzene (**1**), 1,3,5-tris(*N*-morpholinyl)benzene (**2**) 1,3,5-tris(*N*-pyrrolidinyl)benzene (**3**) have been used as carbon neutral nucleophiles and four isomeric chloro-nitrobenzofurazans as electrophiles. The reactions between equimolar amount of reagents, carried out in chloroform at room temperature and in the presence of triethylamine, gave the substitution products with the exception of 5-chloro-6-nitrobenzofurazan which did not react. In the case of the combination between **2** and 5-chloro-4-nitrobenzofurazan, an unexpected product bearing the nitro group shifted in position 5, and the triaminobenzene substituent bound in the original position of the nitro group (C-4), was recovered; this product was not formed when the reaction was carried out in the absence of the amine.

All the reactions were carried out also directly in the NMR spectroscopy tube and monitored with time by ^{1}H NMR. Data obtained showed a **3**>**1**>**2** reactivity order for triaminobenzene derivatives and information on the reactivity of the isomeric chloro-nitrobenzofurazans was also obtained.

Furthermore, during this investigation it was possible to detect and characterize two sigma-cationic intermediates of the aromatic substitution reaction: one derived from the attack of the proton on 1,3,5-tris(*N*-pyrrolidinyl)benzene (**3**) and the second resulting from the C–C coupling between **3** and 4-chloro-7-nitrobenzofurazan after the departure of the chloride from the Wheland-Meisenheimer precursor. This new intermediate represents the first instance of a Wheland intermediate involving a benzofurazan moiety and is highly stable, evolving to the substitution product only after addition of a base.

Experimental

Experimental Details. The ^{1}H and ^{13}C NMR spectra were recorded at 300, 400, or 600 MHz (for ^{1}H NMR) and 75.46, 100.56, or 150.80 MHz (for ^{13}C NMR), respectively. *J* values are given in Hz. Signal multiplicities were established by DEPT or, in some cases, *g*-HSQC experiments. Chemical shifts were referenced to the solvent (δ =7.27 and 77.0 ppm for ^{1}H and ^{13}C NMR in $CDCl_3$, respectively). Chromatographic purifications were carried out on silica gel columns at medium pressure. Aluminum oxide used was activated, basic, Brockmann I, standard grade ca. 150 mesh. Melting points are uncorrected. Compound **6** is commercially available, 1,3,5-tris(*N*,*N*-dialkylamino)benzenes **1–3** and compounds **4**, **5**, and **7** were prepared as previously described by us.[18,21,35]

Reactions between *sym*-triaminobenzene derivatives 1-3 and benzofurazans 4-7. Typical procedure. 5-Chloro-4-nitrobenzofurazan (**4**) (15.0 mg, 0.075 mmol) was dissolved in chloroform (5 mL). Triethylamine (≥ 10 eq.) and tris(*N*-piperidinyl)benzene (**1**) (22.3 mg, 0.075 mmol) were added. The color of the solution turned to pale yellow to dark blue. The reaction mixture was magnetically stirred and the reaction course was monitored by TLC (eluent: petroleum light : ethyl ether 1:1) and by ^{1}H NMR analysis of a little amount of reaction mixture after solvent removal. The crude reaction mixture was then treated with water (5 mL) and the aqueous layer was extracted with dichloromethane (3 x 5 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography of the residue (*n*-hexane/ethyl acetate with increase of gradient starting from 1:1) gave compound **8**. The reactions were also repeated using, instead of triethylamine, basic alumina; after its removal by filtration, the product was purified by FC (in this case no rearrangement was observed). Reactions into the NMR spectroscopy tube have been carried out using equimolar amount (0.007 mmol) of reagents dissolved in 0.7 mL of $CDCl_3$ and monitoring the progress of the reaction over time through ^{1}H NMR spectroscopy.

4-nitro-5-(2,4,6-tripiperidin-1-ylphenyl)-2,1,3-benzoxadiazole (8). Blue-violet solid 0.033 g (90%); m.p.: 227.7–228.8 °C; ^{1}H NMR (400 MHz $CDCl_3$,) δ = 7.83 (d, 1 H, *J* = 9.63 Hz), 7.49 (d, 1 H, *J* = 9.63 Hz), 6.36 (s, 2 H), 3.27-3.12 (m, 4 H), 2.74-2.64 (m, 4 H), 2.64-2.55 (m, 4 H), 1.70-1.60 (m, 4 H), 1.60-1.50 (m, 4 H), 1.33-1.20 ppm (m, 10 H); ^{13}C NMR (100.46 MHz, $CDCl_3$): δ = 155.5, 154.2, 153.6 (CH), 149.1 (CH), 144.3, 140.4, 140.0, 134.0, 117.6, 102.8 (CH), 49.5 (CH_2), 45.8(CH_2), 25.8(CH_2), 25.7(CH_2), 24.2(CH_2), 24.1 ppm (CH_2),; HRMS (ESI-TOF) m/z calcd for $C_{27}H_{35}N_6O_3$: 491.277064 $[M + H]^+$; found: 491.2771; elemental analysis calcd (%) for $C_{27}H_{34}N_6O_3$: C 66.10, H 6.99, N 17.13; found: C 66.32, H 7.01, N 17.08.

5-nitro-4-(2,4,6-tripiperidin-1-ylphenyl)-2,1,3-benzoxadiazole (9). Blue-violet solid 0.034 g (92%); m.p.: 217.4–217.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 (d, 1 H, *J* = 9.5 Hz), 7.80 (d, 1 H, *J* = 9.5 Hz), 6.51 (s, 2 H), 3.32-3.21 (m, 4 H), 2.76-2.64 (m, 4 H), 2.64-2.54 (m, 4 H), 1.80-1.57 (m, 6 H), 1.34-1.08 ppm (m, 12 H); ^{13}C NMR (100.46 MHz, $CDCl_3$): δ = 154.5, 153.94, 153.85, 150.8, 148.9, 147.4, 127.8 (CH), 127.4, 114.3 (CH), 104.0 (CH), 53.5 (CH_2), 49.7 (CH_2), 26.1 (CH_2), 25.9 (CH_2), 24.3 (CH_2), 24.1 ppm (CH_2); ESI MS (ES^+) m/z: 491 (M^+ + 1), 513 (M^+ + Na), 529 (M^+ + K); elemental analysis calcd (%) for $C_{27}H_{34}N_6O_3$: C 66.10, H 6.99, N 17.13; found: C 66.34, H 7.00, N 17.09.

4-nitro-7-(2,4,6-tripiperidin-1-ylphenyl)-2,1,3-benzoxadiazole (10). Blue-violet solid 0.033 g (90%); m.p.: 239.8–240.6 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.47 (d, 1 H, *J* = 7.8 Hz), 7.57 (d, 1 H, *J* = 7.8 Hz), 6.48 (s, 2 H), 3.26-3.12 (m, 4 H), 2.70-2.48 (m, 8 H), 1.77-1.46 (m, 8 H), 1.30-0.93 ppm (m, 10 H); ^{13}C NMR (150.80 MHz, $CDCl_3$) δ = 154.7, 154.5, 151.5, 143.0, 139.8, 133.7, 130.9 (CH), 129.4 (CH), 116.1, 103.4 (CH), 53.6 (CH_2), 49.7 (CH_2), 26.1 (CH_2), 25.8(CH_2), 24.3 (CH_2), 23.9 ppm (CH_2); ESI MS (ES^+) m/z: 491 (M^+ + 1), 513 (M^+ +Na), 529 (M^+ +K); elemental analysis calcd (%) for $C_{27}H_{34}N_6O_3$: C 66.10, H 6.99, N 17.13; found: C 66.36, H 7.01, N 17.07.

4-nitro-5-(2,4,6-trimorpholin-4-ylphenyl)-2,1,3-benzoxadiazole (12). Brown solid 0.012 g (32%); m.p.: 281.3–281.8 °C; ^{1}H NMR (400 MHz $CDCl_3$): δ = 7.98, (d, 1 H, *J* = 9.5 Hz), 7.57 (d, 1 H, *J* = 9.5 Hz), 6.47 (s, 2 H), 3.92–3.86 (m, 4 H), 3.54-3.44 (m, 8 H), 3.30-3.25 (m, 4 H), 2.86-2.77 (m, 4 H), 2.76-2.67 ppm (m, 4 H); ^{13}C NMR (100.46 MHz, $CDCl_3$): δ = 153.9, 152.3 (2 sign. overl.), 149.0, 143.9, 138.8 (CH), 134.7, 118.5 (CH), 117.4, 102.8 (CH), 66.68 (CH_2), 66.66 (CH_2), 52.5 (CH_2), 48.3 ppm (CH_2); ESI MS (ES^+) m/z: 497 (M^+ + 1), 519 (M^+ +Na); elemental analysis calcd (%) for $C_{24}H_{28}N_6O_6$: C 58.06, H 5.68, N 16.93; found: C 58.20, H 5.70, N 16.88.

5-nitro-4-(2,4,6-trimorpholin-4-ylphenyl)-2,1,3-benzoxadiazole (13). Brown solid 0.024 g (64%); m.p.: 289.0–290.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, 1 H, *J* = 9.46 Hz), 7.89 (d, 1 H, *J* = 9.46 Hz), 6.56 (s, 2 H), 3.92-3.85 (m, 4 H), 3.35-3.23 (m, 12 H), 2.81-2.70 (m, 4 H), 2.70-2.60 ppm (m, 4 H); ^{13}C NMR (100.46 MHz, $CDCl_3$): δ = 153.9, 152.6 (2 sign overl.), 150.4, 148.7, 148.0, 127.4 (CH), 125.9, 115.5 (CH), 104.1 (CH), 66.8 (CH_2), 66.7 (CH_2), 52.4 (CH_2), 48.4 ppm (CH_2); HRMS (ESI-TOF) m/z calcd for $C_{24}H_{29}N_6O_6$: 497.214859 $[M + H]^+$; found 497.2150; elemental analysis calcd (%) for $C_{24}H_{28}N_6O_6$: C 58.06, H 5.68, N 16.93; found: C 58.18, H 5.69, N 16.90.

4-nitro-7-(2,4,6-trimorpholin-4-ylphenyl)-2,1,3-benzoxadiazole (14). Brown solid 0.015 g (40%); m.p.: >300 °C (dec); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.56 (d, 1 H, *J* = 7.7 Hz), 7.64 (d, 1 H, *J* = 7.7 Hz), 6.55 (s, 2 H), 3.92-3.88 (m, 4 H), 3.35-3.25 (m, 8 H), 2.75-2.67 ppm (m, 8 H); ^{13}C NMR (150.80 MHz, $CDCl_3$): δ = 154.0, 153.4, 151.3, 142.8, 138.2, 134.5, 130.4 (CH), 129.7 (CH), 117.1, 103.5 (CH), 66.9 (CH_2), 66.7 (CH_2), 52.4 (CH_2), 48.4 ppm (CH_2). HRMS (ESI-TOF) m/z calcd for $C_{24}H_{29}N_6O_6$: 497.214859 $[M + H]^+$; found 497.2150; elemental analysis calcd (%) for $C_{24}H_{28}N_6O_6$: C 58.06, H 5.68, N 16.93; found: C 58.19, H 5.67, N 16.91.

4-nitro-5-(2,4,6-tripyrrolidin-1-ylphenyl)-2,1,3-benzoxadiazole (16). Blue solid 0.028 g (83%); m.p.: 204.1–204.9 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.82, (d, 1 H, *J* = 9.7 Hz), 7.63 (d, 1 H, *J* = 9.7 Hz), 5.99 (s, 2 H), 3.40-3.31 (m, 4 H), 2.95-2.85 (m, 4 H), 2.85-2.74 (m, 4 H), 2.07-1.97 (m, 4 H), 1.79-1.64 ppm (m, 8 H). ^{13}C NMR (150.80 MHz, $CDCl_3$,): δ = 150.5, 149.7, 149.0, 144.5, 141.7, 139.1 (CH), 132.8, 117.6 (CH), 109.7, 95.3 (CH), 51.5 (CH_2), 47.5 (CH_2), 25.5(CH_2), 24.9 ppm (CH_2). ESI MS (ES^+) m/z: 449 (M^+ + 1), 471 (M^+ +Na); elemental

analysis calcd (%) for $C_{24}H_{28}N_6O_3$: C 64.27, H 6.29, N 18.74; found: C 64.45, H 6.31, N 18.80.

5-nitro-4-(2,4,6-tripyrrolidin-1-ylphenyl)-2,1,3-benzoxadiazole (17). Blue solid 0.027 g (80%); m.p.: 190.8–192.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, 1 H, *J* = 9.3 Hz), 7.74 (d, 1 H, *J* = 9.3 Hz), 5.97 (s, 2 H), 3.42-3.30 (m, 4 H), 2.90-2.78 (m, 4 H), 2.68-2.58 (m, 4 H), 1.95-2.04 (m, 4H), 1.69-1.52 ppm (m, 8 H); ^{13}C NMR (100.46 MHz, $CDCl_3$): δ = 150.2, 150.1 ,149.8, 148.8, 146.6, 128.3, 128.2 (CH), 113.7(CH) , 104.7, 95.0 (CH) , 51.1 (CH_2), 47.4 (CH_2), 25.5(CH_2), 25.0 ppm (CH_2); HRMS (ESI-TOF) m/z calcd for $C_{24}H_{29}N_6O_3$ 449.230114 $[M + H]^+$; found 449.2300; elemental analysis calcd (%) for $C_{24}H_{28}N_6O_3$: C 64.27, H 6.29, N 18.74; found: C 64.43, H 6.30, N 18.78.

4-nitro-7-(2,4,6-tripyrrolidin-1-ylphenyl)-2,1,3-benzoxadiazole (18). Blue solid 0.026 g (77%); m.p.: 201.9–202.8 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.50 (d, 1 H, *J* = 7.8 Hz), 7.46 (d, 1 H, *J* = 7.8 Hz), 5.97 (s, 2 H), 3.40-3.34 (m, 4 H), 2.71-2.78 (m, 8 H), 2.05-1.99 (m, 4 H), 1.61-1.53 ppm (m, 8 H); ^{13}C NMR (150.80 MHz, $CDCl_3$): δ = 151.4, 151.3 ,149.9, 142.9, 142.3, 133.2, 131.4 (CH),128.7 (CH), 107.3, 94.4 (CH), 51.8 (CH_2), 47.5 (CH_2), 25.5 (CH_2), 25.0 ppm (CH_2). ESI MS (ES^+) m/z: 449 (M^+ + 1), 471 (M^+ + Na); elemental analysis calcd (%) for $C_{24}H_{28}N_6O_3$: C 64.27, H 6.29, N 18.74; found: C 64.13, H 6.27, N 18.79.

1-(3,5-dipyrrolidin-1-ylphenyl)-1-(7-nitro-2,1,3-benzoxadiazol-4-yl)pyrrolidinium chloride (20). Brown solid, quantitative yield, ^{1}H NMR (600 MHz. $CDCl_3$): δ = 9.07 (d, 1 H, J = 7.5 Hz), 8.56 (d, 1 H, J = 7.5 Hz), 6.39 (s, 1 H), 5.40–4.80 (m, 2 H), 4.92 (s, 2H), 3.70–3.67 (m, 2 H), 3.67–3.60 (m, 2 H), 3.60–2.40 (br. ms, 6 H), 2.40–1.50 ppm (m, 12 H); ^{13}C NMR (150.80 MHz, $CDCl_3$,): δ = 160.8, 157.2, 148.3, 143.1, 136.4, 134.9 (CH), 130.8, 130.4 (CH), 86.4 (CH), 50.0 (CH_2), 49.1 (CH_2), 45.5 (CH), 25.0 (br., CH_2), 24.9 ppm (CH_2). ESI MS (ES^+) m/z: 449 (M^+).

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