Tetrahedron Letters,Vol.24,No.22,pp 2255-2258,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

Π-EXCESSIVE FIVE-MEMBERED RING HETEROAROMATICS ACTING AS CARBON NUCLEOPHILES TOWARDS AN ELECTROPHILIC AROMATIC.

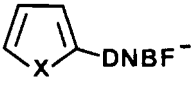
Jean-Claude Hallé, Marie-Paule Simonnin and Marie-José Pouet
Laboratoires de Physicochimie des Solutions et de Spectrographie, E.N.S.C.P.,
11 Rue Pierre et Marie Curie 75231 Paris Cedex 05 - France
François Terrier*
Laboratoire de Chimie Organique Physique, Faculté des Sciences de Rouen
76130 Mont Saint Aignan - France.

Abstract : *4,6-Dinitrobenzofuroxan adds rapidly to pyrrole, indole and their N-methyl derivatives as well as to furan to form C-bonded σ-adducts. Diastereomeric $C_\alpha, C_{\alpha'}$-diadducts also form in appreciable amounts. These results represent the first example of electrophilic addition of an aromatic substrate to Π-excessive five-membered rings acting as carbon nucleophiles*

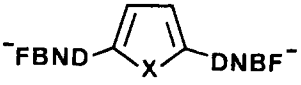
4,6-Dinitrobenzofuroxan (DNBF) is known to exhibit an extremely high electrophilic reactivity which manifests itself in the facile formation of σ-complexes with very weak but common nucleophiles like water, alcohols or enols.[1,2,3] DNBF also reacts with weakly basic heterocycles like imidazoles to yield nitrogen-bonded zwitterionic adducts.[4] In these instances, no electrophilic addition of DNBF at a C-position of the imidazole ring was observed, despite the potential ambident nucleophilic character of these heterocycles. We report here on the facile addition of DNBF at the α or β-carbon atoms of pyrrole, indole and furan derivatives The results provide the first example of electrophilic addition of an aromatic substrate to Π-excessive five-membered ring heteroaromatics acting as carbon nucleophiles.

In a dipolar aprotic solvent such as $(CH_3)_2SO$, pyrrole (1) reacts very rapidly (∿ 10 minutes) with DNBF (1 eq.) to yield a mixture of the C_α mono adduct 2 and the $C_\alpha, C_{\alpha'}$ diadduct 3 where 2 is predominant. The structures have been unambiguously deduced from ^{1}H nmr spectra. For 2, one observes an AKMX system due to the NH and the three pyrrolic protons

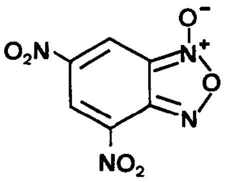
1 X=N-H
5 X=N-Me
10 X=O



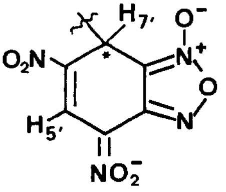
2
6
11



3
7
12



DNBF

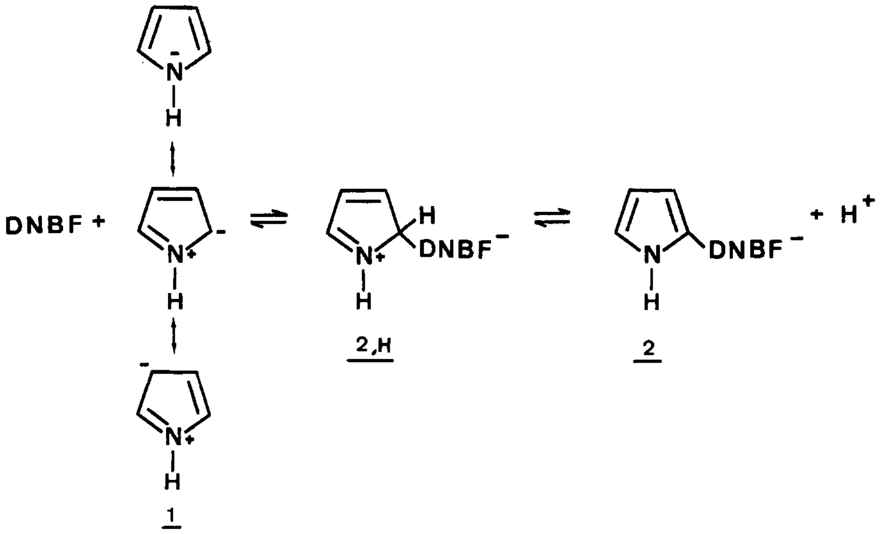


DNBF⁻

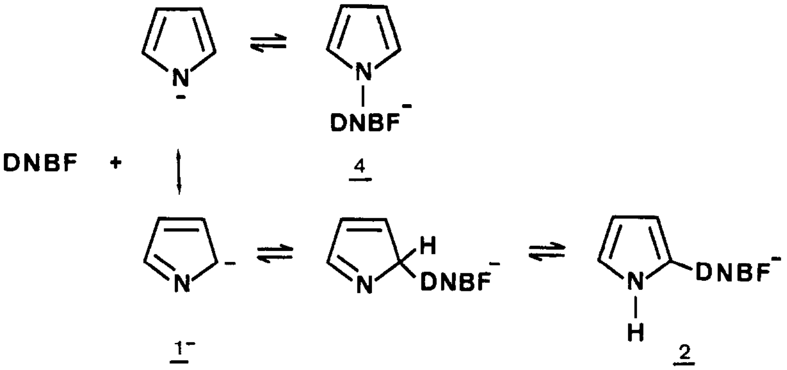
and two singlets at 8.67 and 5.44 ppm associated with the protons bonded to the sp^2 and sp^3 C-5' and C-7' carbons, respectively, of the DNBF moiety. Irradiation of the low-field NH signal changes the four spin system into a three spin one. The observed coupling constants confirm that the substitution occurs at an α position.

The 100 MHz spectrum of the diadduct reveals the presence of a high-field singlet ($\delta_{H_{7'}}$ = 5.42) and a doublet due to the pyrrolic protons ($\delta_{H_{3/4}}$ = 5.59_5). This doublet collapses to a singlet when irradiating the low-field NH signal (δ_{NH} = 10.77). This observation together with the chemical shift of the pyrrolic signal suggest the symmetrical α,α'-disubstituted structure 3. However, the presence of two asymetrical carbons should lead to diastereomeric species. Two close signals are actually observed for the H-5' proton ($\delta_{H_{5'}}$ = 8.65 , 8.64 ; $\Delta\nu \sim 1$ Hz). The presence of two diastereomers, i.e. 3a and 3b, in a 1:1 ratio is further confirmed by a 400 MHz spectrum. Then, the two H-5' signals are separated by $\Delta\nu$ =4.05 Hz and with NH irradiation , there is a doubling of the $H_{3/4}$ signal ($\Delta\nu$ = 2.36 Hz). Only the H-7' protons give a single line ($\Delta\nu < 0.90$ Hz).

There are only two possible pathways for the formation of the pyrrole adducts 2 and 3. The first that we feel the most reasonable is depicted in Scheme 1. It involves direct attack of DNBF at C-2 of the resonance contributor of neutral pyrrole to give the undetected intermediate zwitterion 2,H. This latter must rearrange very fast into 2 since rearomatization of the pyrrole ring acts as a driving force in this process. The second pathway would involve adduct formation from attack of DNBF on the pyrrolide anion generated by the ionization of pyrrole (Scheme 2). Even though equilibrium concentrations of such an anion must be exceedingly small in the absence of a strong base in $(CH_3)_2SO$, it might be argued that this anion has a much higher reactivity than neutral pyrrole and formation of 2 according to Scheme 2 can occur. In addition to the very low acidity of pyrrole,[5,6] there are several



SCHEME 1



SCHEME 2

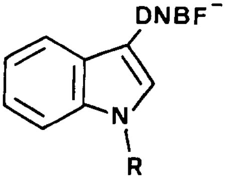
experimental arguments which disfavor this mechanism. Should pyrrolide anion to be the reactive species, this should give rise initially to the nitrogen-bonded adduct 4. Inasmuch as electrophilic attack at the nitrogen atom does not disrupt the aromaticity of the pyrrolide ring, it is always kinetically favored compared to an attack at a C_α position.[7] On this basis, the inobservation of 4 is unexpected. More importantly, we have observed that N-methyl pyrrole 5 behaves as pyrrole to yield mainly the monoadduct 6 and the diadduct 7. There is therefore no doubt that it is the neutral pyrroles which act as carbon nucleophiles towards DNBF. Scheme 1 may also account for the formation of the diadducts 3 and 7. In these instances, the mono adducts 2 and 6 simply behave as 2-substituted pyrroles, adding the electrophile at the free α' position.

These results prompted us to look at the behaviour of other heterocycles. Not surprisingly, unsubstituted indole and N-methyl indole yield the mono adducts 8 and 9. That the DNBF moiety adds to the 3-position of the indole ring is consistent with general reactivity patterns found for reaction of these derivatives with electrophiles.[8] However, a most

Table. ^{1}H NMR Parameters of σ-mono adducts.[a]

σ-Adducts	$\delta_{H_{5'}}$	$\delta_{H_{7'}}$	δ_{H_2}	δ_{H_3}	δ_{H_4}	δ_{H_5}	δ_{NH}	δ_{NCH_3}	$^3J_{H_3H_4}$	$^4J_{H_3H_5}$	$^3J_{H_4H_5}$
2 [b]	8.67	5.44	-	5.78	5.89	6.56_5	10.77	-	3.4	1.6	2.7
6	8.65	5.52	-	5.66	5.85	6.60	-	3.79	3.7	1.9	2.6
11	8.70	5.59	-	6.26	6.29	7.50	-	-	3.2	0.7	1.9
8 [c]	8.72_5	5.63	7.35	-	-	-	11.09	-	-	-	-
9 [d]	8.72	5.61_5	7.33	-	-	-	-	3.73	-	-	-

(a) δ in ppm relative to internal TMS. J in Hz (at 100 MHz, Varian XL-100, probe temperature 31°C) ; (b) $^4J_{H_3NH} = 2.6$, $^4J_{H_4NH} = 2.3$, $^3J_{H_5NH} = 2.8$;(c) $^3J_{H_2NH} = 2.6$; (d) $^4J_{H_2NCH_3} \sim 0.3$.



8 R=H
9 R=Me

noteworthy result which further confirms the mechanism of Scheme 1 is that furan (10) readily forms the monoadduct 11 and the diadduct 12 ($\delta_{H_{7'}}$ = 5.48 ; $\delta_{H_{5'}}$ = 8.67,8.66 ; $\delta_{H_{3/4}}$ = 6.17). The latter exists as a 1:1 mixture of two diastereomers 12a and 12b. The furanic $H_{3/4}$ protons of 12a and 12b which seem to be isochronous at 100 MHz are anisochronous at 400 MHz ($\Delta\nu$ = 1.2 Hz). The nmr parameters of the various monoadducts 2, 6, 8, 9 and 11 are summarized in the Table.

It should be noted that the monoadducts studied also form in acetonitrile. Due to a low solubility in this solvent, they precipitate in their "acid" form as deeply orange crystals which can be isolated. In accord with observations reported for other C-bonded DNBF complexes,[2] such adducts are highly explosive and we abandoned further attempts at isolation or elemental analysis. However, the nmr spectra obtained after an immediate dissolution of the crystals in $(CH_3)_2SO$ were identical to those recorded in the "in situ" generation of the adducts. The visible spectra are also typical of C-bonded DNBF complexes : λ_{max} = 490 nm.

These first results lead us to also examine the behaviour of some thiophenes and selenophenes. Preliminary measurements show that these compounds do react with DNBF but in a more complex manner. Structural studies are in progress.

Acknowledgements. The authors thank Mr. Daniel Davoust (Centre de Spectrochimie, Université Pierre et Marie Curie, Paris) for the 400 MHz spectra which have been recorded on a Bruker WM 400 spectrometer.

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(Received in France 14 March 1983)