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THE CATALYTIC ACTION OF BF_3 IN THE CYCLOADDITION OF BENZONITRILE OXIDE WITH NITRILES AND CARBONYL COMPOUNDS

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In the last few years,several investigations have been carried out on 1,3-dipolar reaction;the various 1,3-dipolar reagents react with systems containing 1,2-dipoles with consequent formation of five membered rings.

One of 1,3-dipoles studied in more detail certianly is benzonitrile oxide,for which a set of reactions is known (type 3 + 2 = 5)with triple- and double-bond systems[1,2], with nitriles,with carbonyl compounds,both aldehydic and ketonic,and others.In some cases, the cycloadditions relating to the systems reported above are not general in character;for example,benzonitrile oxide reacts only with aromatic nitriles[3],or with nitriles activated by an electron-attractor substituent to form oxadiazoles[4],while aliphatic nitriles are not attacked;similarly,carbonyl compounds yield dioxazoles exclusively when the carbonyl group is especially activated[5];therefore,no reaction occurs with aliphatic aldehydes, acetophenone and aliphatic ketones in general.

These considerable limitations,both for the general application of 1,3-dipolar reaction and for all possible synthetic advantage,led us to re-examine this type of reaction with nitriles and with carbonyl compounds,which under the usual conditions do not give rise to cycloaddition.We carried out these type of cycloadditions between benzonitrile oxide and nitriles,ketones and aldeydes by performing the reaction in the presence of boron etherate trifluoride.

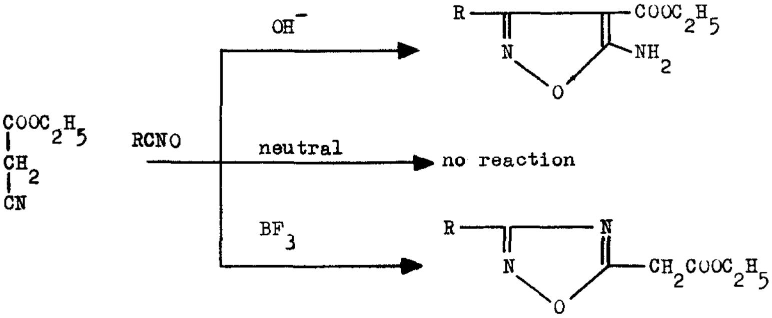
The results obtained by reaction with some nitriles with consequent formation of 1,2,4--oxadiazoles are tabulated hereinafter :

Table I

1,2,4-oxadiazoles ($R = C_6H_5$)

R'CN	**1 . 2 . 4 - oxadiazoles**			
R'=	**Yield %**	m.p.	b.p.	U.V. (EtOH) max. (log ε)
CH_3	35	41° (41°)[6]	--	238 (4.13)
C_2H_5	40	--	120°(1,5 mm)(255°)[7]	238 (4.07)
$n.C_3H_7$	40	--	130°(1.5 mm)(265°)[7]	238 (4.09)
CH_2COOEt	14	--	150° (0.5 mm)	238 (4.15)

It is interesting to observe that ethyl cyanacetate behaves in different manners :in alkaline solution,it reacts with benzonitrile oxide to form 3-phenyl-4-carboxyethyl-5-aminoisoxazole[8];in neutral medium,it is not attacked while in the presence of BF_3,it gives the corresponding oxadiazole :



Reactivity toward carbonyl compounds,both aldehydic and ketonic,has same behaviour when the reaction is carried out in the presence of BF_3 with formation of dioxazoles :

The following table reports the 1,3,4-dioxazoles that were synthesized (Table II).

A typical procedure is as follows : BF_3 etherate (0.04 moles)and later an ether solution of benzonitrile oxide (obtained from 4.5 g(0.03 moles)of chlorooxime and triethylamine) were added in a flask containing propionitrile (20 cm^3);after removing ether by heating, the reaction mixture was refluxed for about two hours[9].By concentration in vacuum,a residue was obtained,which,chromatographed in a column (Silicagel),yielded 2 g of pure 3-phenyl-5-ethyl-1,2,4-oxadiazole with a 40 % yield.

Table II

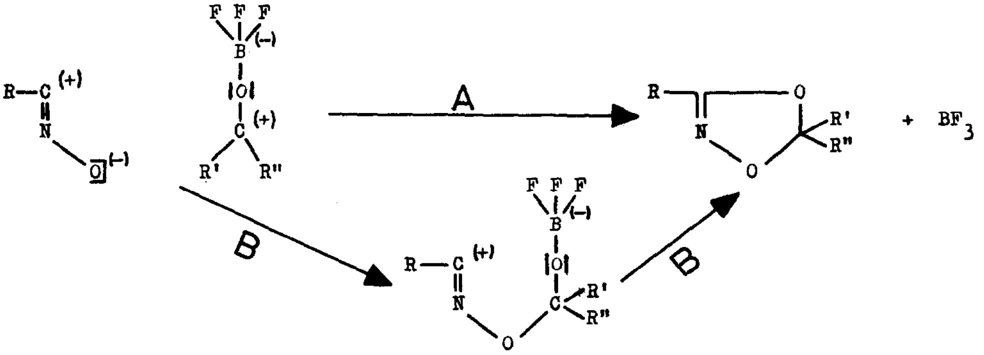
1,3,4 - dioxazoles (R = C_6H_5)

R'-CO-R"		1 , 3 , 4 - dioxazoles			
R'	R"	Yield%	m.p.	b.p.	U.V.(EtOH) max.(logε)
CH_3	H	40	--	80° (0.5 mm)	214 (3.90) 265 (3.76)
n.C_3H_7	H	25	--	140° (2 mm)	216 (4.02) 268 (3.83)
CH_3	CH_3	49	--	90° (1.5 mm)	215 (4.02) 267 (3.87)
CH_2Cl	CH_2Cl	28	48°	150° (1.5 mm)	262 (3.98)
CH_3	C_2H_5	40	--	100° (2 mm)	216 (4.03) 267 (3.87)
CH_3	C_6H_5	15	64°	--	265 (3.93)
cyclohexanone		50	--	140° (2mm)	217 (4.05) 270 (3.86)

The experimental data reported above do not allow a definitive interpretation of the mechanism of the reaction investigated, but consent us to draw some general remarks.

It is actually known that BF_3, in analogy with other Lewis acids, can give co-ordination compounds with aldehydes, ketones and nitriles[10], thus modifying the original system, as it increases its dipole character and electrophilic power. The considerable change in reactivity of benzonitrile oxide toward the BF_3-activated systems experimented by us, makes it clear that, in view of cycloaddition, the change of the substrate is essential.

To account for it, we might say that, along with the planned cycloaddition scheme (scheme A), it would also seem possible an intial nucleophilic attack on the "catalysed" electrophilic carbon, followed by a more or less fast closing of the cycle (scheme B) :



On the other hand, we think it important to notice that a cycloaddition is for the first time carried out in the presence of an electrophilic catalyst, such as a Lewis acid, while other examples are known of formation of products of different nature[11].

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