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A Novel NO Insertion into Cyclopropane Ring by Use of $NOBF_4$. Formation of 2-Isoxazolines

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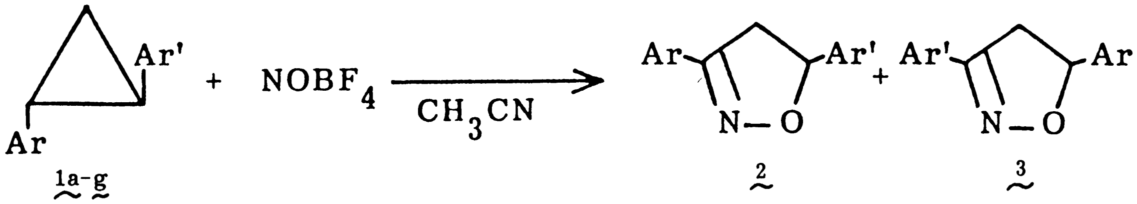
The reaction of 1,2-diarylcyclopropanes with $NOBF_4$ in CH_3CN gave 3,5-diaryl-2-isoxazolines in good yields. For unsymmetrically substituted cyclopropanes, the mixtures of two isomeric isoxazolines were obtained. The mechanism and regioselectivity in this NO insertion into the cyclopropane ring are described.

Nitrosonium salts are known to act as electrophilic nitrosation reagent and as oxidizing reagent for organic compounds.[1-3)] These salts also generate radical cations of organic compounds via one-electron transfer from organic compounds to these salts.[4,5)] However, little is known about the NO insertion to carbon-carbon single bond.[6)] We now report a novel NO insertion reaction into cyclopropane ring of 1,2-diarylcyclopropanes by use of $NOBF_4$ to give 3,5-diaryl-2-isoxazolines.

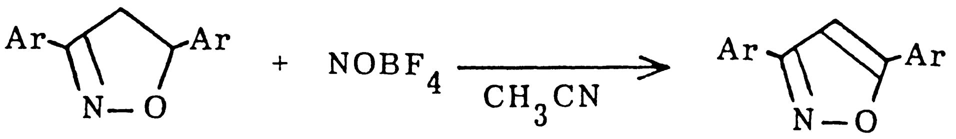
The nitrosonium salt $NOBF_4$ (0.022 mol dm^{-3}) was added to an acetonitrile solution of 1,2-bis(4-methoxyphenyl)cyclopropane **1a** (0.02 mol dm^{-3}) under argon atmosphere. The solution rapidly turned red-violet which gradually disappeared within 30 min. After the disappearance of the color, 10% of aqueous Na_2CO_3 solution 20 cm^3 was added, and the mixture was extracted with two 30 cm^3 portions of benzene. Organic layer was washed with water, dried over Na_2SO_4, and



a : Ar = Ar' = $4\text{-}CH_3OC_6H_4$; **b** : Ar = Ar' = $4\text{-}CH_3C_6H_4$;
c : Ar = Ar' = $4\text{-}ClC_6H_4$; **d** : Ar = Ar' = C_6H_5;
e : Ar = Ar' = $4\text{-}CNC_6H_4$;
f : Ar = C_6H_5, Ar' = $4\text{-}CH_3OC_6H_4$;
g : Ar = $4\text{-}ClC_6H_4$, Ar' = $4\text{-}CH_3C_6H_4$

evaporated under reduced pressure. Recrystallization of the residue from methanol gave 3,5-bis-(4-methoxyphenyl)-2-isoxazoline (**2a** 88%), and a small amount of 3,5-bis(4-methoxyphenyl)-2-isoxazole (**4a** < 5%). The structures of these products were determined by elemental analyses, spectral properties,[7)] and also by the following chemical transformations. The pyrolysis of **2a** at > 200 °C gave 4-methoxybenzonitrile, 4-methoxyacetophenone, and a small amount of 4-methoxybenzaldehyde.[8)] The oxidation of **2a** with DDQ in benzene or CrO_3 in acetic acid gave **4a** in nearly quantitative yield.[8)] The reaction of **1a** with two equiv of $NOBF_4$ gave **4a** which was apparently formed by oxidation of **2a** with $NOBF_4$. Similar treatments of other 1,2-diarylcyclopropanes with $NOBF_4$ afforded the corresponding 3,5-diaryl-2-isoxazolines. The results are summarized in Table 1. The yield of 2-isoxazolines decreased with increasing the oxidation potentials of the starting cyclopropanes. In the case of **1e**, the NO insertion did not occur, but **1e** was recovered.

When unsymmetrically substituted 1,2-diarylcyclopropanes **1f**-**g** were used as substrates, the NO insertion occurred regioselectively, giving **2f**-**g** as major products.



2a **4a**

Ar = 4-$CH_3OC_6H_4$

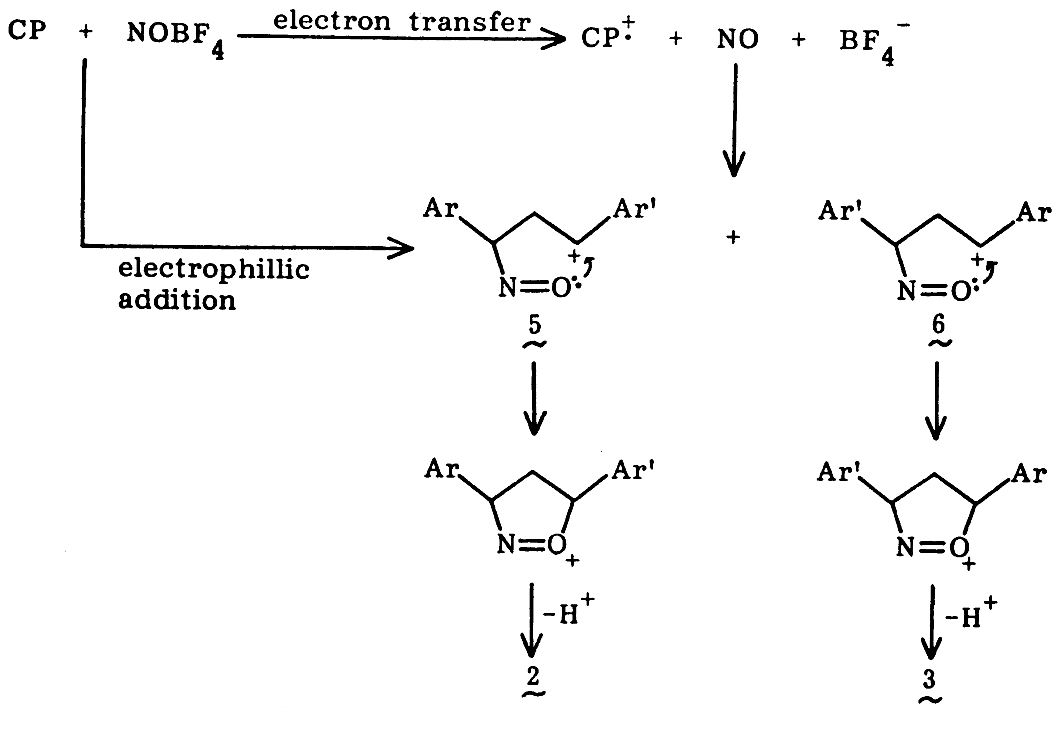
Table 1. The NO Insertion into Cyclopropanes

Compd	$E_{p/2}^{ox}$ /V[a)]	Yield/%[b)]	Isomer ratio[c)]	Mp of **2**/°C
		2 + **3**	**2** : **3**	
1a	0.55	88		141-142
1b	0.90	80		106-107
1c	1.06	38		96-97
1d	1.14	26		73-74
1e	1.26	0		
1f	0.75	70	9 : 1	105-106
1g	1.00	45	7 : 3	

a) Oxidation potentials of cyclopropanes vs. Ag/Ag^+ in acetonitrile. b) Isolated yields of isoxazolines.
c) Determined by 270 MHz ^1H NMR.

A plausible mechanism for the NO insertion reaction is shown in Scheme 1. The first step is the one-electron transfer from 1,2-diarylcyclopropanes (CP) to $NOBF_4$ to produce their radical cations $CP^{+\cdot}$ and NO. This process was rationalized by the following experiments. A catalytic amount of $NOBF_4$ (1/50 equiv.) caused a rapid cis-trans isomerization of 1a giving a stationary state mixture of cis-1a and trans-1a in a 5 : 95 ratio. The formation of radical cation of 1a was also supported by a red-violet coloration of the reaction mixture, whose absorption maximum was at 560-570 nm.[10] The production of NO was recognized by evolution of NO_2 upon introducing air into the reaction mixture. The second step is the attack of NO on $CP^{+\cdot}$ to give cation intermediates 5 and 6. The intramolecular ring closure of these cations, followed by deprotonation, gives 2-isoxazolines. The regioselectivity in the NO insertion into unsymmetrically substituted 1,2-diarylcyclopropanes may be determined by the stability of the cation intermediates: the cation intermediates 5f-g would be more stable than 6f-g by electron-donating substituents on Ar'.

The other mechanism that involved the direct attack of NO^+ to the cyclopropane ring can not be ruled out at present.[6a)]



Scheme 1.

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7) **2a**: mp 141-142 °C. ^{1}H NMR(CDCl$_3$, 270 MHz) δ = 3.30(1H, dd, J = 8.6 and 17.2 Hz), 3.71(1H, dd, J = 10.9 and 17.2 Hz), 3.81(3H, s), 3.84(3H, s), 5.66(1H, dd), 7.11(4H, ABq, J = 8.5 Hz, $\Delta\nu$ = 109.7 Hz), 7.28(4H, ABq, J = 9.3 Hz, $\Delta\nu$ = 195.0 Hz). MS(70 eV) 283(M$^+$). Found: C, 72.13; H, 6.13; N, 4.96%. Calcd for $C_{17}H_{17}O_3N$: C, 72.06; H, 6.05; N, 4.94%.
4a: mp 176-177 °C. ^{1}H NMR(CDCl$_3$, 270 MHz) δ = 3.86(6H, s), 6.65(1H, s), 7.39 (4H, ABq, J = 9.2 Hz, $\Delta\nu$ = 230 Hz), 7.40(4H, ABq, J = 9.2 Hz, $\Delta\nu$ = 224 Hz). MS(70 eV) 281(M$^+$). Found: C, 72.64; H, 5.29; N, 5.06%. Calcd for $C_{17}H_{15}O_3N$: C, 72.58; H, 5.37; N, 4.98%.

8) R. G. Shotter, D. Sesardic, and P. H. Wright, Tetrahedron, 31, 3069(1975); G. Bianchi and M. De Amich, J. Chem. Res. (S), 1979, 311.

9) The ratio of cis-**1a** to trans-**1a** was exactly the same as that obtained from the 9,10-dicyanoanthracene sensitized photoisomerization of **1a** via photoinduced electron transfer: K. Mizuno, Z. Hiromoto, K. Ohnishi, and Y. Otsuji, Chem. Lett., 1983, 1059.

10) The same absorption spectrum of the radical cation of **1a** was observed by the one-electron oxidation of **1a** by use of Cu(BF$_4$)$_2$ or anodic oxidation: N. Ichinose, K. Mizuno, and Y. Otsuji, unpublished results.

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