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Nitrosonium (NO^+) initiated and cation radical-mediated imino Diels–Alder reaction

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Abstract—An efficient aza-Diels–Alder reaction of *N*-arylimines with *N*-vinylpyrrolidinone was achieved using nitrosonium tetrafluoroborate as a cation radical initiator, giving *cis*-4-(2-oxopyrrolidin-1-yl)tetrahydroquinolines in various yields.

Many new approaches for preparing tetrahydroquinoline derivatives have been developed so far,[1] due to the tetrahydroquinoline skeleton being a fundamental structural unit of numerous alkaloids and biologically active compounds. Among these methods, the imino Diels–Alder reaction between *N*-arylimines and electron-rich alkenes probably has been the most powerful synthetic entry to tetrahydroquinolines.[1b,c] These imino Diels–Alder reactions have been reported to be catalyzed by $BF_3{\cdot}Et_2O$ and other Lewis acids,[2] lanthanide triflate,[3] triphenyl phosphonium perchlorate,[4] 2,3-dichloro-5,6-dicyano-*p*-benzoquinone,[5] Ti(IV) complex,[6] chiral copper complex,[7] samarium diiodide,[8] and protic acids.[9] Although cation radical-mediated Diels–Alder reactions have been studied,[10] a requirement for developing synthesis routes accessible to tetrahydroquinolines is still in high demand.[11]

Nitrosonium (NO^+) is a strong one-electron oxidant with a rather high reduction potential of $E^0_{red} = 1.50$ V (vs SCE).[12] Nitric oxide (NO) is its redox partner. The lower reorganization energy of the pair NO^+/NO in acetonitrile, 70 kcal mol^{-1}, argues that NO^+ is predicted to be an effective nonbonding electron transfer oxidant.[13] Our interest in NO^+ has promoted us to investigate NO^+-participating in reactions.[14] Based on previous works on this kind of reaction, we have performed the NO^+-induced and cation radical-mediated aza-Diels–Alder reaction of *N*-arylimines (**1**) with *N*-vinylpyrrolidinone (**2**), which gave tetrahydroquinolines in various yields.

In a typical experiment, 0.5 mmol of *N*-arylimines (**1**) and 0.6 mmol of *N*-vinyl-2-pyrrolidinone (**2**, 1.2 equiv) were dissolved in 20 mL of anhydrous dichloromethane (CH_2Cl_2). At room temperature, 25 μmol of nitrosonium tetrafluoroborate (0.05 equiv) pasted onto a piece of glass was added to the above well-stirred solution. The reaction completed in about 2 h, giving the single products, *cis*-4-(2-oxopyrrolin-1-yl)tetrahydroquinolines (**3**) in various yields (Table 1). All the products were characterized by IR, MS, ^1H and ^{13}C NMR, in good accord with literatures.[15] The production of only one isomer indicated that reactions occurred highly regiospecifically (Scheme 1). The yields of **3** appear good or satisfactory, except for entry 10, where the substituent of *o*-Me seems to be unfavorable for this reaction. Prolonged reaction time of 25 h for **1j** gave a yield of 21%, while 50% of **1j** decomposed to the corresponding benzaldehyde and aniline and the residual part of **1j** was left in the reaction mixture.

It is found that NO^+ itself will oxidize **1** to the corresponding aldehydes and benzenediazonium salts.[14c] However, our present results indicate that the existence of an electron-rich dienophile such as **2** will greatly change the reaction pattern of NO^+. The **2** has a lower oxidation potential of 1.12 V (vs SCE)[15a] for its C–C double bond than **1** ($E_{ox} = 1.50$–1.89 V vs SCE)[15] for its C–N double bond. Therefore, a single electron oxidation of **2** with NO^+ will be expected to occur at its C–C double bond prior to the C–N double bond of **1**, giving the cation radical, $\mathbf{2}^{+\cdot}$. A test of α-methylstyrene used as a dienophile instead of **2** was carried out. Yet, no reaction under consideration took place. The reason is attributed to the higher oxidation potential of

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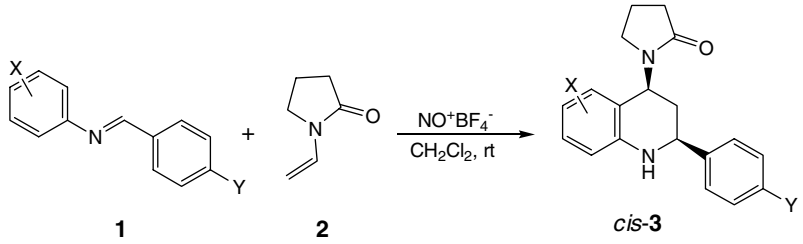
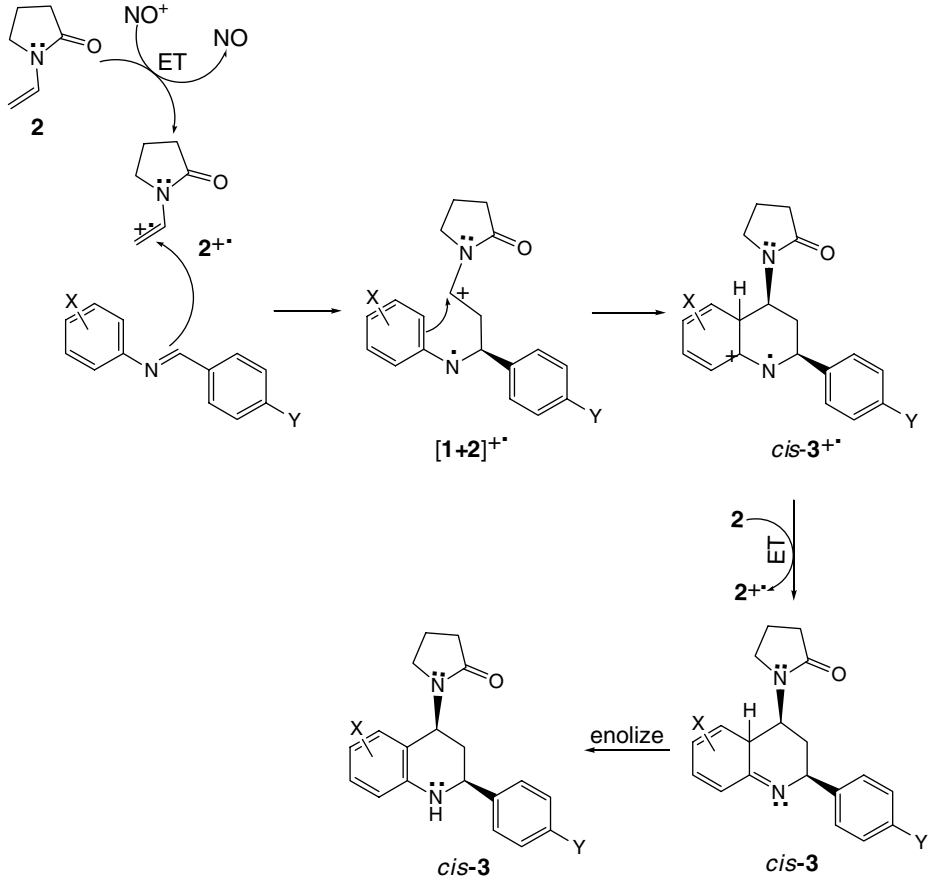
Table 1. NO^+ initiated Diels–Alder reactions of *N*-arylimines with *N*-vinylpyrrolidinone in CH_2Cl_2 at room temperature

Entry	Arylimine			*t* (h)	Yield of *cis*-**3**[a] (%)
		X	Y		
1	**1a**	*p*-OCH_3	H	3	72
2	**1b**	*p*-CH_3	*p*-NO_2	1.5	91
3	**1c**	H	*p*-OCH_3	2	89
4	**1d**	H	H	1	94
5	**1e**	H	*p*-Cl	1.5	79
6	**1f**	H	*p*-NO_2	1	64
7	**1g**	*p*-Br	H	1	95
8	**1h**	*p*-Cl	H	1	96
9	**1i**	*p*-Cl	*p*-NO_2	2	93
10	**1j**	*o*-Me	H	25	21

[a] Isolated yield based on **1**.



Scheme 1.



Scheme 2.

α-methylstyrene ($E_{ox} = 1.72$ V vs SCE).[15b] The stoichiometry study shows that a very small NO^+ amount of 5% will start reactions, which reveals that NO^+ plays a role of initiator in the reaction. The electron transfer (ET) reaction initially occurs between NO^+ and the C–C double bond of **2**, giving $\mathbf{2}^{+\cdot}$. The attack by the C–N π-electrons of **1** on $\mathbf{2}^{+\cdot}$ results in a nucleophilic addition, forming $[\mathbf{1}+\mathbf{2}]^{+\cdot}$. π-Electrons on the benzene ring linked directly to the nitrogen atom of $[\mathbf{1}+\mathbf{2}]^{+\cdot}$ then undergoes an intramolecular nucleophilic attack at its cationic center to give a cyclization compound, *cis*-$\mathbf{3}^{+\cdot}$. The resulting *cis*-$\mathbf{3}^{+\cdot}$ sequentially undergoes an electron transfer reaction with **2**, providing *cis*-**3** and $\mathbf{2}^{+\cdot}$, respectively. The $\mathbf{2}^{+\cdot}$ so produced will participate in the reaction. Studies indicated that there was an 1:1:1 mol relationship between **1**, **2**, and **3**. A more detailed mechanism is proposed as illustrated in Scheme 2.[15] The fact that the *o*-Me substituent in **1j** greatly slowed the reaction indicated that the intramolecular nucleophilic cyclization was the rate-limiting step for the imino Diels–Alder reaction.

As an example, further study was carried out to extend the substrate scope for **1d** and *N*-vinylcarbazole. The oxidation potential of the latter is 1.30 V vs SCE.[15a] The reaction occurred to give a mixture of cis and trans isomers in the ratio of 4:1, determined by ^{1}H NMR spectra, and in 95% total yield. The steric block of carbazole ring promotes the formation of trans isomer.

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