AROMATIC N-OXIDES AS 1,3-DIPOLES AND π-DONORS IN REACTIONS WITH UNSATURATED COMPOUNDS.

REVIEW

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A summary is given for the data on 1,3-dipolar cycloaddition reactions of aromatic N-oxides, which are convenient one-step methods for the synthesis of several heterocyclic compounds. Special attention was given to N-oxides as possible ambident donors in the formation of molecular complexes with dipolarophiles.

The higher activity of aromatic N-oxides in comparison with the corresponding bases both relative to electrophilic and nucleophilic reagents has made these compounds very important synthones in the preparation of pyridine derivatives [1, 2]. However, the synthetic value of N-oxides in ring substitution has not been exhausted. These compounds may also be seen as nitrone analogs characterized by 1,3-dipolarophilic cycloaddition reactions.

The present review covers the reactions of aromatic N-oxides with dipolarophiles proceeding through various mechanisms though all involve initial formation of [3+2]-cycloadducts I and II (Schemes 1 and 2).

1. GENERAL CHARACTERISTICS OF DIPOLAR CYCLOADDITION TO AROMATIC N-OXIDES

Most of the reactions of nitrones with dipolarophiles lead to rather stable five-membered isoxazolidine cycloadducts [3]:

\[ \text{[isoxazolidine]} \]

In contrast to nitrones, the N-oxide 1,3-dipole is often included within an aromatic system, which breaks down upon the formation of new bonds. Thus, on one hand, N-oxides are less reactive than nitrones relative to dipolarophiles and, on the other, when the cycloaddition reaction nevertheless occurs, it is usually accompanied by further rearrangements. The driving force for most of these secondary reactions is the restoration of the aromaticity of the heterocyclic ring lost in the primary cycloadducts. The major directions for such reactions are given in Schemes 1 and 2.

Although primary cycloadducts I and II have been only rarely isolated, their prior formation is assumed in all the reactions described below.

The major condition for cycloaddition is the complementary nature of the reagents. However, in most reported reactions, the electron density in the N-oxide is greater than in dipolarophiles. Thus, there is matching of the reagents: The
most reactive dipolarophiles have the greatest number of electron-withdrawing substituents, while the most reactive N-oxides have the greatest number of electron-donor substituents. Furthermore, the activity of N-oxides increases in going from monocyclic to polycyclic compounds. The question of the possibility of carrying out reactions with inversed electronic nature of the reagents still remains open. In this regard, considerable interest is found in the work of Wittig and Steinhoff [4], who described the reaction of quinoline N-oxide or pyridine N-oxides containing electron-withdrawing substituents with 1,4-epoxy-1,4-dihyronaphthalene:

![Chemical structure](image)

In this case, the reaction occurs between the HOMO of the dipolarophile and LUMO of the N-oxide. We should note that a stable [3+2]-cycloadduct is isolated as the reaction product.

We should also note that some of the most active dipolarophiles are also strong π-acceptors capable of forming charge transfer complexes with potential electron donors, including aromatic N-oxides.

In analyzing the literature data, the major pathways for the reactions of N-oxides with unsaturated compounds may be discerned.

### 2. FORMATION OF A STABLE CYCLOADDUCT

The formation of a stable cycloadduct has been observed in only a few cases upon the reaction of N-oxides with strained ethylenic dipolarophiles. The driving force for such reactions is apparently a reduction in the strain in these molecules [4, 5].

**Scheme 1**

**Mechanism for the Reaction of N-Oxides with Alkenes and Heterocumulenes**

![Diagram](image)

**Scheme 2**

**Mechanism for the Reaction of N-Oxides with Alkynes**

![Diagram](image)

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