



# Regioselectivity of the *ortho*- and *para*-semidine, and diphenylene rearrangements



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## ABSTRACT

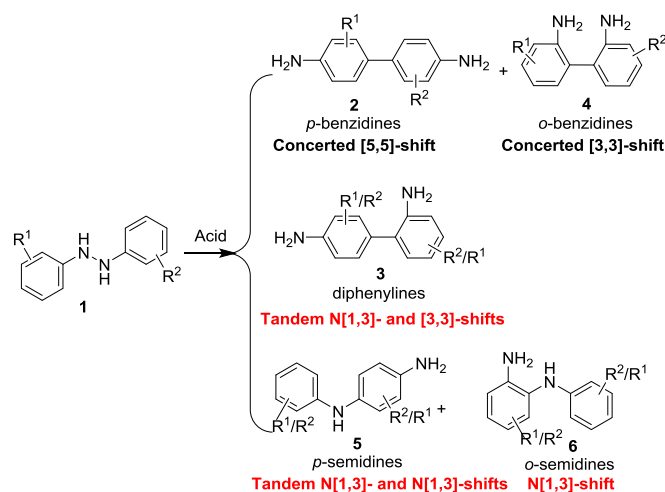
The regioselectivity of the *o*-semidine, *p*-semidine, and diphenylene rearrangements of unsymmetrical *N,N'*-diarylhydrazines was studied experimentally. The results indicate that their electron-rich nitrogen atom is first protonated and then the electron-poor non-protonated nitrogen atom undergoes an N[1,3]-sigmatropic shift to the *ortho*-position of the electron-rich aryl rings, generating key intermediates. The intermediates can undergo (1) a direct proton transfer to give *o*-semidines, (2) a second N[1,3]-shift of the electron-poor nitrogen atom and then proton transfer to furnish *p*-semidines, and (3) a [3,3]-sigmatropic shift and subsequent proton transfer to yield diphenylenes. It is the first N[1,3]-sigmatropic shift step that plays an important role in controlling the regioselectivity in the three rearrangements, further determining the structures of *o*-semidines, *p*-semidines, and diphenylenes. The current results provide new insights into the *o/p*-semidine and diphenylene rearrangements and useful information for controlling and predicting the structures of the rearrangement products.

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## 1. Introduction

The acid-catalyzed benzidine rearrangements have been studied extensively for more than 150 years.<sup>1</sup> Numerous examples have demonstrated that the benzidine rearrangements of *N,N'*-diarylhydrazines **1** gave five types of products, namely *p*-benzidines **2**, diphenylenes **3**,<sup>2,3</sup> *o*-benzidines **4**, *p*-semidines **5**, and *o*-semidines **6** (Scheme 1).<sup>4</sup> The product distribution was dependent on the substituents on the two aryl rings. A large amount of work has been devoted to the mechanisms of the benzidine rearrangements. For *o*-benzidine and *p*-benzidine rearrangements, concerted [3,3]- and [5,5]-sigmatropic shifts were proposed, respectively, on the basis of kinetic isotope effect (KIE) results on nitrogen and carbon atoms.<sup>5–7</sup> Very recently, we proposed the formation mechanisms for *o*-semidines, *p*-semidines, and diphenylenes on the basis of combined experimental and computational investigation.<sup>8</sup> We proposed the N[1,3]-sigmatropic shift for the *o*-semidine rearrangement, the tandem N[1,3]/N[1,3]-sigmatropic shifts for the *p*-semidine rearrangement, and tandem N[1,3]/[3,3]-sigmatropic shifts for the

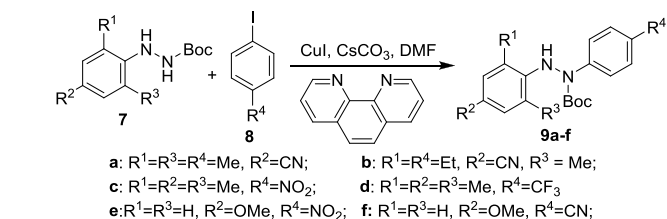
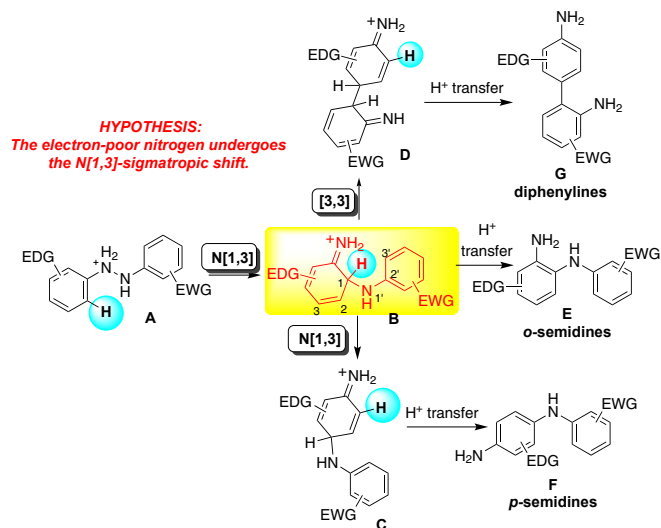
diphenylene rearrangement.<sup>8</sup> Our proposed mechanisms are in good agreement with the Shine's KIE results.<sup>5c,e,7</sup>



**Scheme 1.** The rearrangement products and their established mechanisms in the benzidine rearrangement of *N,N'*-diarylhydrazines.

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**Scheme 3.** Regioselectivity in the *o*-semidine rearrangement of 2,4,4',6-tetrasubstituted *N,N'*-diaryldiazines **9a–d**.

The rearrangements of *N,N'*-diaryldiazines have still been widely applied recently in the preparation of biaryl compounds, such as biphenyl-based cyclophanes<sup>9</sup> and 2,2'-diamino-1,1'-biaryl-type asymmetric catalytic ligands<sup>10</sup> via *p*-benzidine and *o*-benzidine rearrangements. However, the *o*-semidine, *p*-semidine, and/or diphenylene products have been obtained in considerable yields, even as major products, from certain substituted *N,N'*-diaryldiazines,<sup>8,11</sup> providing valuable and metal-free alternative synthetic routes to certain aminodiarylamines and diaminobiaryls, especially halogen-substituted ones. Some halogen-substituted aminodiarylamines and diaminobiaryls, especially bromo substituted ones, are challenging to be accessed via Ullman or Suzuki coupling reactions due to the chemoselective or regioselective control of two halo groups. Thus, the *o*-semidine, *p*-semidine, and diphenylene rearrangements provide a good choice for their preparation. A survey on previously reported and our recent results indicates that the *o*-semidine, *p*-semidine, and diphenylene rearrangements show some regioselectivity.<sup>8,11</sup> To apply these rearrangements efficiently in synthesis of aminodiarylamines and diaminobiaryls, herein, we present our studies on the

regioselectivity of the *o*-semidine, *p*-semidine, and diphenylene rearrangements of unsymmetrical *N,N'*-diaryldiazines.

## 2. Results and discussion

### 2.1. Hypothesis on the regioselectivity

After carefully analyzing the formation mechanisms of *o*-semidines, *p*-semidines, and diphenyline, we can find that all of these three rearrangements start from the first *N*[1,3] sigmatropic shift, however, the competition among the subsequent proton transfer, the second *N*[1,3] sigmatropic shift, and [3,3] sigmatropic shift decides the product distribution. The product distribution (chemoselectivity) is controlled by the properties of substituents of *N,N'*-diaryldiazines. From above analysis, we can suggest that the first *N*[1,3] sigmatropic shift plays an important role in controlling the regioselectivity of the *o*-semidine, *p*-semidine, and diphenylene rearrangements.

According to our formation mechanisms of *o*-semidines, *p*-semidines, and diphenyline,<sup>8</sup> one of two nitrogen atoms in diazines is protonated under acidic conditions, and the other nitrogen atom undergoes the *N*[1,3] sigmatropic shift. Thus, the protonation is reversible, the following *N*[1,3] sigmatropic shift is generally rate-determining step in the rearrangements.<sup>8</sup> There is no regioselective issue in rearrangements of symmetric *N,N'*-diaryldiazines. Unsymmetrical *N,N'*-diaryldiazines would show the regioselectivity in the rearrangements. Since two electronically different nitrogen atoms are present in the unsymmetrical *N,N'*-diaryldiazines (R<sup>1</sup>≠R<sup>2</sup>, Scheme 1), we rationalize that the electron-rich nitrogen atom is protonated favorably and the electron-poor one undergoes the rearrangements for unsymmetrical *N,N'*-diaryldiazines. Thus, we herein hypothesize that the basicity (electron density) of the nitrogen atoms controls the regioselectivity in the *o*-semidine, *p*-semidine, and diphenylene rearrangements of unsymmetrical *N,N'*-diaryldiazines.

The electron-rich nitrogen rather than the electron-poor one of unsymmetrical *N,N'*-diaryldiazines should be protonated to give intermediates **A**, in accordance with calculated results,<sup>8</sup> weakening the N–N bond. Subsequently, the electron-poor nitrogen atom should undergo an *N*[1,3]-sigmatropic shift to the *ortho*-position of the electron-rich aryl rings to form intermediates **B**. The intermediates **B** might evolve toward three directions: (1) the direct proton transfer to afford *o*-semidines **E**; (2) a second *N*[1,3]-sigmatropic shift to give intermediates **C**, and then proton transfer to afford *p*-semidines **F**; (3) a [3,3]-sigmatropic shift to give diphenyline intermediates **D** and then proton transfer to yield diphenyline products **G**. Next, the experimental verification of this hypothesis on the regioselectivity of the *o*-semidine, *p*-semidine, and diphenylene rearrangements will be presented.

### 2.2. Regioselectivity of *o*-semidine rearrangements

To study the regioselectivity of the *o*-semidine rearrangements, we designed 2,4,4',6-tetrasubstituted *N,N'*-diaryldiazines **9**, two nitrogen atoms with different electron densities, since they could only undergo the pericyclic *o*-semidine rearrangements, if possible. *N,N'*-Diaryldiazines **9** were readily synthesized from 2,4,6-trisubstituted *N'*-Boc-*N*-aryldiazines **7** and 4-substituted iodobenzenes **8** via the Cu(I)-catalyzed coupling reaction.<sup>12</sup> Under the acidic conditions, the Boc group of **9** would be deprotected first to release the free diazines Ar<sup>1</sup>NH–NHAr<sup>2</sup>, which would undergo the *o*-semidine rearrangements. Upon reflux in 95% ethanol for 2 h in the presence of concentrated HCl, the *N,N'*-diaryldiazines from **9a** and **9b** underwent the acid-catalyzed rearrangement to afford the *o*-semidine-type products **10a** and **10b** in 35% and 16% yields,

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