

# 2,3-Migration in Rh(II)-Catalyzed Reactions of $\beta$ -Trifluoroacetamido $\alpha$ -Diazocarbonyl Compounds

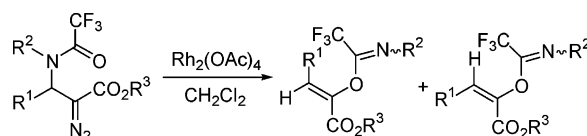
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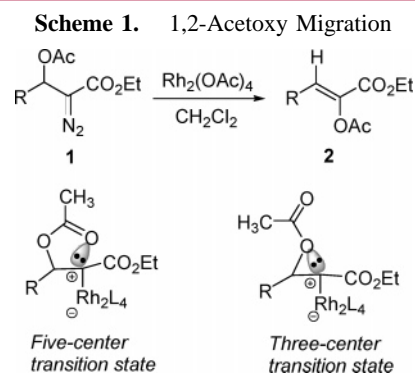
## ABSTRACT



The hydroxy group was directly converted into the trifluoroacetamido group by reacting  $\beta$ -hydroxy- $\alpha$ -diazo carbonyl compounds with trifluoroacetimidoyl chloride in the presence of DBU. Rh(II)-catalyzed reactions of these diazo compounds gave 2,3-migration products in high yields.

1,2-Migration is one of the fundamental reactions in transition-metal-catalyzed reactions of  $\alpha$ -diazo carbonyl compounds.<sup>1</sup> Among the 1,2-migration reactions, the 1,2-hydride migration is generally predominant, but 1,2-alkyl, 1,2-aryl, 1,2-thio group, 1,2-vinyl, and 1,2-acetylenyl migrations are also observed.<sup>2–4</sup> The  $\text{Rh}_2(\text{OAc})_4$ -mediated 1,2-acetoxy group migration was first reported by Ganem and co-workers in 1981,<sup>5a</sup> and later, the synthetic application of this reaction was explored by Lopez-Herrera.<sup>5b,c</sup> Mechanistically, it is believed that the 1,2-migration of acetoxy proceeds through a five-centered transition state, in which the lone pair of the

carbonyl oxygen of the acetoxy group interacts with the electron-deficient Rh(II)–carbene center (Scheme 1). If 1,2-



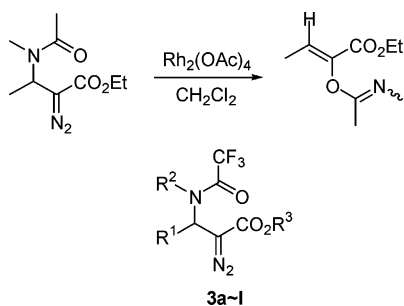
acetoxy group migration indeed proceeds through this mechanism, this should be the first example of 2,3-migration in the Rh(II)–carbene reaction. However, the acetoxy migration may also proceed through a three-centered transition state, as depicted in Scheme 1.<sup>3g</sup> In radical chemistry, a similar problem has been investigated in some detail, and it

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has been found that both three- and five-centered transition states are possible, depending on the substrates and reaction conditions.<sup>6</sup>

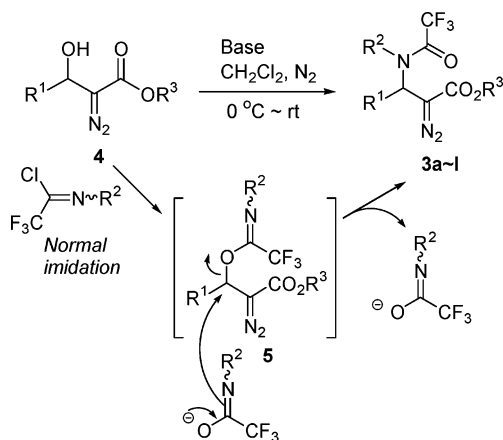
We conceived that an  $\alpha$ -diazo carbonyl compound bearing a  $\beta$ -amido group may also undergo a similar migration in a Rh(II)-catalyzed reaction to give an  $\alpha,\beta$ -unsaturated  $\alpha$ -enamino carbonyl compound. If this is the case, the migration should proceed through a five-centered transition state. In this communication, we report the Rh<sub>2</sub>(OAc)<sub>4</sub>-catalyzed reaction of diazo compounds **3a**–**1**. The results demonstrate facile 2,3-migration in the Rh(II)–carbene reaction.



In our previous study, it was found that the  $\beta$ -hydroxy group of  $\beta$ -hydroxy  $\alpha$ -diazocarbonyl compounds could be directly converted into an amido group under normal imidation conditions.<sup>3d,h</sup> Further study suggested the  $\beta$  position of the  $\alpha$ -diazocarbonyl compound was liable to nucleophilic substitution.<sup>7</sup> Thus, the diazo compounds **3a**–**1** were prepared by a similar reaction as shown in Scheme 2.

The  $\beta$ -hydroxy- $\alpha$ -diazocarbonyl compounds **4** were easily prepared by DBU-catalyzed condensation of an aldehyde with an ethyl or methyl diazo acetate.<sup>8</sup> Methyl 2-diazo-3-hydroxy-3-phenylpropionate (**4**, R<sup>1</sup> = Ph, R<sup>3</sup> = Me) was first subjected to the standard conditions of imidation<sup>9</sup> by treatment with *N*-phenyl trifluoroacetimidoyl chloride<sup>10</sup> with NaH as base and in THF between 0 °C and room temperature. The reaction gave product **3a** in 35% isolated yield. The

## Scheme 2. Preparation of **3a**–**1**



structure of **3a** was established by spectral data and X-ray crystallographic analysis.<sup>11</sup> When DBU was used as base instead of NaH, the isolated yield of **3a** was improved to 95%. For methyl 2-diazo-3-hydroxypentanoate (**4**, R<sup>1</sup> = Et, R<sup>3</sup> = Me), the reaction gave similar product **3b** in 61% yield. The structure of **3b** was also established by X-ray crystallographic analysis.<sup>11</sup>

This direct transformation of the hydroxy group to the amido group was found to be general. The  $\beta$ -trifluoroacetamido- $\alpha$ -diazo carbonyl compounds were obtained in medium to good yields (Table 1).<sup>12</sup> The yields were generally higher

**Table 1.** Preparation of **3a**–**1**

entry	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	product	yield (%) <sup>a</sup>
1	Ph	Ph	Me	<b>3a</b>	95
2	Et	Ph	Me	<b>3b</b>	61(99 <sup>b</sup> )
3	Et	Ph	Et	<b>3c</b>	68(86 <sup>b</sup> )
4	Et	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	Et	<b>3d</b>	65
5	<i>n</i> -hexyl	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	Et	<b>3e</b>	51
6	Ph	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	Et	<b>3f</b>	82
7	<i>p</i> -PhC <sub>6</sub> H <sub>5</sub>	<i>p</i> -MeOC <sub>6</sub> H <sub>4</sub>	Et	<b>3g</b>	92 <sup>c</sup>
8	Et	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	Et	<b>3h</b>	31
9	<i>n</i> -hexyl	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	Et	<b>3i</b>	33
10	Ph	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	Et	<b>3j</b>	62
11	Et	3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	Et	<b>3k</b>	48
12	Ph	3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	Et	<b>3l</b>	90

<sup>a</sup> Yields after column chromatographic purification with silica gel.

<sup>b</sup> Yields after recovering the starting material. <sup>c</sup> Yield after column chromatographic purification with neutral Al<sub>2</sub>O<sub>3</sub>.

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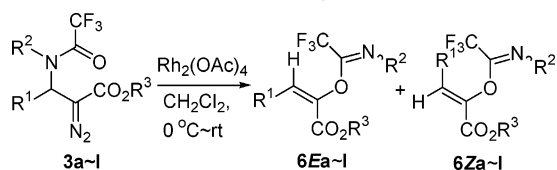
when R<sup>1</sup> was an aryl group rather than an alkyl group. When R<sup>2</sup> was *p*-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>, the diazo products **3h** and **3i** were found to be unstable on a silica gel column, which resulted in relatively low isolated yields (Table 1, entries 8 and 9).

(11) For X-ray structures, see the Supporting Information.

(12) **General procedure:** In a flamed three-necked round-bottom flask, trifluoroacetimidoyl chloride (1.0 mmol) and DBU (1.2 mmol) were added to a solution of  $\beta$ -hydroxy- $\alpha$ -diazo compound (1.0 mmol) in 10 mL of CH<sub>2</sub>Cl<sub>2</sub> under N<sub>2</sub>. The mixture was stirred for 5 h between 0 °C and room temperature. The solution was concentrated under reduced pressure, and the residue was subjected to chromatography on silica gel to afford the products **3a**–**1**.

With these  $\beta$ -trifluoroacetamido- $\alpha$ -diazocarbonyl compounds **3a–l** in hand, we proceeded to study their behaviors under the catalyst of  $\text{Rh}_2(\text{OAc})_4$ . The diazo decomposition of **3a** ( $\text{R}^1 = \text{Ph}$ ,  $\text{R}^2 = \text{Ph}$ ,  $\text{R}^3 = \text{Me}$ ) and **3b** ( $\text{R}^1 = \text{Et}$ ,  $\text{R}^2 = \text{Ph}$ ,  $\text{R}^3 = \text{Me}$ ) occurred smoothly to give a stereoisomeric mixture of products **6Ea,b** and **6Za,b**, whose structures were characterized by spectral data (Scheme 3). Because the

**Scheme 3.**  $\text{Rh}_2(\text{OAc})_4$ -Catalyzed Reaction of **3a–l**



products through a three-centered transition state might give the products with similar NMR spectral data, the structures of **6Ea** and **6Za** were further established by X-ray crystallographic analysis.<sup>11</sup>

The  $\text{Rh}_2(\text{OAc})_4$ -catalyzed reaction of other diazo compounds **3c–l** under the same conditions all gave similar results,<sup>13</sup> as shown in Table 2. In most cases, the  $\text{Rh}_2(\text{OAc})_4$ -

**Table 2.**  $\text{Rh}(\text{II})$ -Catalyzed Reaction of Diazo Compounds **3a–l**

entry	diazo substrate	yield of <b>6</b> ( <i>Z</i> + <i>E</i> ) (%) <sup>a</sup>	ratio ( <i>Z</i> : <i>E</i> ) <sup>b</sup>
1	<b>3a</b>	98	1.4:1
2	<b>3b</b>	90	2.1:1
3	<b>3c</b>	91	2.6:1
4	<b>3d</b>	99	100:0
5	<b>3e</b>	79	100:0
6	<b>3f</b>	83	1.7:1
7	<b>3g</b>	99	1.2:1
8	<b>3h</b>	97	1.6:1
9	<b>3i</b>	95	1.3:1
10	<b>3j</b>	99	2.8:1
11	<b>3k</b>	95	2.0:1
12	<b>3l</b>	99	1.5:1

<sup>a</sup> Yields after column chromatographic purification with silica gel. <sup>b</sup> Ratio determined by <sup>1</sup>H NMR (300 MHz) of the crude product.

catalyzed reaction occurred efficiently to give 2,3-migration products in high yield; however, the *Z/E* selectivity was poor, ranging from 1.2:1 to 2.8:1. The *Z* and *E* isomers were found to be difficult to separate by column chromatography. It is also interesting to note that, for the diazo compounds **3d** and **3e**, the reaction gave only *Z* isomers (Table 2, entries 4 and 5).

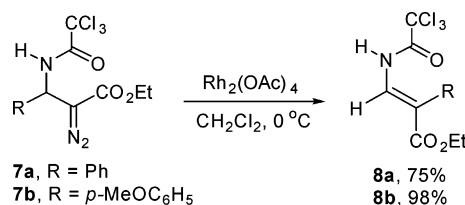
In all cases, the products due to 1,2-H migration and 1,2-aryl migration were not observed as inspected by the <sup>1</sup>H NMR of the crude products. Because previous studies have

(13) **General procedure for the  $\text{Rh}_2(\text{OAc})_4$ -catalyzed reaction:** In a flamed round-bottom flask,  $\text{Rh}_2(\text{OAc})_4$  (1 mol %) was dissolved into 10 mL of anhydrous  $\text{CH}_2\text{Cl}_2$ . A solution of diazo substrates **3a–l** in anhydrous  $\text{CH}_2\text{Cl}_2$  was added dropwise at 0 °C over the course of 15 min. The reaction mixture was stirred until TLC analysis indicated the complete disappearance of the starting material (24 h). The solvent was then removed under reduced pressure, and the crude residue was purified by column chromatography to give the corresponding 2,3-migration products.

demonstrated that 1,2-H and 1,2-aryl migrations are facile processes for  $\text{Rh}(\text{II})$ -carbene,<sup>2,3</sup> the results summarized in Table 2 demonstrate that 2,3-migration is the highly favorable pathway in the  $\text{Rh}(\text{II})$ -catalyzed reaction of **3a–l**. Although the 1,2-migration of the singlet free carbene and metal carbene has been well-known, the corresponding 2,3-migration has only been documented by the  $\text{Rh}(\text{II})$ -catalyzed 1,2-acetoxy shift.<sup>5a–c</sup> The 2,3-migration in the  $\text{Rh}(\text{II})$ -catalyzed reaction of **3a–l** is considered to be due to the favorable conformation of the five-centered transition state as depicted in Scheme 1. The current study supports the five-centered transition state that was proposed by Ganem and co-workers for 1,2-acetoxy migration.

It was interesting to compare the current results of **3a,f** with the similar  $\text{Rh}_2(\text{OAc})_4$ -catalyzed reaction of **7a,b**, which we have reported previously (Scheme 4). In the cases of **7a,b**,

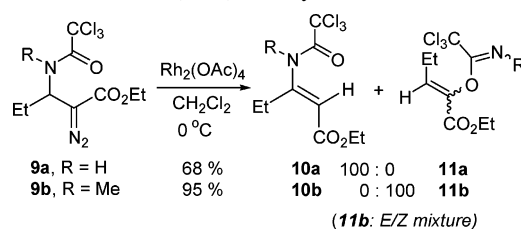
**Scheme 4.**  $\text{Rh}_2(\text{OAc})_4$ -Catalyzed Reaction of **7a,b**<sup>3d</sup>



only the 1,2-aryl migration product could be identified,<sup>3d</sup> whereas in the cases of **3a,f**, the  $\text{Rh}_2(\text{OAc})_4$ -catalyzed reaction only gave 2,3-migration products. The difference in migratory aptitude may be attributed to the N-substitution, which should affect the conformation of the transition states in the migration process. Our recent study suggests that steric factors play an important role in affecting 1,2-migratory aptitude in  $\text{Rh}(\text{II})$ -carbene reactions.<sup>14</sup> Inspection of the X-ray structures of **3a** and **3b** indicates that the amido carbonyl group is pointed to the diazo group, with the distance between the amido carbonyl oxygen and the diazo carbon being 2.815 and 2.897 Å, respectively. If the X-ray structure also represents the stable conformation of the corresponding diazo compound as well as the  $\text{Rh}(\text{II})$ -carbene intermediate in solution, then the facile 2,3-migration in these cases may be attributed to the conformational factors.

The effect of the conformation on the migratory aptitude could be demonstrated by the comparison of  $\text{Rh}_2(\text{OAc})_4$ -catalyzed reactions of **9a** and **9b** (Scheme 5). The diazo

**Scheme 5.**  $\text{Rh}_2(\text{OAc})_4$ -Catalyzed Reaction of **9a,b**<sup>3d</sup>



compound **9a**, in which the N-substitution was H, gave exclusively the 1,2-hydrogen migration product **10a**, whereas **9b**, in which the H was replaced with Me, afforded exclusively the 2,3-migration product **11b** under the same reaction conditions. These results also demonstrate that the N-acyl substituents (CF<sub>3</sub>CO vs Cl<sub>3</sub>CC=O) do not significantly affect the migratory aptitude.

In summary, we have observed 2,3-migration in the Rh(II)–carbene reaction. Similar 2,3-migration may be possible in other systems of metal–carbene reactions as well as in free carbene reactions. Moreover, this also represents a concise two-carbon homologation for converting aldehydes to  $\alpha$ -keto ester derivatives,<sup>15</sup> which are useful structural units in organic synthesis.

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**Supporting Information Available:** Experimental details and characterization data for all new compounds and X-ray crystallographic data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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