ORGANIC LETTERS

2001
Vol. 3, No. 19
2989−2992

1,2-Aryl and 1,2-Hydride Migration in Transition Metal Complex Catalyzed Diazo Decomposition: A Novel Approach to α-Aryl-β-enamino Esters

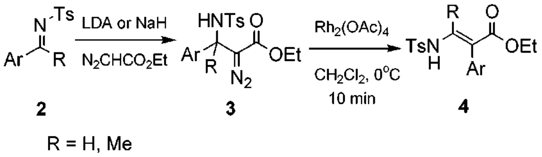
Nan Jiang, Zhaohui Qu, and Jianbo Wang*

Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, Department of Chemistry, Peking University, Beijing 100871, China

wangjb@pku.edu.cn

Received June 22, 2001

ABSTRACT



N-Tosyl diazoketamines were prepared by addition of the ethyl α-diazoacetate anion to N-sulfonylimines. The diazo decomposition of the diazoketamines with $Rh_2(OAc)_4$ complex resulted in aryl migration to give α-aryl-β-enamino esters in good yields and high stereoselectivity. The effect of the catalysts on the migratory aptitude of 1,2-aryl over 1,2-hydride migration was studied. A reaction mechanism involving a "bridged" phenonium ion is proposed.

Diazocarbonyl compounds can be decomposed by transition metal complex to generate metal carbenes, which can subsequently undergo diverse chemical transformation, including cyclopropanation, X−H (X = C, O, S, N, etc) insertion, and ylide formation.[1] In addition to these typical transformations, one can also encounter rearrangement reactions in diazo carbonyl chemistry, which involves Wolff rearrangement and 1,2-hydride or 1,2-alkyl migration. The 1,2-hydride migration, also referred to as β-hydride shift, has been frequently a competing side reaction with other metal carbene reactions when β-hydrogen is present.[2] In some cases, β-elimination can find useful application in organic synthesis. For example, Hudlicky and co-workers have devised a route to β-methoxy enones from acid chloride, based on the $Rh_2(OAc)_4$-mediated 1,2-hydride migration of α-diazo carbonyls.[3] On the other hand, 1,2-alkyl migration has been reported in the Rh(II)- or acid-promoted decomposition of diazoketols.[4] This migration has been an efficient route to β-ketoesters.

We have been interested in the α-diazo carbonyl compounds with a functional group other than carbonyl group adjacent to the diazo group **1**, since it is possible to expect new chemical properties from this type of diazo compounds, as demonstrated by the above-mentioned diazoketols and other examples.[5] In this communication, we wish to report

---

(1) For reviews, see: (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley-Interscience: New York, 1998. (b) Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091.

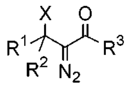
(2) (a) Franzen, V. *Liebigs Ann. Chem.* **1957**, *602*, 199. (b) Ikota, N.; Takamura, N.; Young, S. D.; Ganem, B. *Tetrahedron Lett.* **1981**, *22*, 4163. (c) Taber, D. F.; Hoerrner, R. S. *J. Org. Chem.* **1992**, *57*, 441. (d) Taber, D. F.; Hennessy, M. J.; Louey, J. P. *J. Org. Chem.* **1992**, *57*, 436. (e) Taber, D. F.; Herr, R. J.; Pack, S. K.; Geremia, J. M. *J. Org. Chem.* **1996**, *61*, 2908. (f) Ohno, M.; Itoh, M.; Umeda, M.; Furuta, R.; Kondo, K.; Eguchi, S. *J. Am. Chem. Soc.* **1996**, *118*, 7075.

(3) Hudlicky, T.; Olivo, H. F.; Natchus, M. G.; Umpierrez, E. F.; Pandolfi, E.; Volonterio, C. *J. Org. Chem.* **1990**, *55*, 4767.

(4) (a) Nagao, K.; Chiba, M.; Kim, S.-W. *Synthesis* **1983**, 197. (b) Ye, T.; McKervey, M. A. *Tetrahedron* **1992**, *48*, 8007.

10.1021/ol016324p CCC: $20.00

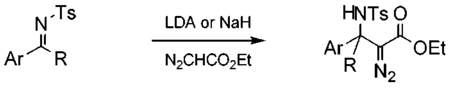
the transition metal complex catalyzed decomposition of *N*-tosyl α-diazoketamines (**1**, X = NHTs). The results show an efficient 1,2-aryl migration leading to the formation of α-aryl-*β*-enamino esters, which could serve as precursors for the synthesis of α-substituted *β*-amino acids.[6]



1 X = OH, OAc, NR'R'', etc

The *N*-tosyl diazoketamines were prepared by the addition of ethyl α-diazoacetate (EDA) anion to *N*-sulfonylimines. The deprotonation of the α-diazo acetate was generally achieved by LDA at low temperature.[7] We found that NaH was a better base for this purpose in our case. The reaction can be performed in THF at 50 °C to give the expected *N*-tosyl diazoketamines in good yields (Table 1). *N*-Sulfonylimines have attracted considerable attention in recent years, since these highly electrophilic species are capable of undergoing some unique transformations, including nucleophilic additions and cycloadditions.[9] However, as far as we know, there has been no report on the addition of the α-diazocarbonyl anion to imines.

Table 1. Addition of EDA Anion to *N*-Sulfonylimines[a]



2 R = H, Me; Ar = XC_6H_4-, $X_2C_6H_3$- **3**

entry	*N*-sulfonylimines	yield (%)[b]
1	**2a**, X = H, R = H	74
2	**2b**, X = *p*-MeO, R = H	85
3	**2c**, X = *p*-Cl, R = H	68
4	**2d**, X = *p*-Ph, R = H	79
5	**2e**, X = *m*-Br, R = H	83
6	**2f**, X = *o*-Me, R = H	87
7	**2g**, X = 2,4-dichloro, R = H	32
8	**2h**, X = 3,5-dimethoxy, R = H	70
9	**2i**, X = H, R = Me	81

[a] For general procedure, see ref 8. [b] Yield after column chromatography.

With the diazoketamines **3a**−**i** in hand, we next proceeded to examine the transition metal catalyzed diazo decomposition of these newly formed α-diazo carbonyl compounds. The α-diazoketamine **3a** was first taken as a model substrate in the investigation. In the presence of a catalytic amount of $Rh_2(OAc)_4$ in CH_2Cl_2 at 0 °C, it decomposed cleanly to give three products, which were separated by column chromatography. The structure of the main product was confirmed by spectroscopic data to be phenyl migration product **4a**, whose configuration was assigned to be *trans* on the basis of the NOSEY spectra information.[10] Two minor products, hydride migration product **5a** and the *cis* isomer of the phenyl migration product **6a**, were also confirmed. The ratio of **4a**:**6a**:**5a** was found to be 91:4:5 (Table 2).

Scheme 1

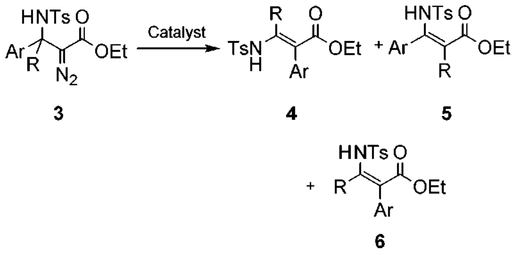


Table 2. Effect of Catalyst on 1,2-Phenyl and 1,2-Hydride Migration

entry	entry catalyst	reaction condition	product ratio[a] **4a**:**6a**:**5a**	yield[b] (%)
1	$Rh_2(OAc)_4$	CH_2Cl_2, 0 °C	91:4:5	98
2	$Rh_2(acam)_4$	CH_2Cl_2, 0 °C	85:6:9	95
3	$Rh_2(O_2CCF_3)_4$	CH_2Cl_2, 0 °C	57:4:39	97
3	$Cu(acac)_4$	CH_2Cl_2, 25 °C	56:32:12	91
5	$Cu(hfacac)_4$	CH_2Cl_2, 25 °C	38:44:18	94
6	$Cu(MeCN)_4PF_6$	CH_2Cl_2, 25 °C	64:7:29	89
7	AgO_2CPh	Et_3N, THF, reflux	23:10:67	81
8	no catalyst	$h\nu > 300$ nm, benzene, rt	42:40:18	94

[a] Product ratio was determined by ^1H NMR (400 MHz) of the crude product. [b] Yields refer to **4a**, **5a**, and **6a** combined after column chromatography.

Since the catalysts can exert significant influence over the regio- and chemoselectivity of the corresponding metal carbene reactions,[11] we then investigated the diazo decom-

---

(5) Pellicciari, R.; Natalini, B.; Sadeghpour, B. M.; Rosato, G. C.; Ursini, A. *J. Chem. Soc., Chem. Commun.* **1993**, 1798. (b) Pellicciari, R.; Natalini, B.; Sadeghpour, B. M.; Marinozzi, M.; Snyder, J. P.; Williamson, B. L.; Kuethe, J. T.; Padwa, A. *J. Am. Chem. Soc.* **1996**, *118*, 1. (c) Lopez-Herrera, F. J.; Sarabia-Garcia, F. *Tetrahedron* **1997**, *53*, 3325.

(6) Cimarelli, C.; Palmieri, G. *J. Org. Chem.* **1996**, *61*, 5557. (b) Zhu, G.; Chen, Z.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 6907.

(7) Pellicciari, R.; Castagnino, E.; Fringuelli, R.; Corsano, S. *Tetrahedron Lett.* **1979**, 481.

(8) **General procedure** for the preparation of *N*-tosyl diazoketamines **3a**−**j**. To a solution of **2** (1.0 mmol) in anhydrous THF (20 mL) at 50−55 °C was added sodium hydride (1.0 mmol) under N_2. The mixture is stirred for 5 min, and a solution of ethyl diazoacetate (1.2 mmol) in anhydrous THF (5 mL) was added dropwise during 30 min. The mixture was then stirred until TLC analysis indicated the disappearance of the starting material. The solution was cooled to −30 °C, and saturated aqueous $NaHCO_3$ (20 mL) was carefully added. Usual workup gave a crude product, which was purified by column chromatography with silica gel.

(9) For review, see: Weinreb, S. M. *Top. Curr. Chem.* **1997**, *190*, 131. For a recent example, see: Lu, W.; Chan, T. H. *J. Org. Chem.* **2001**, *66*, 3467.

(10) The *cis* isomer has intramolecular hydrogen bonding between N−H and the carbonyl oxygen. The spectra data for all diazo compounds and the α-aryl-*β*-enamino esters are submitted as Supporting Information.

position of **3a** with several transition metal catalysts commonly used in diazo carbonyl chemistry. First, two other typical Rh(II) catalysts, $Rh_2(O_2CCF_3)_4$ and $Rh_2(acam)_4$, were compared with $Rh_2(OAc)_4$. The data show that although they all promote the aryl migration efficiently, the ligands of the catalyst do have influence over the migratory aptitude of the phenyl group over the hydride group (Table 2). The electron-withdrawing trifluoacetate ligand slightly enhances the hydride migration.[12] For copper catalysts, the phenyl migration is again predominant, although the *cis* isomer of the phenyl migration product **6a** was formed in considerable amount in these cases (entries 4−6).

Finally, silver benzoate AgO_2CPh, which is an efficient catalyst for Wolff rearrangement in α-diazo carbonyl chemistry, was investigated. Under typical Wolff rearrangement conditions, AgO_2CPh/Et_3N,[13] **3a** decomposed to give hydride migration isomer **5a** as main product (entry 7). It is likely that the hydride migration occurs through a free carbene intermediate rather than a silver complexed carbene species. To confirm this point, a photolysis experiment was conducted. However, contrary to our prediction, when the α-diazoketamine was photolyzed ($\lambda > 300$ nm) at room temperature, the phenyl migration product was formed as major product (entry 8).

Having confirmed that $Rh_2(OAc)_4$ is the effective catalyst to promote phenyl migration, we then carried out the diazo decomposition of *N*-tosyl diazoketamines **3b−i** with this catalyst. As shown by the data collected in Table 3, the aryl migration products were predominant for all these substrates. Except in one case the hydride migration **5e** was isolated as minor product (entry 5), the hydride migration product **5a−d**, **5f−i** and the *cis* isomer of the phenyl migration products **6a−i** could only be detected on TLC and in ^{1}H NMR spectra of the crude product, but they were not be isolated because of their tiny amounts.

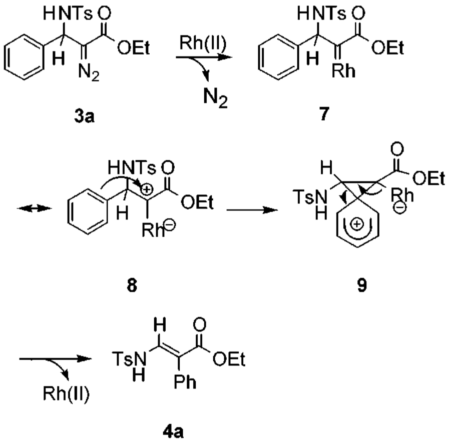
Table 3. 1,2-Aryl Migration Catalyzed by $Rh_2(OAc)_4$[a]

		yield (%)[a]	
entry	*N*-tosyl α-diazoketamines	**4**	**5**
1	**3a**, X = H, R = H	71^{b}	*c*
2	**3b**, X = *p*-MeO, R =H	89^{b}	
3	**3c**, X = *p*-Cl, R = H	83^{b}	
4	**3d**, X = *p*-Ph, R = H	86^{b}	
5	**3e**, X = *m*-Br, R = H	53^{b}	29^{b}
6	**3f**, X = *o*-Me, R = H	81^{d}	
7	**3g**, X = 2,4-Cl, R =H	84^{d}	
8	**3i**,X = 3,5-OMe, R = H	82^{d}	
9	**3j**, X = H, R = Me	90^{d}	

[a] For general procedure, see ref 14. [b] Yields after column chromatography. [c] 1,2-Hydride migration products **5** and the *cis* isomer of the aryl migration products **6** were detectable in TLC and the ^{1}H NMR spectra of the crude products, but they were not isolated because of their tiny amounts. [d] Yields after single recrystallization of the crude product.

A possible reaction mechanism could be tentatively proposed on the basis of the information now available. The aryl migration promoted by Rh(II) or copper catalysts should occur through a metal-bound carbene **8** as intermediate (Scheme 2). It has been suggested that in this metal carbene intermediate, the carbon attached to the metal has a partial positive charge.[15] It is possible that aryl migration may go through a “bridged” intermediate or transition state, in which the orbital system of the aryl group is expected to assist in the stabilization of a bridged carbonium ion or partial carbonium ion through delocalization.[16] This situation is similar as the well-known 1,2-shift in carbonium ions, in which the phenyl group also has higher migratory aptitude than an alkyl group.[17] The 1,2-shift in carbonium ions has been extensively studied, and the aryl participation through the formation of phenonium ion has been experimentally confirmed. However, since electronic structure of the Rh(II) carbene or Cu(I) carbene is still controversial,[15,18] further experiments will be needed to confirm if a “bridged” phenonium ion is truly involved in the migration process.

Scheme 2



In the end, it is worthwhile to mention that the presence of the X group in diazo compound **1** has a significant impact

---

[11] Wang, J.; Chen, B.; Bao, J. *J. Org. Chem.* **1998**, *63*, 1853 and references therein.

[12] $Rh_2(O_2CCF_3)_4$ has been reported to be more effective in promoting 1,2-hydride migration than $Rh_2(OAc)_4$; see ref 2c.

[13] Wang, J. Hou, Y. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1919 and references therein.

[14] **General procedure** for the $Rh_2(OAc)_4$-catalyzed diazo decomposition of *N*-tosyl diazoketamines **3a−j**. A solution of **3** (0.5 mmol) in CH_2Cl_2 (20 mL) was stirred at 0 °C under N_2, and then $Rh_2(OAc)_4$ (1 mg) was added. The reaction mixture was stirred at 0 °C for 10 min. The solvent was removed under vacuum, and the residue was purified by chromatography or recrystallization.

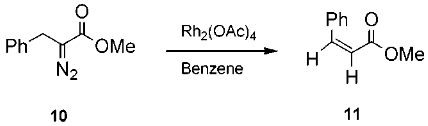
[15] Doyle, M. P.; Westrum, L. J.; Wolthuis, W. N. E.; See, M. M.; Boone, W. P.; Bagheri, V.; Pearson, M. M. *J. Am. Chem. Soc.* **1993**, *115*, 958.

[16] However, we could not rule out the possibility that migration concerted with rhodium dissociation, as one of the referees suggested.

[17] Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper Collins Publishers: New York, 1987.

[18] Pirrung, M. C.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **1994**, *116*, 8991.

Scheme 3



over the migratory aptitude of the migrating group. Without an OH, OAc, or NHTs, the hydride shift will be predominant, as shown by the example in Scheme 3.[2b] The exact driving force for this switch of migratory aptitude, however, is not clear at present.

Acknowledgment. The project is generously supported by Natural Science Foundation of China (grant 29972002).

Supporting Information Available: Experimental details and characterization data for all diazo compounds **3a**−**j**, β-enamino esters **4a**−**j**, and **5e**, **5h** and **6a**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL016324P