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Unusual Reaction of β-Hydroxy α-Diazo Carbonyl Compounds with Cl_3CCN/NaH and Rh(II)-Catalyzed Reaction of β-Trichloroacetylamino α-Diazo Carbonyl Compounds

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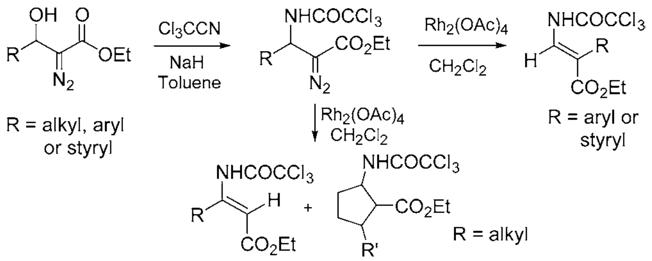
ABSTRACT



The hydroxyl group was directly converted into the trichloroacetylamino group by reacting β-hydroxy α-diazo carbonyl compounds with Cl_3CCN and NaH. Rh(II)-catalyzed reactions of the β-amino α-diazo carbonyl compounds were discussed.

1,2-Migration is frequently encountered in a photoinduced or transition metal catalyzed reaction of α-diazo carbonyl compounds.[1,2] The migrating group can be a hydride, aryl, or acetoxy group. The $Rh_2(OAc)_4$-mediated 1,2-acetoxy group migration was first reported by Ganem in 1981,[2b] and later the synthetic application of this reaction was explored by Lopez-Herrera.[2e] Mechanistically, it is believed that the 1,2-migration of acetoxy proceeds through a five-membered-ring transition state, in which the carbonyl oxygen of the acetoxy group interacts with the Rh(II)-carbene center.[2b] As a natural extension of this reaction, we conceived that an imino group may undergo similar migration as the carbonyl group to give enamino ester **5** in Rh(II)-catalyzed reaction (Scheme 1). When COR′ is an ester group, hydrogenation and hydrolysis will lead to amino acids.

However, in the process of preparing α-diazo carbonyl compound **4** by imidation of **1**, we unexpectedly observed a direct conversion of the hydroxyl group into the trichloroacetylamino group. In this paper, we report this unprec-

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(1) For comprehensive 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) For examples of 1,2-hydride migration, see: (a) Taber, D. F.; Herr, R. J.; Pack, S. K.; Geremia, J. M. *J. Org. Chem.* **1996**, *61*, 2908. (b) Ikota, N.; Takamura, N.; Young, S. D.; Ganem, B. *Tetrahedron Lett.* **1981**, *22*, 4163. For examples of 1,2-alkyl or 1,2-aryl migration, see: (c) Kanemasa, S.; Kanai, T.; Araki, T.; Wada, E. *Tetrahedron Lett.* **1999**, *40*, 5055. (d) Jiang, N.; Ma, Z.; Qu, Z.; Xing, X.; Xie, L.; Wang, J. *J. Org. Chem.* **2003**, *68*, 893. For an example of 1,2-acetoxy migration, see: (e) Lopez-Herrera, F. J.; Sarabia-Garcia F. *Tetrahedron* **1997**, *53*, 3325.

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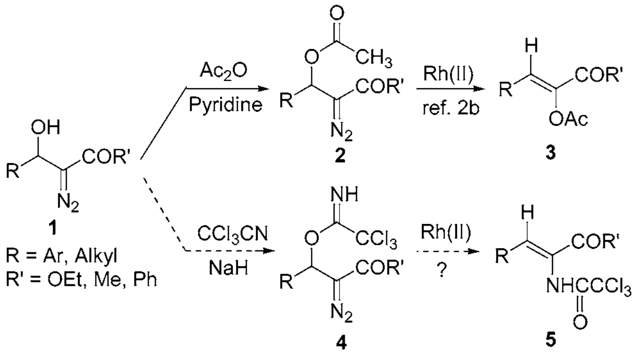
Scheme 1



edented reaction, as well as the $Rh_2(OAc)_4$-catalyzed reaction of the resulting β-(trichloroacetyl)amino α-diazo carbonyl compound **7** (vide infra).

The β-hydroxy α-diazo carbonyl compounds **6a−i** were easily prepared by DBU-catalyzed condensation of aldehyde with ethyl diazoacetate.[3] The diazo compound **6a** was first subjected to the standard condition of imidation[4] by treatment with trichloroacetonitrile and 25 mol % of DBU in CH_2Cl_2 between 0 °C and room temperature. The reaction proceeded cleanly to give a major product in 60% isolated yield; however, ^{1}H NMR data of the product suggested that it was not the expected imidate **8a** (R = *trans*-PhCH=CH−). The peak at δ 5.41, which corresponds to the proton of the carbon attached to the styryl group, was a doublet doublet (J = 7.0 and 6.6 Hz), rather than the expected doublet. The data were consistent with those of trichloroacetamide **7a**, which was unambiguously determined by X-ray crystallographic analysis (Figure 1). When 2 equiv of NaH were used as base instead of catalytic DBU, the reaction time was shortened considerably and the isolated yield of **7a** was 67%. For the diazo compound **6b**, the reaction gives a similar product **7b** in 77% yield. The structure of **7b** was also established by X-ray crystallography data (Figure 1). This direct transformation of the hydroxyl group to the amino group was found to be general, the β-(trichloroacetyl)amino α-diazocarbonyl compounds were obtained in good yields with all the β-hydroxy α-diazo substrates **6a−i** examined in our study.[5] The substrates with β-aryl substituents **7g−i** gave higher yields in general.

This unexpected reaction raises an intriguing question concerning its reaction mechanism. Since for normal hydroxyl compounds the same reaction conditions gave the corresponding trichloroacetimidate without exception,[4,6] it is apparent that the α-diazo group is crucial in this reaction.

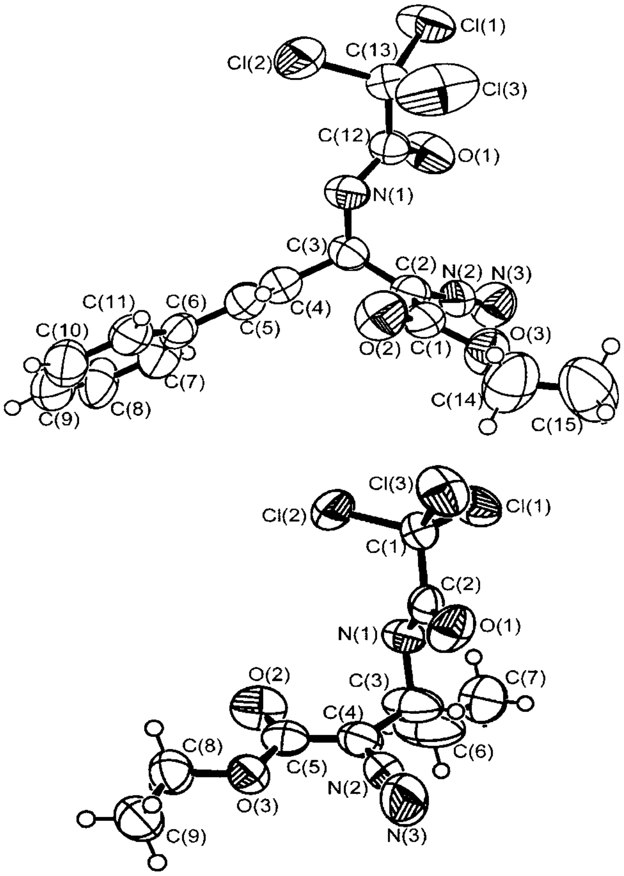
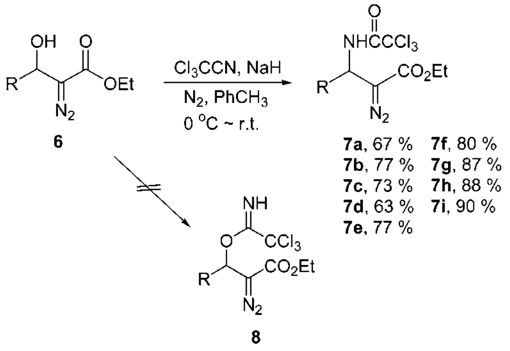


Figure 1. X-ray structure of **7a** and **7b**.

To confirm this, compound **9** was submitted to the same reaction conditions, and the normal imidation product **10** was obtained together with dehydration product (Scheme 3). No trace trichloroacetamide could be detected. To gain insight into the mechanism, an optically active **6g** (67% ee) was subjected to the above-mentioned reaction conditions.[7] The product **7g** was found to have an optical purity of 53% ee

Scheme 2



a. R = *trans*-PhCH=CH; **b**. R= CH_3CH_2; **c**. R = $CH_3(CH_2)_2$; **d**. R = $CH_3(CH_2)_3$; **e**. R = $CH_3(CH_2)_5$; **f**. R = $CH_3(CH_2)_{10}$; **g**. R = C_6H_5; **h**. R = p-FC_6H_4; **i**. R = p-$MeOC_6H_4$

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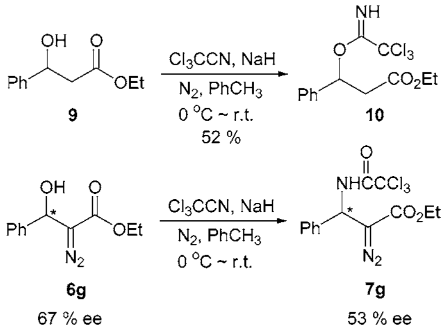
[3] Jiang, N.; Wang, J. *Tetrahedron Lett.* **2002**, *43*, 1285.

[4] For a recent example, see: Chen, Y. K.; Lurain, A. E.; Walsh, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 12225.

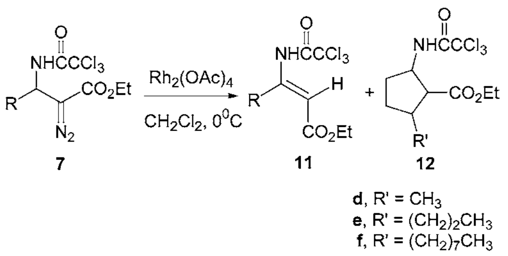
[5] **General procedure:** In a flamed three-necked round-bottom flask, trichloroacetonitrile (3.0 mmol, 98%) and hydride sodium (2.0 mmol, 60%) were added to a solution of β-hydroxy-α-diazo compound (1.0 mmol) in 5 mL of toluene at 0 °C. The mixture was stirred for 6 h between 0 °C and room temperature. The reaction was quenched with saturated $NaHCO_3$ and extracted with Et_2O. The crude product was purified by flash chromatography on silica gel (petroleum ether: ethyl ether 5:1) to afford the pure **7a−i**.

Scheme 3



(Scheme 4). Therefore, the reaction proceeded with little racemization at the reaction center.

Scheme 4



It is convenient to speculate that an imidate such as **8** is an intermediate in the reaction. This intermediate then undergoes rapid rearrangement to give the amide product **7** since monitoring the reaction with ^{1}H NMR did not reveal the presence of an intermediate. Two mechanisms can be envisioned for the rearrangement of the intermediate to amide **7**. An intramolecular S_N2 type mechanism is not plausible due to the four-member-ring structure in the transition state.[8] On the other hand, a tight ion-pair S_N1 mechanism seems reasonable and is consistent with the stereochemical data.[9] It should be pointed out that this mechanistic hypothesis is conjectural and further mechanistic study is under way.

The diazocarbonyl compounds thus obtained were subjected to $Rh_2(OAc)_4$-mediated diazo decomposition.[10] When the β-substituent was an alkyl group, the reaction was complicated by the competition of intramolecular C−H insertion (Scheme 4, Table 1).[11] In the case of **7b** and **7c**, where intramolecular C−H insertion is not possible or not competitive due to the insertion into a primary C−H bond,[12] the 1,2-hydride migration was the only reaction pathway (Table 1, entries 1 and 2). When the C−H bond insertion became competitive, as in the cases of **7d**, **7e**, and **7f**, product **12** became predominant.[13] The ratio of 1,2-hydride shift to C−H insertion is affected by the reaction temperature and the catalyst. High temperature and $Rh_2(acam)_4$ favor the 1,2-hydride shift.

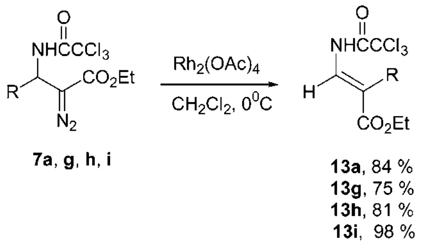
Table 1. Rh(II)-Catalyzed Reaction of Diazo Compounds **7a**−**f**

entry	diazo substrate	Rh(II)	solvent	temp (°C)	**11**:**12**^{a}	yield (%)^b
1	**7b**	$Rh_2(OAc)_4$	CH_2Cl_2	0	100:0	68
2	**7c**	$Rh_2(OAc)_4$	CH_2Cl_2	0	100:0	73
3	**7d**	$Rh_2(OAc)_4$	CH_2Cl_2	0	0:100	41^c
4	**7e**	$Rh_2(OAc)_4$	CH_2Cl_2	0	12:88	89
5	**7e**	$Rh_2(OAc)_4$	C_6H_6	80	50:50	87
6	**7e**	$Rh_2(acam)_2$	C_6H_6	80	71:29	95
7	**7e**	$Rh_2(O_2CCF_3)_4$	CH_2Cl_2	0		−^{d}
8	**7f**	$Rh_2(OAc)_4$	CH_2Cl_2	0	16:84	94
9	**7f**	$Rh_2(OAc)_4$	C_6H_5	80	50:50	99
10	**7f**	$Rh_2(acam)_4$	C_6H_5	80	60:40	98
11	**7f**	$Rh_2(O_2CCF_3)_4$	CH_2Cl_2	0		−^{d}

[a] Product ratio was determined by ^{1}H NMR (300 MHz) of the crude product. [b] Combined yield after column chromatography. [c] The reaction with this substrate was exceptionally slow. About 50% of **7d** was recovered after stirring at rt for 2 days. [d] Starting material was recovered after stirring for 2 days.

For the substrates with β-aryl groups, **7g**−**i**, the diazo decomposition gave predominantly the 1,2-aryl migration product of *trans*-α-aryl-β-enamino esters (Scheme 5). This result was similar to our previous study on the β-(tosyl)-amino α-diazo carbonyl compounds.[2d] It is worthwhile to note that only the trans isomer was obtained in all cases, and the trans-to-cis isomerization on silica gel column chromatography was not observed. On the other hand, the

Scheme 5



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(6) The rearrangement of allyl trichloroacetimidate into allyl trichloroacetamide, namely the Overman rearrangement, is well-known. See: Overman, L. E. *Acc. Chem. Res.* **1980**, *13*, 218.

(7) The enantiomerically enriched **6g** was prepared by condensation of benzaldehyde with ethyl diazoacetate catalyzed by *L*-(+)-6,6′-Br$_2$-BINOL + Zr(O^{t}Bu)$_4$. Yao, W.; Wang, J. *Org. Lett.* **2003**, *5*, 1527−1530.

(8) Beak, P. *Acc. Chem. Res.* **1992**, *25*, 215−222.

(9) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; HarperCollinsPublishers: New York, 1987; pp 342−344.

(10) **General procedure for the $Rh_2(OAc)_4$-catalyzed reaction:** In a flamed round-bottom flask, $Rh_2(OAc)_4$ (1 mol %) was dissolved into 10 mL of anhydrous CH_2Cl_2. A solution of diazo substrate **7a**−**i** in anhydrous CH_2Cl_2 was added dropwise at 0 °C over the course of 15 min. Upon stirring for another 20 min, the solution was concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel to afford the products.

(11) Taber, D. F.; Hennessy, M. J.; Louey, J. P. *J. Org. Chem.* **1992**, *57*, 436

(12) Taber, D. F.; Ruckle, R. E., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7686.

(13) Only one diastereoisomer of the C−H insertion product could be detected from the crude product.

$Rh_2(OAc)_4$-mediated reaction of **7a** gave only the 1,2-styryl migration product.[14]

In summary, we have discovered an unusual reaction in which the hydroxyl group is directly converted into a trichloroacetyl-protected amino group under mild conditions. In connection with the subsequent transformations of the resultant α-diazo carbonyl compounds,[1] this reaction may find synthetic applications. Moreover, the direct conversion of a hydroxyl group to an amino group may be possible in other hydroxyl compounds. Investigation along this line is underway in our laboratories and the results will be reported in due course.

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Supporting Information Available: Experimental details and characterization data for all new compounds, X-ray crystallographic data of **7a** and **7b** (CIF files). This material is available free of charge via the Internet at http://pubs.acs.org.

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[14] As far as we know, this is the first example of 1,2 migration of a double bond in the Rh(II)-mediated carbenoid reaction.