Unusual Reaction of $\beta$-Hydroxy $\alpha$-Diazo Carbonyl Compounds with Cl$_3$CCN/NaH and Rh(II)-Catalyzed Reaction of $\beta$-Trichloroacetylamino $\alpha$-Diazo Carbonyl Compounds

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ABSTRACT

The hydroxyl group was directly converted into the trichloroacetylamino group by reacting $\beta$-hydroxy $\alpha$-diazo carbonyl compounds with Cl$_3$CCN and NaH. Rh(II)-catalyzed reactions of the $\beta$-amino $\alpha$-diazo carbonyl compounds were discussed.

1,2-Migration is frequently encountered in a photoinduced or transition metal catalyzed reaction of $\alpha$-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 $\alpha$-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-
edented reaction, as well as the Rh\(_2\)(OAc)\(_4\)-catalyzed reaction of the resulting \(\beta\)-(trichloroacetyl)amino \(\alpha\)-diazocarbonyl compound 7 (vide infra).

The \(\beta\)-hydroxy \(\alpha\)-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\(_2\)Cl\(_2\) 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 \(\delta 5.41\), 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 \(\beta\)-(trichloroacetyl)amino \(\alpha\)-diazoacarbonyl compounds were obtained in good yields with all the \(\beta\)-hydroxy \(\alpha\)-diazo substrates 6a–i examined in our study.\(^5\)

The substrates with \(\beta\)-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 \(\alpha\)-diazo group is crucial in this reaction.

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(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 \(\beta\)-hydroxy-\(\alpha\)-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\(_2\)O. The crude product was purified by flash chromatography on silica gel (petroleum ether: ethyl ether 5:1) to afford the pure 7a–i.

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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.
Since monitoring the reaction with 1H NMR did not reveal an intermediate in the reaction. This intermediate then undergoes rapid rearrangement to give the amide product 7. The rearrangement of the intermediate to amide product 7 is envisioned for the rearrangement of the intermediate to amide product 7. An intramolecular SN2 type mechanism is not plausible due to the four-member-ring structure in the transition state. It is convenient to speculate that an imidate such as 7b which is enantiomerically enriched, undergoes rapid rearrangement to give the amide product 7.


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 result was similar to our previous study on the β-(tosyl)-amino α-diazo carbonyl compounds. It is convenient to speculate that an imidate such as 7b, the diazo decomposition gave predominantly the 1,2-aryl migration product of trans-α-aryl-β-enamino esters (Scheme 5). This

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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.

$^{14}$ 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.

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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.