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=CHCOCl/Et$_3$N gave β-(*p*-tolylsulfonyl) α,β-
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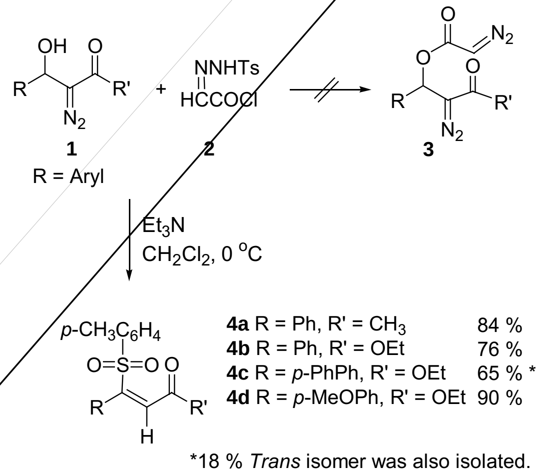
hemistry of β-hydroxy α-diazo
s, we have intended to convert the
diazo compound **1** into a diazoester
well-established diazotization reaction
[4] Since there are two diazo functional
the resulting diazoester compound **3**, novel
may be expected. However, when trying to
the β-hydroxyl group into diazoester group, we
ved quite unexpected results.

Initially, the β-hydroxy-β-phenyl α-diazo ester **1** (R = Ph, R′ = OEt) was treated with glyoxylic acid chloride *p*-toluenesulfonylhydrazone **2** in the presence of triethylamine in CH$_2$Cl$_2$ at 0 °C to room temperature.[4] The reaction proceeded cleanly to give a major product in 76% isolated yield. The structure of this product was elucidated to be ethyl *cis*-3-(*p*-tolylsulfonyl)-3-phenyl-2-propenoate **4b**, rather than the expected bisdiazo compound **3** (R = Ph, R′ = OEt), based on the spectral data.



Scheme 1.

The formation of β-(*p*-tolylsulfonyl) α,β-unsaturated carbonyl compounds were found to be general for β-aryl β-hydroxy diazo substrates **1** (R = Ph, R′ = CH$_3$; R = *p*-PhPh, *p*-MeOPh, R′ = OEt). The normal diazotization reactions with these substrates all proceeded in

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0040-4039/$ - see front matter
doi:10.1016/j.tetlet.2004.04.037

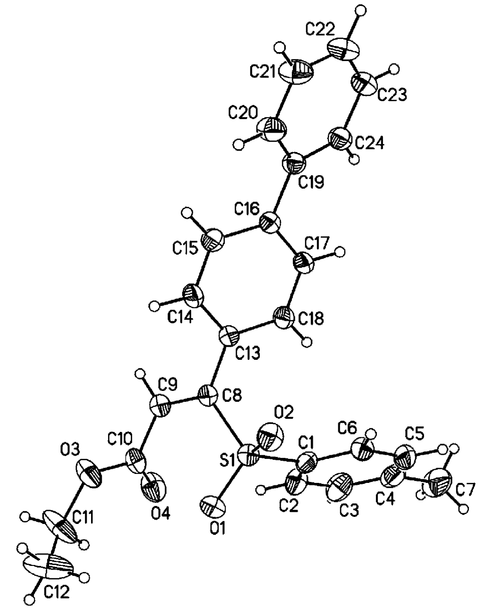


Figure 1. X-ray structure of **4c**.

good isolated yields of **4b–d**. For **1** (R = *p*-PhPh, R′ = OEt), the reaction gave an isomeric mixture in a ratio of 78:22. In other cases, only *cis* isomers were isolated.[5] For **4c**, the structure was further confirmed by single crystal X-ray diffraction (Fig. 1).[6]

We then examined the reaction of β-hydroxy α-diazo carbonyl compounds bearing β-alkyl substituents (Scheme 2). Unexpectedly again, the isolated products in this case were neither bisdiazo esters **3**, nor β-(*p*-tolylsulfonyl) α,β-unsaturated carbonyl compounds **4**. The spectral data suggested their structures as β-(*p*-tolylsulfonyl) α-diazo esters **5a–c**.[5] The structure of α-diazo compound **5b** was confirmed by single crystal X-ray diffraction (Fig. 2).[6]

The X-ray structure of **5b** shows some interesting features. The O=C–C=N_2 group is found to have *s–Z* conformation, while the other β-substituted α-diazo carbonyl compounds that we have studied all have *s–E* conformation.[3c,7] The diazo group and the carbonyl group are almost coplanar with a dihedral angle of −0.93°. The dihedral angle between β C–H bond and the diazo group is −169.5°. Thus, the β C–H is in an antiperiplanar position, which is not favorable for 1,2-hydride shift in diazo decomposition.[8] The diazo compounds **5a–c** are found to be exceptionally stable. In EI-MS spectra, they all give molecular ion peak. They are stable when refluxed in 1,2-dichloroethane. When catalyzed with $Rh_2(OAc)_4$ in CH_2Cl_2 at room temperature, **5b** reacted very slowly to give an oxidized product **6b**, rather than the product due to 1,2-hydride shift, in 45% yield after 12 h (Scheme 3).

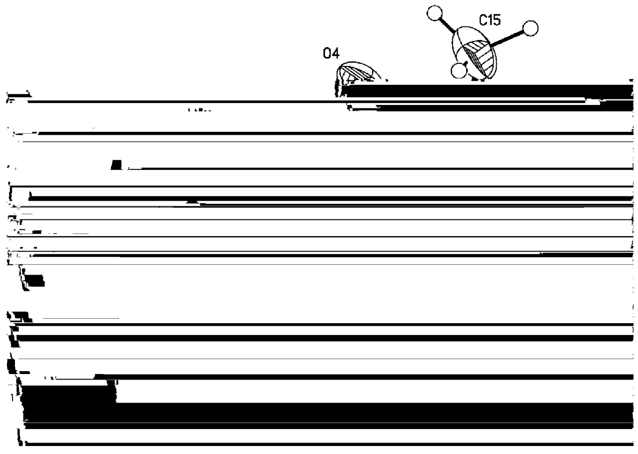
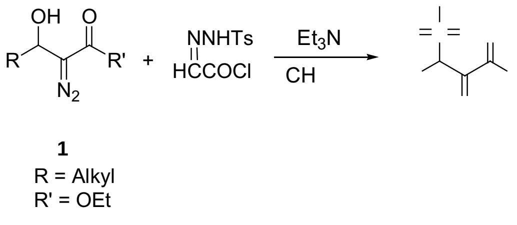


Figure 2. X-ray structure of **5b**.

A reaction mechanism is proposed to account for the formation of **4** and **6** (Scheme 4). As suggested by Corey and Mayers, the reaction of β-hydroxy diazo compound **1** with TsNHN=CHCOCl/Et_3N gave bisdiazo ester **3** together with *p*-toluenesulfinate ester **9**.[4b] We speculate that the existence of the neighboring electron-withdrawing diazo group and the carbonyl group makes the β-position in **3** and **9** liable to nucleophilic attack. The *p*-toluenesulfinate group in **9** is a good leaving group, which is easily replaced by the *p*-toluenesulfinyl anion through the attack of the more nucleophilic sulfur. The diazo ester group in **3**, on the other hand, may also be easily replaced by the *p*-toluenesulfinyl anion after protonation. The S_N2 type nucleophilic substitution gives the β-(*p*-tolylsulfonyl) α-diazo ester **5**. When R of **5** is an aryl group, the diazo decomposition occurs under the reaction conditions to give the 1,2-hydride shift product **4**.[9]

The important point in this mechanism is the suggestion that the β-position is liable to nucleophilic attack in these compounds. This speculation is supported by the fact that β-acetoxy group in compound **7** is readily replaced by $p\text{-}CH_3C_6H_4SO_2$ group when treating with sodium *p*-toulenesulfinate (Scheme 5) in DMF at room temperature.[10]



In our previous study, we have observed a direct conversion of hydroxyl group to trichloroacetylamino group by treatment of β-hydroxy α-diazo carbonyl compound **1** with Cl_3CCN and NaH (Scheme 6).[3c] Similar S_N2 type mechanism is most likely followed in that case too, thereby supporting the argument made in this paper that the β-position in α-diazo carbonyl compounds is liable to nucleophilic attack.

In summary, we have observed unexpected reactions of β-hydroxy α-diazo carbonyl compounds with $TsNHN{=}CHCOCl/Et_3N$, which give β-(*p*-tolylsulfonyl) α-diazo esters or β-(*p*-tolylsulfonyl) α-diazo esters. These transformations may find synthetic applications.[11] Moreover, the fact that the β-hydroxyl group in diazo compound **1** can be easily replaced by other functional group through nucleophilic substitution opens the way to the diazo compounds with more diverse β-substitutions. These diazo compounds may have novel reactivities when catalyzed with transition metal complex or acid. The investigation along this line is under the way in our laboratory and the results will be reported in due course.

Acknowledgements

The project is generously supported by Natural Science Foundation of China (Grant No. 20225205, 20172002, 20390050).

References and notes

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*, 1091–1160.
2. (a) Schollkopf, U.; Frasnelli, H.; Hoppe, D. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 300–301; (b) Schollkopf, U.; Banhidai, B.; Frasnelli, H.; Meyer, R.; Beckhaus, H. *Liebigs Ann. Chem.* **1974**, 1767–1783; (c) Pellicciari, R.; Natalini, B. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1822–1824; (d) 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*, 1–12; (e) Moody, C. J.; Taylor, R. J. *Tetrahedron Lett.* **1987**, *28*, 5351–5352; (f) Wenkert, E.; McPherson, A. A. *J. Am. Chem. Soc.* **1972**, *94*, 8084–8090; (g) Burkoth, T. L. *Tetrahedron Lett.* **1969**, *10*, 5049–5052; (h) Woolsey, N. F.; Khalil, M. H. *J. Org. Chem.* **1972**, *37*, 2405–2408; (i) Jiang, N.; Wang, J. *Tetrahedron Lett.* **2002**, *43*, 1285–1287.
3. (a) Jiang, N.; Qu, Z.; Wang, J. *Org. Lett.* **2001**, *3*, 2989–2992; (b) Jiang, N.; Ma, Z.; Qu, Z.; Xing, X.; Xie, L.; Wang, J. *J. Org. Chem.* **2003**, *68*, 893–900; (c) Shi, W.; Jiang, N.; Zhang, S.; Wu, W.; Du, D.; Wang, J.

25, 3559–3562; (c) Corey, E. J.; Mayers, A. G. *J. Am. Chem. Soc.* **1985**, *107*, 5574–5576; (d) Clive, D. L. J.; Daigneault, S. *J. Org. Chem.* **1991**, *56*, 3801–3814.

5. General procedure for the reaction of β-hydroxy α-diazo carbonyl compounds with TsNHN=CHCOCl/Et_3N. In a flamed three-necked round bottom flask, β-hydroxy-α-diazo compound (1.0 mmol) was dissolved in 5 mL CH_2Cl_2. Triethylamine (4.0 mmol) was added to the solution at 0 °C, after 10 min the glyoxylic acid chloride *p*-toluenesulfonylhydrazone (3.0 mmol) was added dropwise. The mixture was allowed to stir for 8 h between 0 °C and room temperature. The reaction mixture was concentrated under reduced pressure with rotvap. The residue was subjected to silica gel chromatography (petroleum ether–acetone = 12:1) to afford the pure products. Representative analytical data:
   (*E*)-Ethyl 3-(*p*-tolylsulfonyl)-3-phenyl-3-buten-2-one (**4a**). IR 3058, 1706, 1147, 700, 561 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.37 (s, 3H), 2.60 (s, 3H), 6.44 (s, 1H), 7.21 (d,wTD(d)Tj(J-r3)Tone