

Diazo Decomposition in the Presence of Tributyltin Hydride. Reduction of α -Diazo Carbonyl Compounds

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Table 1. Diazo decomposition in the presence of Bu₃SnH under Cu(acac)₂-catalytic and photochemical conditions

Entry	Substrate	Reaction Conditions ^a and Yields ^b	Product
1		A 85 % B 75 %	
2		A 93 % B 85 %	
3		B 61 %	
4		A 95 % B 95 %	
5		A 88 %	
6		A 78 %	
7		A 68 %	
8		A 76 %	
9		A B	
10		A B	

^a A: Diazo compound (1.0 mmol), Cu(acac)₂ (0.01 mmol) and Bu₃SnH (2.5 mmol) in dry benzene (20 mL) were refluxed for 5 h; B: Diazo compound (1.0 mmol) and Bu₃SnH (2.5 mmol) in dry benzene (20 mL) were irradiated with 300 W high pressure mercury lamp at rt.

^b Isolated yields.

group has been the object of scattered studies. In 1950, Wanger and Tome reported the reduction of an α -diazo carbonyl compound to the corresponding CH₂ group with concentrated HI.⁵ After 20 years Horner and Schwarz reported another diazo reduction. The reaction was suggested to follow a radical chain mechanism, with isopropyl alcohol as hydrogen donor and peroxide as radical initiator.⁶ More recently, Pellicciari demonstrated that diazo group can be reduced in methanol in the presence of palladium on charcoal,⁷ and Moody et al. reported a diazo reduction as a side reaction in the Rh(II)-mediated diazo decomposition in the presence of 2-propanol.⁸

The efficient reduction of α -diazo carbonyl compounds with Bu₃SnH brings up some interesting questions concerning the mechanism of the diazo decomposition. For the Cu(acac)₂ catalyzed reaction, the experiments clearly

indicated that the copper catalyst was involved in the initial diazo decomposition process, since the diazo compound did not decompose in the absence of Cu(acac)₂ under the same conditions.

In order to gain some insight into the mechanism of this reaction, the diazo decomposition was studied in some detail. First, the diazo decomposition was monitored by ¹H NMR spectroscopy for identifying reaction intermediates (Fig. 1). Thus, an equimolar amount of diazoacetophenone and Ph₃SnH, together with a catalytic amount of Cu(acac)₂ were mixed in sodium-dried C₆D₆ at room temperature. ¹H NMR spectra suggested that there was no detectable reaction at room temperature. However, upon heating at about 50°C for 3 min, the light yellow solution turned to be slight brown and in the ¹H NMR spectra the absorption of α -stannyl ketone **28** (see Scheme 4)

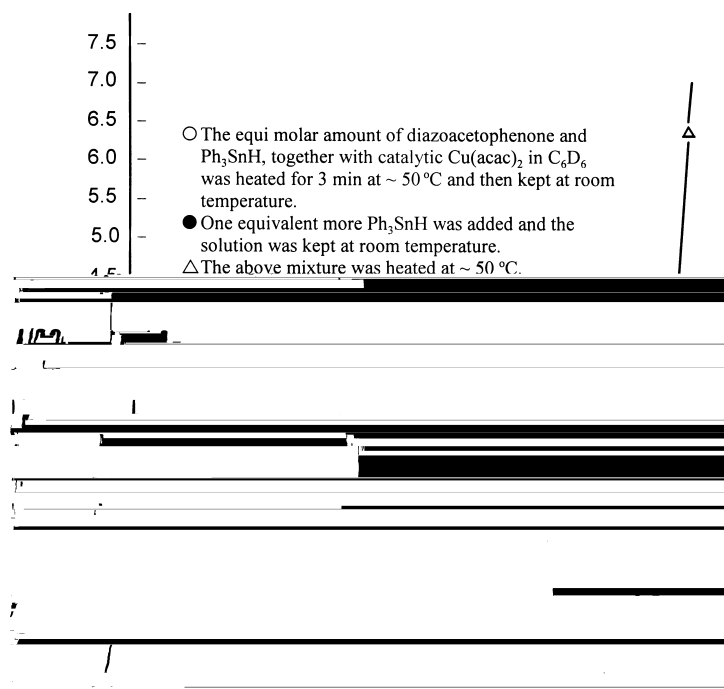
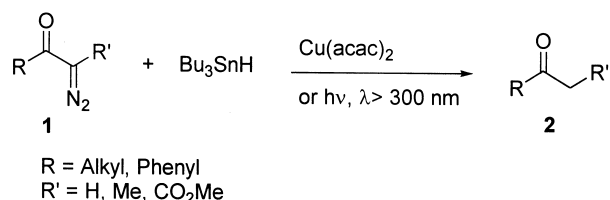


Figure 1. The $\text{Cu}(\text{acac})_2$ -catalyzed diazo decomposition of diazoacetophenone in the presence of Ph_3SnH monitored by ^1H NMR spectroscopy.

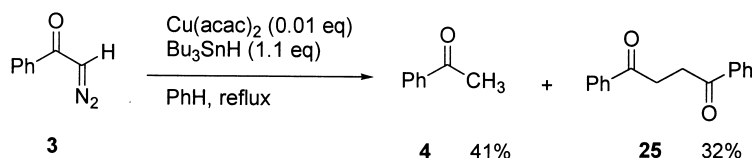


Scheme 1.

could be observed, together with acetophenone and starting diazoacetophenone.⁹ The molar ratio for the three compounds was estimated by the ^1H NMR integration to be **28**:**3**:**4**=13:80:7. The reaction mixture was then kept in NMR tube at room temperature and was monitored by NMR spectrum. It was found that the diazoacetophenone gradually decreased and completely disappeared after 15 min at room temperature. During this period, both α -stannyl ketone **28** and acetophenone **4** increased while the ratio of **28** to **4** slightly decreased. The ratio of **28** to **4** was then found to be almost constant under the same condition. After 35 min, one more equivalent of Ph_3SnH was added and the mixture was further kept at room temperature for another 20 min. In this period, the α -stannyl ketone **28** is slowly changed to acetophenone **4**. This indicates that α -stannyl ketone **28** is relatively stable at room temperature. The experiment also proves that the formation of acetophenone **4** was not due to the decomposition of α -stannyl

ketone **28** by trace amounts of H_2O in the mixture, since our independent experiment showed that H_2O can immediately hydrolyze the α -stannyl ketone to generate the acetophenone. Finally, when the mixture was heated again at 50°C , the α -stannyl ketone **28** was found to change to the acetophenone rapidly, and it totally disappeared upon heating for about 20 min (Scheme 1).

To further prove the existence of the radical intermediate **30** (vide infra) in the reaction mechanism, we then carried out the $\text{Cu}(\text{acac})_2$ catalyzed diazo decomposition of diazoacetophenone in the presence of 1 equiv. of Bu_3SnH in refluxing benzene. In this case, acetophenone **4** (41 %) together with diketone **25** (32 %) were isolated as major products (Scheme 2). The formation of diketone might arise from the coupling of the α -carbonyl radical intermediate **30** (vide infra). However, when the diazoacetophenone alone was decomposed with catalytic $\text{Cu}(\text{acac})_2$ in refluxing benzene, the coupling product **26** was isolated in 42% yield as the major product. When this coupling product was further refluxed with Bu_3SnH and $\text{Cu}(\text{acac})_2$ in benzene, and product **25** was isolated (Scheme 3). This experiment indicates that the formation of diketone **25** does not prove the involvement of the radical intermediate. When Bu_3SnH was added dropwise to a refluxing solution of 2.5 equiv. of diazoacetophenone in benzene containing catalytic $\text{Cu}(\text{acac})_2$, both **26** and **25** were isolated as major products.



Scheme 2.

5H); ^{13}C NMR (50 MHz, CDCl_3) δ 24.3, 30.9, 31.7, 35.5, 37.4, 73.3, 125.6, 128.2, 128.2, 142.0, 207.0. This compound was unstable and was used in the diazo decomposition immediately after column chromatography.

Pentyl 5-diazo-4-oxo-pentanoate 17. Oil; IR (Neat): ν 2958, 2105, 1734, 1645, 1382, 1174 cm^{-1} ; ^1H NMR (200 MHz, CDCl_3) δ 0.90 (t, $J=6.6$ Hz, 3H), 1.28–1.35 (m, 4H), 1.55–1.66 (m, 2H), 2.65 (s, 4H), 4.08 (t, $J=6.8$ Hz, CH_2), 5.32 (s, br, 1H); ^{13}C NMR (50 MHz, CDCl_3) δ 192.6, 172.3, 64.6, 54.3, 34.7, 28.4, 28.0, 27.7, 22.0, 13.7; MS m/z (relative intensity) 184 $[(\text{M}-\text{N}_2)^+, 7\%]$, 156 (4), 125 (3), 114 (4), 101 (21); HRMS calcd for $(\text{M}-\text{N}_2)^+$, $\text{C}_{10}\text{H}_{16}\text{O}_3$ 184.1099, found 184.1102.

Diazo α -ketoester **11** was prepared by standard diazo transfer reaction ($\text{TsN}_3/\text{Et}_3\text{N}/\text{MeCN}$, room temperature).^{3a}

Methyl 2-diazo-3-oxo-7-phenylheptanoate 11. Oil; IR (Neat) ν 2930, 2129, 1727, 1656, 1435, 1308, 1220 cm^{-1} ; ^1H NMR (200 MHz, CDCl_3) δ 1.65–1.70 (m, 4H), 2.63 (t, $J=6.4$ Hz, 2H), 2.87 (t, $J=6.2$ Hz, 2H), 3.82 (s, 3H), 7.15–7.31 (m, 5H); ^{13}C NMR (50 MHz, CDCl_3) δ 23.95, 30.88, 35.63, 39.91, 52.10, 125.66, 128.23, 128.34, 142.19, 161.74, 192.64; MS m/z (relative intensity) 232 $[(\text{M}-\text{N}_2)^+, 6\%]$, 200 $[(\text{M}-\text{N}_2-\text{MeOH})^+, 29\%]$, 172 (15), 144 (20), 117 (41), 91 (100); HRMS calcd for $(\text{M}-\text{N}_2)^+$, $\text{C}_{14}\text{H}_{16}\text{O}_3$ 232.1099, found 232.1099.

General procedure for the $\text{Cu}(\text{acac})_2$ catalyzed diazo decomposition in the presence of Bu_3SnH

Method A. The diazo compound (1.0 mmol), $\text{Cu}(\text{acac})_2$ (0.01 mmol) and Bu_3SnH (2.5 mmol) was dissolved in dry benzene (20 mL). The solution was refluxed until the completion of the diazo decomposition, as indicated by TLC. The reaction mixture was cooled down and the solvent was removed under reduced pressure to give a crude mixture, which was subjected to column chromatography.

General procedure for the diazo decomposition in the presence of Bu_3SnH under photochemical conditions

Method B. The diazo compound (1.0 mmol) and Bu_3SnH (2.5 mmol) was dissolved in benzene (20 mL) in a Pyrex tube. The solution was irradiated with a 300 W high pressure Hg lamp at room temperature. Upon completion of the reaction, the solvent was removed and the crude residue was purified by column chromatography.

Compounds **10**, **18**, **20**, **21**, **23** and **24** are known^{3f,17,18,19,20} and their data were consistent with that reported in the literature.

Acknowledgements

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