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

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Abstract—The diazo group of a series of α-diazo carbonyl compounds can be reduced to the corresponding CH_2 group by Bu_3SnH under $Cu(acac)_2$-catalytic or photochemical conditions. The mechanistic aspects of this reaction were investigated in some detail, and a possible reaction pathway was discussed. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

The decomposition of α-diazo carbonyl compounds has been widely studied under thermal, photochemical and transition-metal catalyzed conditions. The resulting free carbene or carbenoids can undergo diverse synthetically useful transformations, including cyclopropanations, ylide generations, and insertion reactions.[1] In contrast with intramolecular C–H insertion and inter- or intramolecular Si–H insertion reactions, which have been well established as synthetically useful transformations, there have been only a few isolated reports on the intermolecular insertion of carbenes or carbenoids into the related Sn–H bond.[2] Doyle and Padwa investigated the reaction between free carbene and Bu_3SnH and showed that Sn–H bond insertion was an efficient process.[2b,c,d] More recently, Landais reported an example in which an α-stannyl ester was isolated in high yield when diazo ethylacetate was decomposed by catalytic $Rh_2(OAc)_4$ in the presence of Bu_3SnH.[2e] This example suggests that carbenoid intermolecular Sn–H insertion can be a highly efficient process. In connection with our interest in the synthetic application and the reaction mechanism of the reactions of diazo carbonyl compounds,[3] we investigated the diazo decomposition in the presence of Bu_3SnH under thermal, photochemical and transition-metal catalyzed conditions. Our results demonstrate that α-diazo group can be efficiently reduced to the corresponding CH_2 group by Bu_3SnH.

Results and Discussion

First, we examined the diazo decomposition under thermal conditions in the presence of Bu_3SnH. Thus, diazoacetophenone **3** was refluxed in benzene with 2.5 equiv. of Bu_3SnH. We found that diazo decomposition did not proceed to any detectable extent and the starting material was recovered after refluxing for 5 h. The experiment suggests that Bu_3SnH neither directly reacts with diazo group[4] nor facilitates its decomposition in refluxing benzene. This result is not unexpected because α-diazo carbonyl compounds are generally stable up to 100°C upon heating.[1a] However, when the reaction was conducted in refluxing toluene for 3 h, the diazo compound was decomposed and acetophenone **4** was isolated in 59% yield.

We next inspected the diazo decomposition under transition metal catalyzed conditions. The diazoacetophenone was refluxed in benzene containing 0.01 equiv. of $Cu(acac)_2$ and 2.5 equiv. of Bu_3SnH. The diazo compound disappeared after refluxing for 2 h and acetophenone was isolated in 85% yield. Encouraged by the clear diazo reduction under these conditions, we then proceeded to investigate the generality of this reaction. Thus, α-diazo carbonyl compounds with different structures were prepared and subjected to the same diazo decomposition conditions. The results are summarized in Table 1. As shown in the table, in most cases the diazo reduction occurred to give the corresponding reduced products in good to excellent yields. For the substrates with a tosyl protected amino group in the α-diazo carbonyl molecule, both reduction and intramolecular N–H insertion products[3f] were observed (entries 9 and 10).

The diazo reduction was then investigated under photochemical conditions. Thus, the α-diazo carbonyl compounds and Bu_3SnH (2.5 equiv.) were dissolved in benzene and irradiated with a 300 W high pressure mercury lamp through a Pyrex filter. As shown in Table 1, clean reduction also occurred under these conditions within 2 h.

The reduction of the diazo group to the corresponding CH_2

Keywords: diazo compounds; carbene and carbenoids; reduction.

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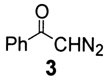
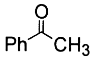
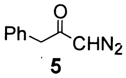
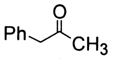
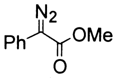
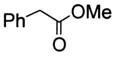
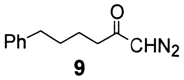
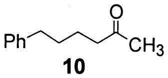
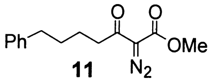
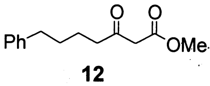
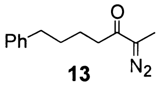
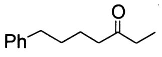
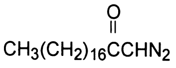
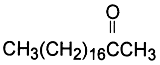
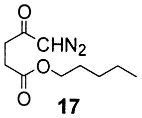
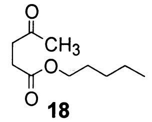
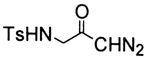
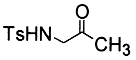
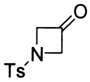
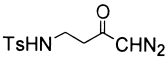
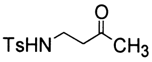
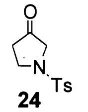
Table 1. Diazo decomposition in the presence of Bu_3SnH under $Cu(acac)_2$-catalytic and photochemical conditions

Entry	Substrate	Reaction Conditions[a] and Yields[b]	Product	
1	 **3**	A 85 % B 75 %	 **4**	
2	 **5**	A 93 % B 85 %	 **6**	
3	 **7**	B 61 %	 **8**	
4	 **9**	A 95 % B 95 %	 **10**	
5	 **11**	A 88 %	 **12**	
6	 **13**	A 78 %	 **14**	
7	 $CH_3(CH_2)_{16}\overset{\overset{O}{\|}}{C}CHN_2$ **15**	A 68 %	 $CH_3(CH_2)_{16}\overset{\overset{O}{\|}}{C}CH_3$ **16**	
8	 **17**	A 76 %	 **18**	
9	 **19**		 **20**	 **21**
		A	31 %	63 %
		B	51 %	0 %
10	 **22**		 **23**	 **24**
		A	17 %	57 %
		B	56 %	0 %

[a] A: Diazo compound (1.0 mmol), $Cu(acac)_2$ (0.01 mmol) and Bu_3SnH (2.5 mmol) in dry benzene (20 mL) were refluxed for 5 h; B: Diazo compound (1.0 mmol) and Bu_3SnH (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 CH_2 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 Bu_3SnH 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 Ph_3SnH, together with a catalytic amount of $Cu(acac)_2$ were mixed in sodium-dried C_6D_6 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)

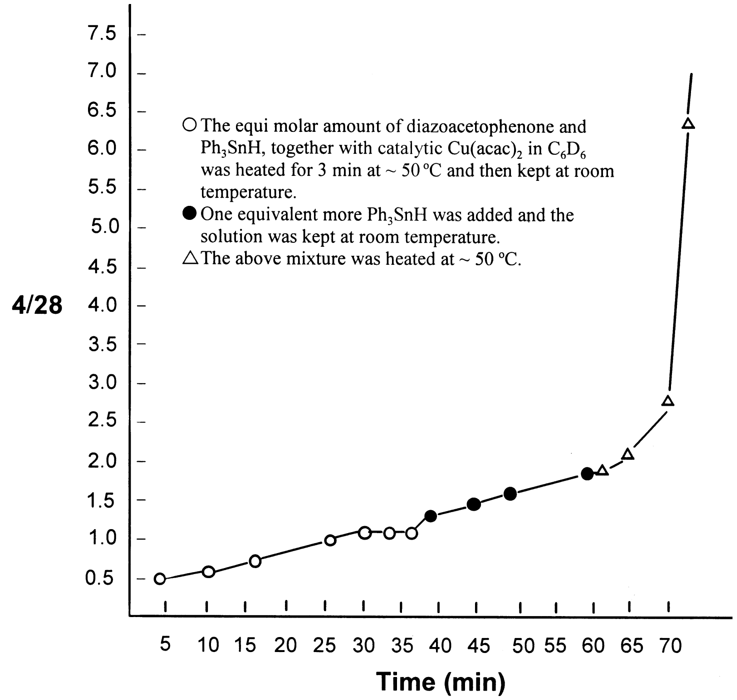
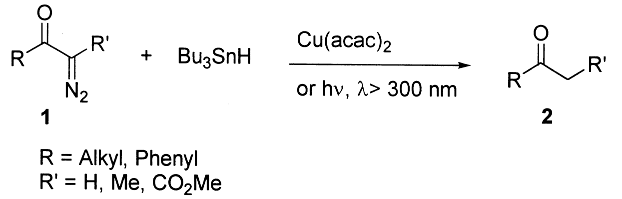


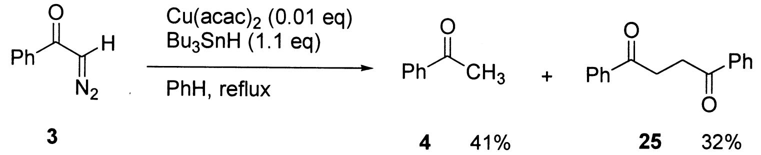
Figure 1. The Cu(acac)$_2$-catalyzed diazo decomposition of diazoacetophenone in the presence of Ph$_3$SnH monitored by ^{1}H NMR spectroscopy.



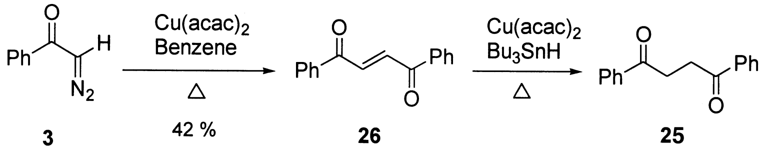
Scheme 1.

could be observed, together with acetophenone and starting diazoacetophenone.[9] The molar ratio for the three compounds was estimated by the ^{1}H 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$_3$SnH 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$_2$O in the mixture, since our independent experiment showed that H$_2$O 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).

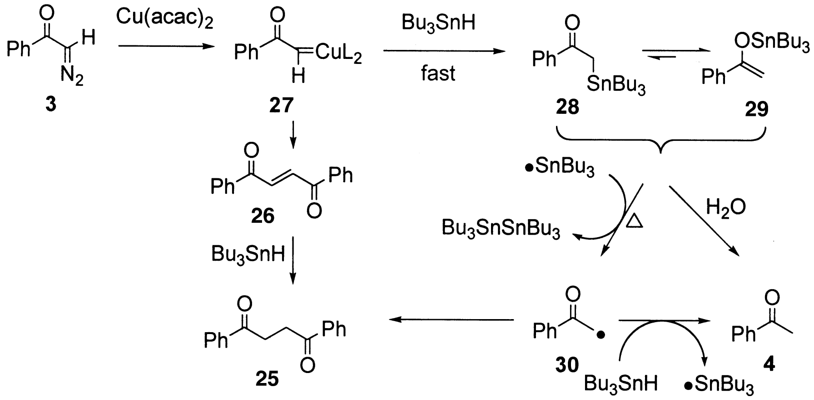
To further prove the existence of the radical intermediate **30** (vide infra) in the reaction mechanism, we then carried out the Cu(acac)$_2$ catalyzed diazo decomposition of diazoacetophenone in the presence of 1 equiv. of Bu$_3$SnH in refluxing benzene. In this case, acetophenone **4** (41 %) together 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 Cu(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$_3$SnH and Cu(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$_3$SnH was added dropwise to a refluxing solution of 2.5 equiv. of diazoacetophenone in benzene containing catalytic Cu(acac)$_2$, both **26** and **25** were isolated as major products.



Scheme 2.



Scheme 3.



Scheme 4.

A mechanism to account for the above experimental observations is proposed in Scheme 4. As generally accepted, the metal carbene forms through nitrogen extrusion in the diazo decomposition process.[1,10] The α-stannyl carbonyl is then formed by carbenoid Sn–H insertion reaction. In comparison, the Sn–H insertion by Rh(II)-carbene has been reported to be an efficient process.[2e] The relatively unstable α-stannyl carbonyl **28** then decomposes in refluxing benzene to generate an α-carbonyl radical which can abstract hydrogen from Ph_3SnH.[11] Since the α-stannyl carbonyl is easily hydrolyzed by H_2O, we cannot rule out the possibility that some of the product is formed by the hydrolysis due to trace amounts of H_2O in the reaction system. The formation of the diketone **25** might be due to the coupling of the radical intermediate **30**, but a different route through direct coupling of metal-carbene with diazo carbonyl and then reduction by Ph_3SnH is more likely (**27** to **26** to **25**).

For the reaction under photochemical conditions, it is possible that the reaction follows a similar mechanism in which the initial Sn–H insertion is carried out by a free carbene generated photochemically from the diazo substrate. The resulting α-stannyl carbonyl could decompose to generate the α-carbonyl radical under photochemical conditions.[11] If the reaction indeed follows this mechanism, the Sn–H insertion by the α-carbonyl carbene must be a highly efficient process. This is consistent with the previous investigations by Doyle et al., which showed that phenylchlorocarbene could insert into the Sn–H bond with rate a constant greater than its insertion into Si–H bond of organosilane.[2b,c,d]

This efficient reduction of the diazo group by Bu_3SnH might find synthetic applications. With this reaction, we can transform a carboxylic group into a methyl ketone group (entries 1,2,4,8, Table 1) or an ethyl ketone group (entry 6, Table 1) in three steps through the diazo compounds. The same transformation was conventionally achieved by converting the carboxylic acid to acyl chloride and then treating it with organocuprates.[12] The α-diazo carbonyl route provides an alternative method to achieve this transformation.

Experimental

All reactions with air- and moisture-sensitive components were performed under a nitrogen atmosphere in a flame-dried reaction flask, and the components were added via syringe. All solvents were distilled prior to use. The boiling point of petroleum ether is between 30 and 60°C. THF was distilled from sodium prior to use. For chromatography, 100–200 mesh silica gel (Qingdao, China) was employed. For preparative TLC, 10–40 μm silica gel GF_{254} (Qingdao, China) was used. Recrystallization was from petroleum ether–ethyl acetate. Diazomethane and diazoethane solutions in dry ether was prepared from *N*-methyl-*N*-nitrosourea and *N*-ethyl-*N*-nitrosourea,[13,14] respectively. ^1H and ^{13}C NMR spectra were recorded at 200 and 50 MHz with a Varian Mercury 200 spectrometer, or at 400 and 100.6 MHz with a Brucker ARX400 spectrometer. Chemical shifts are reported in ppm using tetramethylsilane as internal standard. IR spectra were recorded with a Nicolet 5MX-S infrared spectrometer. Mass spectra were obtained on a VG ZAB-HS mass spectrometer.

α-Diazo ketones **3**,**5**,**9**,**13**,**15**,**17**,**19**,**22** were prepared by converting an acid into the corresponding acyl chloride and then treating it with an ethereal solution of diazomethane or diazoethane.[3e] Compounds **3**, **5**, **9** and **15** are known[15,16] and their data were consistent with that reported in the literature.

2-Diazo-7-phenyl-3-heptanone 13. Yellow oil. ^1H NMR (200 MHz, $CDCl_3$): δ 1.55–1.80 (m, 4H), 1.92 (s, 3H), 2.40–2.60 (m, 2H), 2.62 (t, J=6.5 Hz, 2H), 7.09–7.35 (m, 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}; ^{1}H 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 [$(M-N_2)^+$, 7%], 156 (4), 125 (3), 114 (4), 101 (21); HRMS calcd for $(M-N_2)^+$, $C_{10}H_{16}O_3$ 184.1099, found 184.1102.

Diazo α-ketoester **11** was prepared by standard diazo transfer reaction (TsN_3/Et_3N/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}; ^{1}H 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 [$(M-N_2)^+$, 6 %], 200 [$(M-N_2-MeOH)^+$, 29], 172 (15), 144 (20), 117 (41), 91 (100); HRMS calcd for $(M-N_2)^+$, $C_{14}H_{16}O_3$ 232.1099, found 232.1099.

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

Method A. The diazo compound (1.0 mmol), $Cu(acac)_2$ (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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References

1. For recent comprehensive reviews on the reaction of α-diazo carbonyl compounds, 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) McKervey, M. A.; Ye, T. *Chem. Rev.* **1994**, *94*, 1091.

2. (a) Lesbre, M.; Buisson, R. *Bull. Soc. Chim. Fr.* **1957**, 1204. (b) Padwa, A.; Eastman, D. *J. Org. Chem.* **1969**, *34*, 2728. (c) Doyle, M. P.; Taunton, J.; Oon, S.-M.; Liu, M. T. H.; Soundararajan, N.; Platz, M. S.; Jacson, J. E. *Tetrahedron Lett.* **1988**, *29*, 5863. (d) Jackson, J. E.; Soundararajan, N.; Platz, M. S.; Doyle, M. P.; Liu, M. T. H. *Tetrahedron Lett.* **1989**, *30*, 1335. (e) Andrey, O.; Landais, Y.; Planchenault, D.; Weber, V. *Tetrahedron* **1995**, *44*, 12083.

3. (a) Wang, J.; Chen, B.; Bao, J. *J. Org. Chem.* **1998**, *63*, 1853. (b) Wang, J.; Liang, F.; Chen, B. *J. Org. Chem.* **1998**, *63*, 8589. (c) Chen, B.; Liang, F.; Chen H.; Wang, J. *J. Chem. Res., Synop.* **1998**, 410. (d) Wang, J.; Liang, F. *Chin. Chem. Lett.* **1998**, *9*, 701. (e) Wang, J.; Hou, Y. *J. Chem. Soc. Perkin Trans. 1* **1998**, 1919. (f) Wang, J.; Hou, Y. *J. Chem. Soc. Perkin Trans. 1* **1999**, 2277. (g) Wang, J.; Hou, Y.; Wu, P.; Qu, Z.; Chen, A. S. C. *Tetrahedron: Asymmetry* **1999**, *10*, 4553.

4. Bu_3SnH is known to react with isonitriles and nitro groups, see: Barton, D. H. R.; Mortherwell, W. B. *Pure Appl. Chem.* **1981**, *53*, 15. (b) Ono, N.; Kaji, A. *Synthesis* **1986**, 693. The addition of Bu_3SnH to C=N group is also known, see: Palmisano, G.; Lesma, G.; Nali, M.; Rindone, B.; Tollari, S. *Synthesis* **1985**, 1072.

5. Wanger, R. W.; Tome, J. M. *J. Am. Chem. Soc.* **1950**, *72*, 3477.

6. (a) Horner, L.; Schwarz, H. *Tetrahedron Lett.* **1966**, 3579. (b) Horner, L.; Schwarz, H. *Liebigs Ann. Chem.* **1971**, *747*, 1.

7. Pellicciari, R.; Natalini, B.; Cecchetti, S.; Fringuelli, R. *J. Chem. Soc. Perkin Trans. 1* **1985**, 493.

8. Cox, G. G.; Miller, D. J.; Moody, C. J.; Sie, E. H. B.; Kulagowski, J. J. *Tetrahedron* **1994**, *50*, 3195.

9. The α-stannyl ketone can be easily identified by a singlet at δ 3.24, with characteristic tin statellites corresponding to J_{119Sn}=69.6 Hz and J_{117Sn}=67.2 Hz, due to the α-CH_2SnPh_3 group. The acetophenone was identified by the singlet of the methyl group at δ 2.06. Ph_3SnH was used in the NMR study instead of Bu_3SnH because of the simplicity of the spectra in the high field.

10. Pirrung, M. C.; Morehead Jr., A. T. *J. Am. Chem. Soc.* **1996**, *118*, 8162.

11. Watanabe, Y.; Yoneda, T.; Ueno, Y.; Toru, T. *Tetrahedron Lett.* **1990**, *31*, 6669.

12. March, J. *Advanced Organic Chemistry*; 4th ed.; Wiley-Interscience: New York, 1992, p 487.

13. Arndt, F. *Organic Synthesis Collective Volume 3*, 1943; pp 165 and 461.

14. Wilds, A. L.; Meader Jr., A. L. *J. Org. Chem.* **1948**, *13*, 763.

15. Kennedy, M.; McKervey, M. A.; Maguire, A. R.; Tulladhar, S. M.; Twohig, M. F. *J. Chem. Soc. Perkin Trans. 1* **1990**, 1047.

16. Pellicciari, R.; Natalini, B.; Cecchetti, S.; Santucci, S. *Tetrahedron Lett.* **1984**, *25*, 3103.

17. Ho, T.-L.; Wong, C. M. *Synth. Commun.* **1975**, *5*, 91.

18. Kise, N.; Suzumoto, T.; Shono, T. *J. Org. Chem.* **1994**, *59*, 1407.

19. Kasturi, T. R.; Mathew, L.; Sattigeri, J. A. *Indian J. Chem., Sect. B* **1990**, *29*, 1004.

20. Molander, G. A.; Stengel, P. J. *J. Org. Chem.* **1995**, *60*, 6660.