

Reaction of β -trimethylsiloxy α -diazocarbonyl compounds with trimethylsilyl halides: a novel diazo decomposition process

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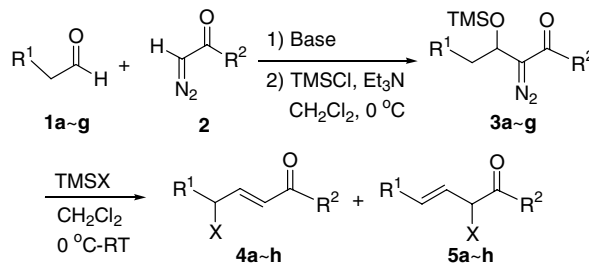
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Abstract—When β -trimethylsiloxy α -diazocarbonyl compounds were treated with trimethylsilyl halide, a mixture of α - and γ -halide substituted unsaturated carbonyl compounds was obtained. The mechanism of this novel diazo decomposition process was discussed.

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α -Diazocarbonyl compounds as the metal carbene precursors in catalytic reactions have attracted great attention over the past decades.¹ On the other hand, the relatively stable α -diazocarbonyl compounds can tolerate a number of chemical transformations with the diazo functionality keeping unchanged. For example, ethyl diazoacetate can be deprotonated with LDA or NaH, and the resulting anion can further react with C=O or C=N groups to give α -diazocarbonyl compounds with β -hydroxy or β -amino substituent.² Our recent study suggests that β position of the α -diazocarbonyl compound is liable to nucleophilic substitution.³ This observation makes it possible to prepare the diazo compounds with various β -substituents. We have used this strategy to prepare some new α -diazocarbonyl compounds with different β -substituents such as Ts and SR, and their reactions catalyzed by Rh(II) have been studied.^{4,5}

To further explore the utility of α -diazocarbonyl compounds in organic synthesis, we have converted the β -hydroxyl group in diazo compound into β -siloxy group to afford β -siloxy substituted diazo compound **3a–g** (Scheme 1).⁶ When **3a–e** was further treated with trimethylsilyl halide, a novel diazo decomposition process occurred to give α - and γ -halide substituted unsaturated carbonyl compounds **4a–h** and **5a–h**.



Scheme 1.

The nucleophilic addition of acyldiazomethane **2** with aldehyde **1a–g** gave β -hydroxy α -diazocarbonyl compounds, which were followed by the reaction with TMSCl in the presence of triethylamine in CH₂Cl₂ at 0 °C to room temperature. The β -trimethylsiloxy α -diazocarbonyl compounds **3a–g** were obtained in high yields (Table 1).^{6,7} The diazo compounds **3a–g** are relatively stable and can be kept at room temperature for days without detectable decomposition.

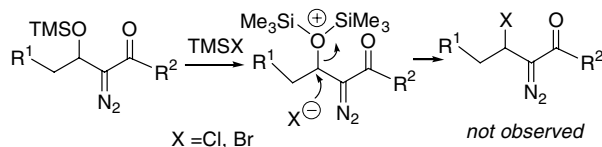
β -Trimethylsiloxy α -diazocarbonyl compounds **3a** were further treated with trimethylsilyl chloride with the expectation that β -chloro substituted α -diazo compounds may be obtained, as shown in Scheme 2.

However, when **3a** was treated with TMSCl in CH₂Cl₂ at 0 °C to room temperature, the diazo compound was decomposed to give two major products, none of them was the expected β -chloro substituted α -diazo compound. Inspection of the two products with IR, ¹H

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Table 1. Reaction of β -hydroxy α -diazo esters with trimethylsilyl chloride

Entry	Aldehyde R^1	Diazo R^2	Product	Yield ^a (%)
1	CH ₃	OEt	3a	91
2	CH ₃ CH ₂	OEt	3b	90
3	CH ₃ (CH ₂) ₂	OEt	3c	90
4	CH ₃ (CH ₂) ₄	OEt	3d	89
5	Ph	OEt	3e	88
6	CH ₃	CH ₃	3f	89
7	CH ₃ (CH ₂) ₂	CH ₃	3g	88

^a Yields after column chromatographic purification with silica gel.**Scheme 2.**

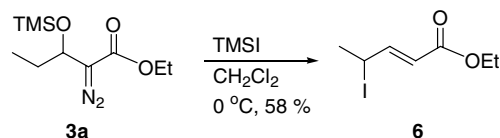
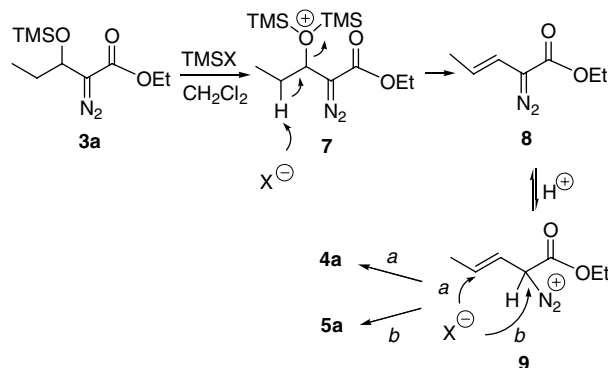
NMR and MS spectra indicated one product was (*E*)-ethyl 4-chloropent-2-enoate **4a** ($R^1 = \text{CH}_3$, $R^2 = \text{Et}$, $X = \text{Cl}$), the other one was (*E*)-ethyl 2-chloropent-3-enoate **5a** ($R^1 = \text{CH}_3$, $R^2 = \text{OEt}$, $X = \text{Cl}$). The diazo decomposition with TMSCl was surprising, and to the best of our knowledge, this type of reaction of α -diazo-carbonyl compound has not been reported before. The reaction of TMSCl with other β -trimethylsiloxy α -diazo-carbonyl compounds gave similar results (Table 2),⁸ except in the case of **3e**, in which case a complex mixture was formed. For the reactions with substrates **3f** and **3g**, same results were obtained but the products were all volatile and unstable compounds. Accurate data of yields could not be determined for these two cases.

When trimethylsilyl bromide was used instead of trimethylsilyl chloride, the corresponding mixture of bromide **4** ($X = \text{Br}$) and **5** ($X = \text{Br}$) were obtained in similar yields (Table 2). It was noted that the reaction had no selectivity with two isomeric products **4** and **5** isolated in almost 1:1 ratio.

It was also noted that compound **4a–h** was not stable even in refrigerator. Partial conversion of **4** to **5** was observed. Trimethylsilyl iodide (TMSI) could also react with **3**. Compound **3a** was treated with TMSI in CH_2Cl_2 at 0 °C to give (*E*)-ethyl 4-iodopent-2-enoate **6** as the

Table 2. Reaction of **3a–e** with TMSCl or TMSBr

Entry	3	TMSX ($X =$)	Products	Yield ^a (%)	Ratio ^b (4:5)
1	a	Cl	4a+5a	56	41:59
2	a	Br	4b+5b	52	48:52
3	b	Cl	4c+5c	64	39:61
4	b	Br	4d+5d	63	57:43
5	c	Cl	4e+5e	55	35:65
6	c	Br	4f+5f	60	47:53
7	d	Cl	4g+5g	64	50:50
8	d	Br	4h+5h	55	45:55

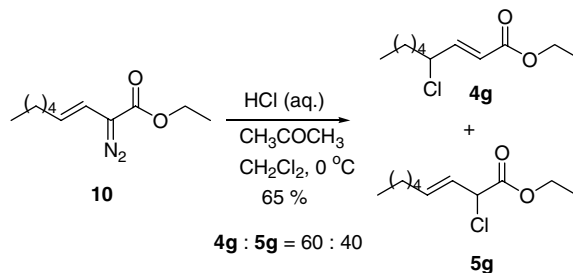
^a Yields after column chromatographic purification with silica gel.^b Ratios after column chromatographic purification with silica gel.**Scheme 3.****Scheme 4.**

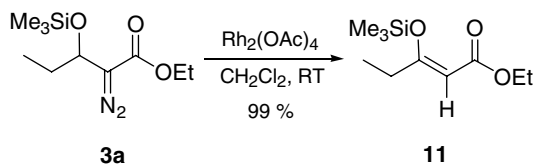
only product in 58% yield. No isomeric product similar to **5** could be identified from the reaction mixture. The γ -iodo substituted product **6** was highly unstable at room temperature (Scheme 3).

A plausible reaction mechanism was proposed to account for the formation of **4** and **5** (Scheme 4). The reaction of **3a** with TMSX generated an intermediate **7**, in which the β substituent became a better leaving group. E2 type elimination gave vinyl diazo carbonyl compound **8**, which could be further protonated at the diazo carbon. Nucleophilic attack by X^- could occur at both α - and γ -position to give **4a** and **5a** with the extrusion of N_2 .

This proposed mechanism was supported by the following experiments. When vinyl diazocarbonyl compound **10** was treated with aqueous HCl in acetone, a mixture of **4g** and **5g** was isolated in moderate yield (combined yield of 65 %) with a ratio of 60:40 (Scheme 5).

On the other hand, when **3a** was treated with $\text{Rh}_2(\text{OAc})_4$ (1 mol %) in CH_2Cl_2 at room temperature, 1,2-hydrogen shift product **11** was isolated in almost quantitative yield (Scheme 6). Other diazo compounds gave similar results

**Scheme 5.**



Scheme 6.

when treated with $\text{Rh}_2(\text{OAc})_4$. This reaction may be served as a good method for preparing this type of enol trimethylsilyl ethers.

In summary, we have observed a novel reaction of β -trimethylsiloxy α -diazocarbonyl compounds with TMSX ($\text{X} = \text{Br}, \text{Cl}$), which give α - and γ -halide substituted unsaturated carbonyl compounds. This reaction may find synthetic application as a new entry to these halides. As far as our knowledge is concerned, there are only limited methods to prepare these halides.⁹

Acknowledgements

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- General procedure for the reaction of β -hydroxy α -diazocarbonyl compounds with TMSCl*: In a flamed three-necked round bottom flask, β -hydroxy α -diazocarbonyl compound (1.0 mmol) was dissolved in CH_2Cl_2 (5 mL). Triethylamine (3.0 mmol) was added to the solution at 0 °C. After stirring for 10 min, TMSCl (1.2 mmol) was added with syringe. The mixture was allowed to stir for 4 h between 0 °C and room temperature. The reaction mixture was quenched by water and was extracted twice with CH_2Cl_2 , washed with saturated brine and dried. After evaporation of the solvent, a residue was obtained which was purified by column chromatography on silica gel (petroleum ether/acetone = 100:0.1) to afford pure products **3a–g**. Ethyl 2-diazo 3-trimethylsiloxy pentanoate (**3a**): ^1H NMR (300 MHz, CDCl_3): δ 0.00 (s, 9H), 0.79 (t, $J = 7.5$ Hz, 3H), 1.13–1.15 (t, $J = 7.2$ Hz, 3H), 1.49–1.56 (m, 2H), 4.10 (qd, $J = 7.2$, 1.5 Hz, 2H), 4.40 (t, $J = 6.8$, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ –0.31, 9.87, 14.16, 29.29, 60.62, 67.84, 165.86.
- General procedure for the reaction of **3a–d** with TMSX*: In a flamed three-necked round bottom flask, β -trimethylsiloxy α -diazocarbonyl compound **3a–d** (1.0 mmol) was dissolved in CH_2Cl_2 (5 mL). TMSX ($\text{X} = \text{Cl}$ or Br , 1.0 mmol) was added by syringe at 0 °C. The mixture was allowed to stir at 0 °C until all the diazo substrate disappeared as judged by IR spectra. Evaporation of the solvent gave a residue, which was purified by column chromatography on silica gel (petroleum ether/ether = 200:1) to afford the pure products of **4a–h** and **5a–h**. Representative data: (*E*)-ethyl 2-chlorohept-3-enoate (**4e**). IR (film): ν 1264, 1743 cm^{-1} ; ^1H NMR (200 MHz, CDCl_3): δ 0.91 (t, $J = 7.2$ Hz, 3H), 1.30 (t, $J = 7.2$ Hz, 3H), 1.38–1.49 (m, 2H), 2.02–2.13 (m, 2H), 4.21 (q, $J = 7.2$, 2H), 4.74 (d, $J = 8.6$ Hz, 1H), 5.61–5.74 (m, 1H), 5.82–5.96 (m, 1H); ^{13}C NMR (50 MHz, CDCl_3): δ 3.52, 13.96, 21.71, 34.09, 58.10, 62.15, 124.66, 137.82, 168.56; MS m/z (EI) 155 [(M–Cl) $^+$, 75], 127 (23), 117 (2), 109 (11), 97 (4), 81 (100), 75 (58). (*E*)-Ethyl 4-chlorohept-2-enoate (**5e**). IR (film): ν 228, 1268, 1723 cm^{-1} ; ^1H NMR (200 MHz, CDCl_3): δ 0.94 (t, $J = 7.2$ Hz, 3H), 1.30 (t, $J = 7.2$ Hz, 3H), 1.40–1.55 (m, 2H), 1.78–1.89 (m, 2H), 4.22 (q, $J = 7.2$, 2H), 4.40–4.51 (m, 1H), 6.02 (dd, $J = 1.0$, 15.4 Hz, 1H), 6.89 (dd, $J = 7.8$, 15.4 Hz, 1H); ^{13}C NMR (50 MHz, CDCl_3): δ 3.34, 14.18, 19.41, 39.59, 59.61, 60.65, 122.31, 146.2, 165.84; MS m/z (EI) 190 (M^+ , 6), 162 (15), 155 (71), 145 (35), 127 (30), 120 (30), 109 (24), 81 (97), 29 (100).
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