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

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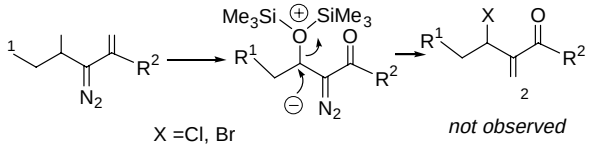
Abstract— hen β-trimethylsiloxy α-diazocarbonyl compounds were treated with trimethylsilyl halide, a mixture of α- and γ-halide substituted unsaturated carbonyl compounds was obtained. The mechanism of this novel diazo decomposition process was discussed.

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. e have used this strategy to prepare some new α-diazocarbonyl compounds with different β-substitP31HH–wY,TH))D4-sFcth a

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_3CH_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** ($R^1 = CH_3$, $R^2 = Et$, X = Cl), the other one was (*E*)-ethyl 2-chloropent-3-enoate **5a** ($R^1 = CH_3$, $R^2 = OEt$, X = Cl). The diazo decomposition with TMSCl was surprising, and to the best of our knowledge, this type of reaction of α-diazocarbonyl compound has not been reported before. The reaction of TMSCl with other β-trimethylsiloxyl α-diazocarbonyl 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.

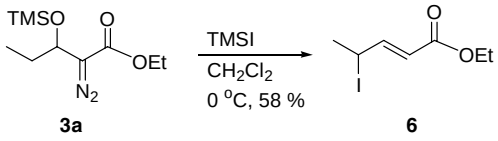
hen trimethylsilyl bromide was used instead of trimethylsilyl chloride, the corresponding mixture of bromide **4** (X = Br) and **5** (X = Br) were obtained in similar yields (Table 2). It was noted that the reaction had no selectivity with two isomeric products **4** and **5** isolated in almost 1:1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

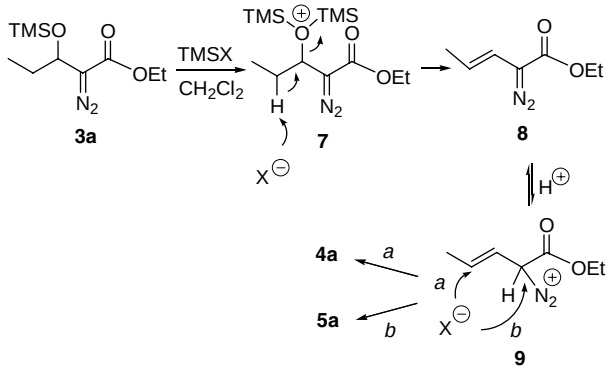
Table 2. Reaction of

				[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.

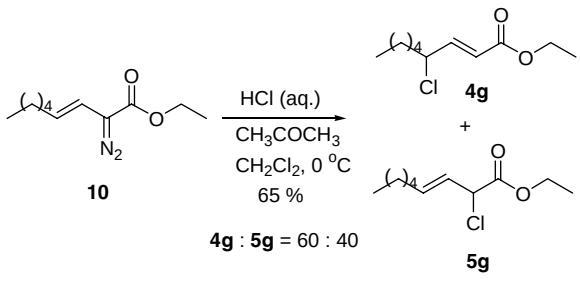


Scheme 4.

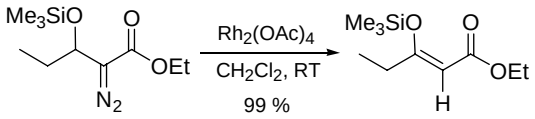
A plausible reaction mechanism was proposed to account for the formation of **4** and **5** (Scheme 4). The reaction of **3a** with TMSX generated an intermediate **7**, in which the β substituent became a better leaving group. E2 type elimination gave vinyl diazo carbonyl compound **8**, which could 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. hen 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 $Rh_2(OAc)_4$ (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.



3a 11

Scheme 6.

when treated with $Rh_2(OAc)_4$. 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-trimethylsiloxyl α-diazocarbonyl compounds with TMSX (X = Br, 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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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*; iley-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.; illiamson, 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) enkert, E.; McPherson, A. A. *J. Am. Chem. Soc.* **1972**, *94*, 8084–8090; (g) Burkoth, T. L. *Tetrahedron Lett.* **1969**, *10*, 5049–5052; (h) oolsey, N. F.; Khalil, M. H. *J. Org. Chem.* **1972**, *37*, 2405–2408; (i) Jiang, N.; Qu, Z.; ang, J. *Org. Lett.* **2001**, *3*, 2989–2992; (j) Jiang, N.; ang, J. *Tetrahedron Lett.* **2002**, *43*, 1285–1287; (k) Jiang, N.; Ma, Z.; Qu, Z.; Xing, X.; Xie, L.; ang, J. *J. Org. Chem.* **2003**, *68*, 893–900.
3. Shi, .; Zhang, B.; Liu, B.; Xu, F.; Xiao, F.; Zhang, J.; Zhang, S.; ang, J. *Tetrahedron Lett.* **2004**, *45*, 4563–4566.
4. Shi, .; Zhang, B.; Zhang, J.; Liu, B.; Zhang, S.; ang, J. *Org. Lett.* **2005**, *7*, 3103–3106.
5. Xu, F.; Shi, .; ang, J. *J. Org. Chem.* **2005**, *70*, 4191–4194.
6. Sarabia García, F.; Pedraza Cebrián, G. M.; Heras López, A.; López Herrera, F. J. *Tetrahedron* **1998**, *54*, 6867–6896.
7. *General procedure for the reaction of β-hydroxy α-diazo carbonyl 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**): ^{1}H 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.
8. *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 (X = 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}; ^{1}H 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}; ^{1}H 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).
9. (a) Duclos, J. F.; Outurquin, F.; Paulmier, C. *Tetrahedron Lett.* **1993**, *34*, 7417–7420; (b) Dussault, P. H.; Eary, C. T.; Lee, R. J.; Zope, U. R. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2189–2204; (c) Tunge, J. A.; Mellegaard, S. R. *Org. Lett.* **2004**, *6*, 1205–1207.