March, 1987] © *1987 The Chemical Society of Japan* *Bull. Chem. Soc. Jpn.*, ***60***, *1063—1066 (1987)* 1063

A Convenient Reduction Method of *β*-Phenyl *α*,*β*-Unsaturated Carbonyl Compounds with Me_3SiCl-NaI-ROH Reagent

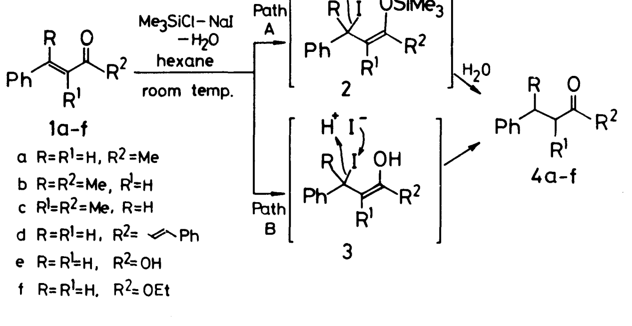
Takashi Sakai, Kazuyoshi Miyata, Masanori Utaka, and Akira Takeda*
Department of Synthetic Chemistry, School of Engineering, Okayama University,
Tsushima, Okayama 700

(Received July 23, 1986)

Treatment of *β*-phenyl *α*,*β*-unsaturated ketones, cinnamic acid and its ester with Me_3SiCl-NaI-ROH reagent in hexane at room temperature gave the corresponding saturated carbonyl compounds in good yields. A similar reaction of 2,4-hexadienoic acid afforded 4-hexanolide.

A Me_3SiCl-NaI reagent has been applied to a variety of organic syntheses as a Me_3SiI equivalent,[1)] where beside the application to cleavage of ether, ester and amide,[2)] it can be used effectively in the deoxygenation of sulfoxide,[3)] alcohol,[4)] epoxide,[5)] and vicinal diol[6)] as well as in the dehalogenation of *α*-halo ketone.[7)] The reagent is also effective for the conversion of *α*,*β*-unsaturated carbonyl compounds to *β*-iodo carbonyl compounds. Thus, the reaction of conjugated enones with Me_3SiI gives *β*-iodo ketones,[8)] and a similar treatment of 2-alkenoic acids affords trimethylsilyl 3-iodoalkanoates.[9)] Recently, Larson et al.[10)] have reported that acrylaldehyde and methyl vinyl ketone were transformed into ethylene acetals of 3-iodopropanal and 4-iodo-2-butanone, respectively, by the action of Me_3SiCl-NaI-ethylene glycol reagent in CH_3CN. However, reduction of carbon-carbon (C-C) double bond of *α*,*β*-unsaturated carbonyl compounds with the reagent has not been reported.

In relation to our continuing investigations[11,12)] to extend the applicability of the Me_3SiCl-NaI reagent in organic synthesis, we have found that *β*-phenyl *α*,*β*-unsaturated ketones, ester, and acid (**1a—f**) can be reduced to the corresponding saturated carbonyl compounds (**4a—f**) in good yields by using an excess of Me_3SiCl-NaI-ROH reagent in hexane at room temperature (Scheme 1 and Table 1). It is interesting that water or poly alcoholic compounds such as 2,3-butanediol, (*R*,*R*)-diethyl tartrate, and cellulose are used for ROH as hydrogen sources.



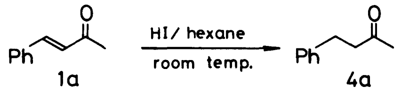
Scheme 1.

Although such transformation can be done by using several known methods, for example, alkali metals in liquid ammonia,[13)] amalgamated zinc in hydrochloric acid,[14)] Me_3SiH in CF_3CO_2H,[15)] combination of $LiAlH_4$ and CuI,[16)] 2-phenylbenzothiazoline,[17)] Hantzsch ester-silica gel,[18)] and so on, the present method offers the significant advantages that the reagent is inexpensive and the reaction can be done conveniently under mild conditions. Furthermore, products obtained after washing with aqueous $Na_2S_2O_3$ have sufficient purity, as checked by using ^1H NMR.

The present reaction was usually carried out by adding Me_3SiCl (6—10 mmol) with stirring to a mixture of substrate 1 (1 mmol), NaI (6—10 mmol), H_2O (6—10 mmol), and hexane (2 ml) as shown in Table 1. Since the amount of water added was equimolar with those of Me_3SiCl and NaI, it would completely be consumed to produce HI. The reaction was retarded by using a large excess of water. When 10 mmol of water and 6 mmol of Me_3SiCl-NaI were used in the reduction of 1 mmol of **1a**, **4a** was obtained still in an 80% yield. However, an increase in the amount of water to 30 mmol (five equivalents of Me_3SiCl-NaI) decreased the yield of **4a** to 23% accompanied by unidentified impurities. A further increase in the amount of water to 60 mmol resulted merely in recovery of **1a**.

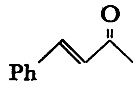
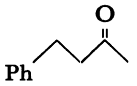
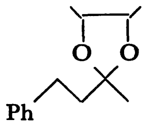
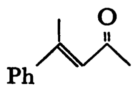
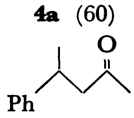
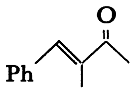
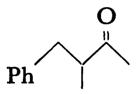
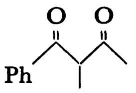
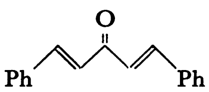
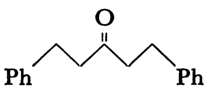
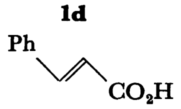
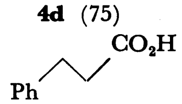
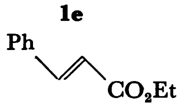
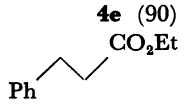
Scheme 1 shows a possible mechanism for the reduction which involves two pathways. In path A, the reaction is initiated by 1,4-addition of Me_3SiI generated in situ to **1** to produce *β*-iodo enol silyl ether intermediate **2**, whose allylic and benzylic iodo substituent would be extremely labile and attacked by an iodide anion existing in excess to generate iodine molecule in parallel with hydrogenation. The compound having the same functionality as that of **2** has been isolated by Miller[8)] in the reaction of *α*,*β*-unsaturated ketone with Me_3SiI under anhydrous conditions, and identified by using ^1H NMR. In the present reaction, however, the intermediate **2** seems to make relatively small contribution because, as described above, the reaction in the presence of 1.67 equivalent of water to Me_3SiCl-NaI gave **4a** in 80% yield in spite of the fact that Me_3SiCl and Me_3SiI are readily hydrolysed by water.[19] In path B, HI generated in situ adds to the C–C double bond of **1** to give β-iodo ketone intermediate **3** as reported in the literatures.[9,10] Subsequent reduction of **3** with HI leads to **4** in a manner similar to path A. Path B is supported on the basis of two facts: a) addition of **1a** to a stirred mixture of Me3SiCl, NaI, H2O, and hexane also gave **4a** in an 80% yield, and b) the reaction of **1a** with dry HI, generated by adding 55% aqueous HI to phosphorus pentoxide, also afforded **4a** in a 57% yield (Scheme 2). Comparison of the yield between the two methods indicates the obvious advantage of the present method using Me3SiCl-NaI-H2O.

Table 1 shows several examples of the reactions by using olefins whose C–C double bond is conjugated with phenyl group and carbonyl moiety. When 2,3-butanediol was employed instead of water for the reduction of **1a**, cyclic acetal **5** was obtained predominantly. The work-up procedure becomes more convenient by using cellulose (absorbent cotton), which is easily removable from the reaction mixture. It is worthy to note here that asymmetric induction



Scheme 2.

Table 1. Reduction of β-Phenyl α,β-Unsaturated Carbonyl Compounds **1a**—**f** with Me_3SiCl-NaI-ROH Reagent

Substrate[a]	ROH[b] (Molar ratio vs. 1)	Reaction time/h	Product[c] (Yield/%)[d]
 **1a**	A (6)	30	 **3a** (86)
1a	A (6)[e]	30	**4a** (95)[f]
1a	B (10)	38	**4a** (29) +  **5** (51)
1a	C[g]	20	**4a** (60)
 **1b**	A (10)	22	 **4b** (52)
1b	C[g]	22	**4b** (70)[h]
1b	D (3)	7	**4b** (81)[i]
 **1c**	A (10)	31	 +  **4c** (42) **6** (31)
 **1d**	A (10)	100	 **4d** (75)
 **1e**	A (10)	100	 **4e** (90)
 **1f**	A (10)	108	 + **4e** (27) **4f** (66)

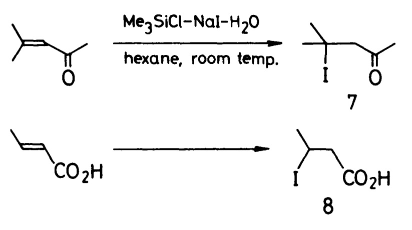
a) 1 mmol of substrate was generally used. b) A: H_2O; B: 2,3-butanediol; C: cellulose (absorbent cotton); D: (*R*,*R*)-diethyl tartrate. c) Products obtained are known compounds excepting 5. d) Isolated yield by preparative TLC. e) 10 mmol of substrate was used. f) After purification by distillation. g) Against 1 mmol of **1a** or **1c**, 1.8 g of cellulose (absorbent cotton) was used. h) $[\alpha]_D^{23}$ −1.2° (*c* 3.06, C_6H_6) [maximun rotation, $[\alpha]_D$ −75.5° (*c* 1, C_6H_6) for *R*-(−)-**4b**: F. Leyendercker, F. Jesser, and B. Ruhland, *Tetrahedron Lett.*, **22**, 3601 (1981)]. i) $[\alpha]_D^{21}$ −1.8° (*c* 4.1, C_6H_6).

was observed, though very slight, in the reduction of **1b** by using (*R*,*R*)-diethyl tartrate or cellulose. Reaction of **1c** with Me_3SiCl–NaI–H_2O reagent afforded **4c** and oxidation product **6**, which may be formed via addition of generated iodine to **1c** and subsequent hydrolysis. The methyl group at C-3 would retard 1,4-addition of iodide anion by the electron donating effect.[20]

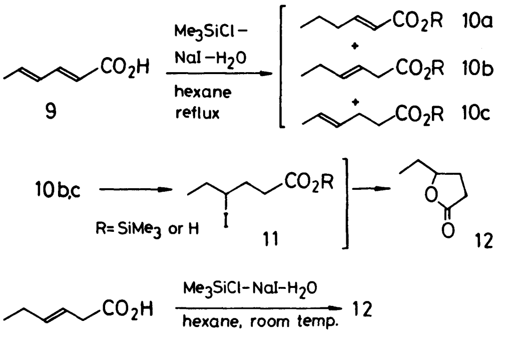
Unfortunately, the present reduction method is not applicable to β-alkyl α,β-unsaturated ketone and acid. For example, the reactions with mesityl oxide and crotonic acid gave merely 4-iodo-4-methyl-2-pentanone (**7**) (70% yield) and 3-iodobutanoic acid (**8**) (94% yield), respectively, as expected[8,9,10] (Scheme 3).

The reactions listed in Table 1 were generally done in a small scale by using 1 mmol of substrates. The crude products obtained were therefore purified by preparative TLC. The preparative scale of 10 mmol order was exemplified by employing typical enone **1a**. In this case, vacuum distillation of the crude product gave **4a** with 98% purity (GLPC and ^{1}H NMR analysis) in a 95% yield.

The Me_3SiCl–NaI–H_2O reagent was also found to be effective for the transformation of 2,4-hexadienoic acid (**9**) to 4-hexanolide (**12**) (54% yield), although it required refluxing. The formation of **12** suggests the occurrence of the reduction of **9** to a mixture of regioisomers of hexenoic acids and/or their trimethylsilyl esters (**10a**—**c**), addition of HI to **10b**, **c** to give 4-iodohexanoic acid and/or its trimethylsilyl ester (**11**), and lactonization to **12** in a successive way (Scheme 4). We confirmed that the treatment of 3-hexenoic acid with the reagent at room temperature also gave **12** in a 66% yield.



Scheme 3.



Scheme 4.

Experimental

General. IR spectra were taken on a JASCO Model A-102 spectrometer. ^{1}H NMR spectra (60 MHz) were measured with a JEOL Model JNM-60 SI spectrometer using Me_4Si as an internal standard. Optical rotation was recorded with a JASCO Model DIP-4 apparatus. GLPC analysis was done with a Hitachi Model 163 gas chromatograph. The preparative TLC was carried out on silica gel (Kieselgel 60 PF_{254}, Merck A. G. Darmstadt). Elemental analysis was performed by Eiichiro Amano of our laboratory. Starting materials **1b**,[21] **1c**,[22] and **1d**[23] were prepared according to the methods reported and **1a**, **1e**, and **1f** are commercially available.

General Procedure for the Reaction of 1a—f with Me_3SiCl-NaI-H_2O Reagent. To a mixture of NaI (1.5 g, 10 mmol), olefin **1** (1 mmol), water (0.18 ml, 10 mmol) and hexane (2 ml), was added Me_3SiCl (1.28 ml, 10 mmol) dropwise with stirring. Then, stirring was continued at room temperature for the time indicated in Table 1. During the course of the reaction, the mixture was colored dark purple gradually due to liberated iodine. After addition of water (3 ml), the ether extract was washed with aqueous $Na_2S_2O_3$ and brine, dried over $MgSO_4$, and concentrated. Purification of the residue by preparative TLC (hexane–ether 3:1) gave product, whose IR and ^{1}H NMR spectral data were identical with those reported (compounds **4a**,[24] **4b**,[25] **4c**,[24] **4d**,[26] **6**,[27] **7**,[28] and **8**[29]) or with those of authentic samples commercially available (**4e** and **4f**).

Reactions by using 2,3-butanediol, (*R*,*R*)-diethyl tartrate, or cellulose for ROH were done in a similar way to that described above and the quantities of ROH used are indicated in Table 1.

Reaction of 1a with Me_3SiCl-NaI-2,3-Butanediol. Crude products were fractionated by preparative TLC (hexane–ether, 3:1) to give **4a** (R_f 0.45, 29% yield) and **5** (R_f 0.67, 51% yield). **5**: IR (neat) 1583, 1604 cm^{-1}; ^{1}H NMR (CCl_4) $\delta=1.18$ (6H, d, $J=6$ Hz), 1.30 (3H, s), 1.84 (2H, m), 2.66 (2H, m), 3.53 (2H, m), 7.08 (5H, s). Anal. ($C_{14}H_{20}O_2$)C, H.

Effects of the Amount of Water on the Yield of 4a. The reaction of **1a** (146 mg, 1 mmol) with Me_3SiCl (0.77 ml, 6 mmol), NaI (900 mg, 6 mmol) and water (0.18 ml, 10 mmol) in hexane (4 ml) was carried out in a manner similar to that described above. The crude product was distilled [bp 105—110 °C (5 mmHg) (1 mmHg=133.322 Pa)] to give **4a** (119 mg, 80% yield).

A similar reaction with an increased amount of water (540 mg, 30 mmol) gave a 88:12 (by ^{1}H NMR) mixture (38 mg) of **4a** (23% yield) and **1a** (3% recovered) after distillation [bp 110 °C (5 mmHg)]. A considerable amount of tarry material remained as a still residue.

The reaction with a large excess of water (1.1 g, 60 mmol) was done in a similar way and the recovery of the most of **1a** with a small amount of unidentified material was confirmed by using ^{1}H NMR.

Reduction of 1a by Addition to a Mixture of Me_3SiCl-NaI-H_2O. A mixture of Me_3SiCl (0.77 ml, 6 mmol), NaI (900 mg, 6 mmol), water (0.108 ml, 6 mmol) and hexane (4 ml) was stirred for 1 h at room temperature and then **1a** (146 mg, 1 mmol) was added. The mixture was stirred for additional 24 h at room temperature and treated in a usual way to give **4a** (120 mg, 80% yield) after distillation.

Reduction of 1a in a Preparative Scale. A similar reaction using **1a** (1.46 g, 10 mmol) and Me_3SiCl–NaI–H_2O each with 60 mmol gave **4a** (1.40 g, 95% yield) after distillation [bp 100—110 °C (5 mmHg)]. GLPC analysis (SE-30, 1.0 m×5 mm o.d., N_2 27 ml min^{-1}, oven temperature 100 °C) of the product showed a peak at the retention time of 4.5 min with an relative intensity of 98%.

Reduction of 1a with Dry HI. To a mixture of **1a** (292 mg, 2 mmol) and hexane (5 ml) was introduced dry HI, which was generated by dropping 55% aqueous HI solution (5 ml, 37 mmol) to phosphorus pentoxide (13 g, 92 mmol).[30] The mixture was stirred for 24 h at room temperature and then poured into aqueous $NaHCO_3$. The organic layer was extracted with ethyl acetate and treated in a usual way to give **4a** (167 mg, 57% yield) after distillation. A tarry material was remained as a still residue.

4-Hexanolide (12) from 2,4-Hexadienoic Acid (9). To a mixture of acid **9** (224 mg, 2 mmol), NaI (3.0 g, 20 mmol), water (0.36 ml, 20 mmol) and hexane (4 ml), was added Me_3SiCl (2.56 ml, 20 mmol) at room temperature. After being stirred under reflux for 18 h, the mixture was washed with aqueous $NaHCO_3$ and treated in a usual way. Kugelrohr distillation [bp 120—130 °C (18 mmHg)] of the residual oil gave **12** (123 mg, 54% yield), whose IR and ^1H NMR spectra were identical with those reported.[31] The aqueous $NaHCO_3$ layer was acidified and the ether extract was treated in a similar way to give 189 mg of a mixture of acidic materials, whose separation and structual identification were unsuccessful.

Lactone 12 from 3-Hexenoic Acid. A mixture of 3-hexenoic acid[32] (228 mg, 2 mmol), Me_3SiCl (2.56 ml, 20 mmol), NaI (3.0 g, 20 mmol), water (360 mmol), and hexane (4 ml) was allowed to react for 44 h at room temperature and treated in a usual way to give **12** (152 mg, 66% yield) after distillation. Attempts to purify the acidic material (87 mg) by preparative TLC was failed.

References

1) Review: G. A. Olah, and S. C. Narang, *Tetrahedron*, **38**, 2225 (1982).

2) G. A. Olah, S. C. Narang, B. G. B. Gupta, and R. Malhotra, *J. Org. Chem.*, **44**, 1247 (1979).

3) G. A. Olah, B. G. B. Gupta, and S. C. Narang, *Synthesis*, **1977**, 583; G. A. Olah, S. C. Narang, B. G. B. Gupta, and R. Malhotra, *Synthesis*, **1979**, 61.

4) W. Ando and M. Ikeno, *Tetrahedron. Lett.*, **1979**, 4941.

5) J. N. Denis, R. Magnane, M. Van Eenoo, and A. Krief, *Nouv. J. Chim.*, **3**, 705 (1979).

6) N. C. Barua, J. C. Sarma, R. P. Sharma, and J. N. Barua, *Chem. Ind.*, **1982**, 956; N. C. Barua and R. P. Sharma, *Tetrahedron Lett.*, **23**, 1365 (1982).

7) G. A. Olah, M. Arvanaghi, and Y. D. Vankar, *J. Org. Chem.*, **45**, 3531 (1980).

8) R. D. Miller and D. R. McKean, *Tetrahedron Lett.*, **1979**, 2305.

9) T. Azuhata and Y. Okamoto, *Synthesis*, **1983**, 461.

10) G. L. Larson and R. Klesse, *J. Org. Chem.*, **50**, 3627 (1985).

11) T. Sakai, K. Miyata, M. Ishikawa, and A. Takeda, *Tetrahedron Lett.*, **26**, 4727 (1985).

12) T. Sakai, K. Miyata, and A. Takeda, *Chem. Lett.*, **1985**, 1137.

13) A. J. Birch, *Quart. Rev. Chem. Soc.*, **4**, 69 (1950).

14) J. G. St. C. Buchanan and P. D. Woodgate, *Quart. Rev. Chem. Soc.*, **23**, 522 (1969).

15) D. N. Kursanov, Z. N. Parnes, and N. M. Loim, *Synthesis*, **1974**, 633.

16) E. C. Ashby, J. J. Lin, and R. Kovar, *J. Org. Chem.*, **41**, 1939 (1976).

17) H. Chikashita, M. Miyazaki, and K. Itoh, *Synthesis*, **1984**, 308.

18) K. Nakamura, M. Fujii, A. Ohno, and S. Oka, *Tetrahedron Lett.*, **25**, 3983 (1984).

19) a) D. A. Armitage, "Comprehensive Organometalic Chemistry," ed by G. Wilkinson, Pergamon Press (Oxford), Vol. 2, p. 155; b) W. Patnode and D. F. Wilcock, *J. Am. Chem. Soc.*, **68**, 358 (1946); c) M. J. Hunter, E. L. Warrick, J. F. Hyde, and C. C. Curre, *ibid.*, **68**, 2284 (1946).

20) For example, the yields of the hydrocyanation of methacryronitrile and methyl methacrylate were greatly reduced as compared with those of acrylonitrile and methyl acrylate: a) W. Nagata and M. Yoshioka, "Organic Reactions," ed by W. G. Dauben, John Wiley & Sons, Inc., New York (1977), Vol. 25, Chap. 3, pp. 300—305; b) P. Kurtz, *Ann. Chem.*, **572**, 23 (1951).

21) S. N. Huckin and L. Weiler, *Can. J. Chem.*, **52**, 2157 (1974).

22) H. Muller, *Chem. Ber.*, **35**, 970 (1902).

23) C. R. Conard and M. A. Polliver, *Org. Synth.*, Coll. Vol. II, 167 (1943).

24) L. E. Hightower, L. R. Glasgow, K. M. Stone, D. A. Albertson, and H. A. Smith, *J. Org. Chem.*, **35**, 1881 (1970).

25) Y. Yamamoto, S. Yamamoto, H. Yatagai, Y. Ishihara, and K. Maruyama, *J. Org. Chem.*, **47**, 119 (1982).

26) D. Sovoia, C. Trombini, and A. Umani-Ronchi, *J. Org. Chem.*, **43**, 2907 (1978).

27) R. Howe and D. Johnson, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 977.

28) J. N. Marx, *Tetrahedron*, **39**, 1529 (1983).

29) G. A. Olah, R. Karpeles, and S. C. Narang, *Synthesis*, **1982**, 963.

30) G. K. Rollefson and J. E. Booher, *J. Am. Chem. Soc.*, **53**, 1728 (1931).

31) W. Sucrow and U. Klein, *Chem. Ber.*, **108**, 48 (1975).

32) S. E. Boxer and R. P. Linstead, *J. Chem. Soc.*, **1932**, 740.