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Dehalogenation of α-Halo Carbonyl Compounds by a New Efficient Reagent, Triphenylphosphonium Iodide

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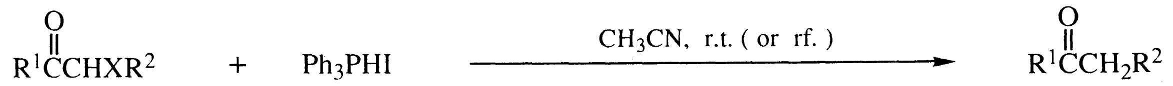
Triphenylphosphonium iodide, Ph_3PHI, was found to be an efficient reagent for the dehalogenation of α-halo carbonyl compounds. α-Halo esters, which were difficult to be reduced with Me_3SiCl/NaI reagent, was smoothly debrominated by Ph_3PHI. Treatment of α-halocarbonyl compounds with Ph_3PDI produced the corresponding α-deuterated compounds.

Dehalogenation of α-halo carbonyl compounds has long been recognized as a useful synthetic transformation. Therefore a number of methods have been developed for this purpose.1) Hydrogen iodide equivalents derived from sodium iodide and sulfuric acid2) or phosphoric acid3) and iodotrimethylsilane4) have been shown to be efficient reagents for the dehalogenation of α-halo carbonyl compounds. Previously, we have reported that chlorotrimethylsilane/sodium iodide/water ($Me_3SiCl/NaI/H_2O$) reagent in acetonitrile provides a convenient method for *in situ* generation of hydrogen iodide (HI) under mild conditions in short time,5) and that the HI thus generated can be used in a variety of synthetic reactions.6)

In this paper, we wish to report the dehalogenation of α-halo carbonyl compounds by a efficient reagent, Ph_3PHI,7) which was easily obtained from Ph_3P and HI generated from $Me_3SiCl/NaI/H_2O$ in CH_3CN at room temperature.8)

$$\mathrm{Me_3SiCl} \quad + \quad \mathrm{NaI} \quad \xrightarrow[\text{2) Ph}_3\text{P, r.t., 2 h}]{\text{1) 1/2 H}_2\text{O, CH}_3\text{CN, r.t., 5 min}} \quad \underset{94\ \%}{\mathrm{Ph_3PHI}}$$

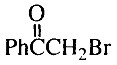
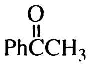
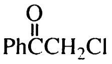
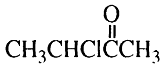
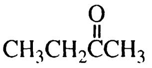
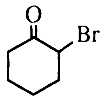
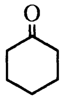
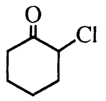
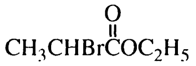
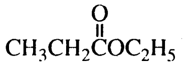
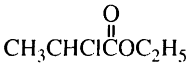
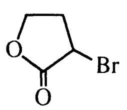
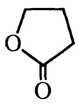


$$\mathrm{R^1\overset{\overset{O}{\|}}{C}CHXR^2} \quad + \quad \mathrm{Ph_3PHI} \quad \xrightarrow{\text{CH}_3\text{CN, r.t. (or rf.)}} \quad \mathrm{R^1\overset{\overset{O}{\|}}{C}CH_2R^2}$$

A typical reaction was carried out as follows. To a solution of α-bromoacetophenone (1.0 g, 5 mmol) in CH_3CN (10 ml) was added Ph_3PHI (2.34 g, 6 mmol). The solution was stirred at room temperature for 3 h. The reaction was quenched with water (10 ml), and the product was extracted with ether (10 ml X 3). The ether solution was washed with 10% $Na_2S_2O_3$ (20 ml), and dried over $MgSO_4$. Column chromatography on silica gel with hexane eluent afforded acetophenone in 85% yield.

Table 1 shows the dehalogenation of a variety of α-halo carbonyl compounds with Ph3PHI reagent.

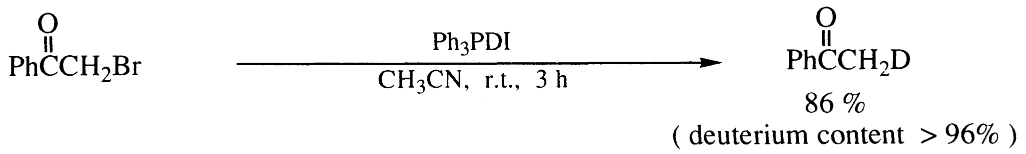
Table 1. Dehalogenation of α-Halo Carbonyl Compounds with Ph_3PHI [a]

Run	Substrate	Time / h	Temp / °C	Product	Yield / % [b]
1	**1**  $\mathrm{Ph\overset{O}{\overset{\|}{C}}CH_2Br}$	3	r.t.	**2**  $\mathrm{Ph\overset{O}{\overset{\|}{C}}CH_3}$	85
2	**3**  $\mathrm{Ph\overset{O}{\overset{\|}{C}}CH_2Cl}$	4	r.t.	**2**	83
3	**4**  $\mathrm{CH_3CHCl\overset{O}{\overset{\|}{C}}CH_3}$	5	r.t.	**5**  $\mathrm{CH_3CH_2\overset{O}{\overset{\|}{C}}CH_3}$	60
4	**4**	24	r.t.	**5**	89
5	**4**	3	rf.	**5**	87
6	**6** 	4	r.t.	**7** 	80
7	**8** 	5	rf.	**7**	72
8	**9**  $\mathrm{CH_3CHBr\overset{O}{\overset{\|}{C}}OC_2H_5}$	3	r.t.	**10**  $\mathrm{CH_3CH_2\overset{O}{\overset{\|}{C}}OC_2H_5}$	80
9	**11**  $\mathrm{CH_3CHCl\overset{O}{\overset{\|}{C}}OC_2H_5}$	6	rf.	**10**	78
10	**12** 	6	r.t.	**13** 	82

a) Substrate (5 mmol) was allowed to react with Ph_3PHI (6 mmol) in acetonitrile.
b) Based on the substrate used.

2-Bromo- and 2-chloroacetophenones were dehalogenated at room temperature to give acetophenone in good yields. 3-Chloro-2-butanone was difficult to be reduced at room temperature with short time reaction, but after 24 h 2-butanone was obtained in 89% yield. The same reaction under refluxing gave 2-butanone in good yield. Similar results were also observed in the reaction of α-halocycloalkanones and α-halo esters, *i.e.*, bromo compounds were easily reduced at room temperature, but for chloro derivatives the temperature must be raised to refluxing temperature of CH_3CN (ca. 80 °C).

It is of interest to note that Ph_3PDI was easily prepared from the reaction of DI, derived from Me_3SiCl/NaI and D_2O,[6d)] and PPh_3. The reaction of 2-bromoacetophenone with Ph_3PDI gave acetophenone-2-*d* whose ^1H-NMR showed that the deuterium was incorporated more than 96%.



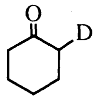
$$Ph\overset{O}{\overset{\|}{C}}CH_2Br \xrightarrow[CH_3CN,\ r.t.,\ 3\ h]{Ph_3PDI} Ph\overset{O}{\overset{\|}{C}}CH_2D$$

86 %

(deuterium content > 96%)

Table 2 shows the dehalogenation of ethyl 2-bromopropionate (**9**) to ethyl propionate (**10**) by several hydrogen iodide equivalents.

Table 2. Dehalogenation of α-Halo Carbonyl Compounds with Several Reagents[a)]

Run	Substrate	Reagent	Time/ h	Temp / °C	Product	Yield / %[b)]
1	**9**	Ph_3PHI	3	r.t.	**10**	80
2	**9**	Me_3SiCl / NaI / H_2O - Ph_3P	3	r.t.	**10**	83
3	**9**	Me_3SiCl / NaI / H_2O(= HI)	6	r.t.	**10**	17
4	**9**	Me_3SiCl / NaI	3	r.t.	**10**	4
					14 $CH_3CHI\overset{O}{\overset{\|}{C}}OC_2H_5$	65
5	**9**	Me_3SiCl / NaI / H_2O - Et_3N	6	r.t.	**14**	69
6	**9**	Ph_3PDI	3	r.t.	**15** $CH_3CHD\overset{O}{\overset{\|}{C}}OC_2H_5$	88
7	**8**	Ph_3PDI	6	rf.	**16** 	72

a) Substrate (5 mmol) was allowed to react with several reagents (6 mmol) in acetonitrile.
b) Based on the substrate used.

The dehalogenation was found to be carried out without isolation of Ph_3PHI. To an acetonitrile solution of HI generated from $Me_3SiCl/NaI/H_2O$ system was added PPh_3, and the mixture was stirred for 3h at room temperature. The Ph_3PHI thus generated in situ was allowed to react with **9** to give **10** in almost the same yield as that of the debromination of **9** with the isolated Ph_3PHI. However, **9** was difficult to be reduced by treating with $Me_3SiCl/NaI/H_2O$ reagent (HI), and most of **9** was recovered unchanged. On the other hand, treatment of **9** with Me_3SiCl/NaI reagent induced the substitution reaction rather than the debromination, forming ethyl 2-iodopropionate (**14**) with a small amount of debrominated product **10** (4%), although

Me_3SiCl/NaI system was an efficient reagent for the dehaloganation of 2-haloalkanones and 2-halocycloalkanones.[4)] In the similar manner as Me_3SiCl/NaI reagent, triethylammonium iodide (Et_3NHI), generated *in situ* from $Me_3SiCl/NaI/H_2O$-Et_3N system, promoted also the substitution of **9** to **14**. The reactivity of Ph_3PHI and Et_3NHI toward **9** may reflect the difference between phosphorus atom having vacant d-orbital and nitrogen atom lacking d-orbital, *i.e.,* phosphonium salt is capable to coordinate to the carbonyl oxygen by taking five coordination sites, but not ammonium salt does.

The reaction of **9** and **8** with Ph_3PDI afforded the corresponding deuterated compounds, **15** and **16,** in good yields.

References

1) I.Pri-Ban and O. Buchman, *J. Org. Chem.*, **51**, 734 (1986); G. A. Molander and G. Hahn, *ibid.*, **51**, 1135 (1986); T. Oriyama and T. Mukaiyama, *Chem. Lett.*, **1984,** 2069; A. Osuka and H. Suzuki, *ibid.*, **1983**, 119; S. K. Chung and Q. Y. Hu, *Synth. Commun.*, **12**, 261 (1982); D. Savoia, E. Tagliavini, C. Trombini, and A. U. Roachi, *J. Org. Chem.*, **47**, 876 (1982); D. L. J. Clive and P. L. Beaulieu, *ibid.*, **47**,1124 (1982); J. N. Dennis and A. Krief, *Tetrahedron Lett.*, **22**, 1431 (1981); T. H. Luh, C. H. Lai and S. W. Tam, *J. Org. Chem.*, **44**, 641 (1979); H. Alper and L. Petene, *ibid.*, **44**, 2568 (1979); G. Cainelli, F. Manescalchi A. U.Rondii, and M. Panunzio, *ibid.*, **43**, 1598 (1978).
2) A. L. Gamal and J. L. Luche, *Tetrahedron Lett.*, **21**, 3195 (1980).
3) A. K. Mandal and A. K. Nijasure, *Synlett*, **1990**, 554.
4) T. L. Ho, *Synth. Commun.*, **11**, 101 (1981); G. A. Olah, A. Arranghi, and Y. Vanker, *J. Org. Chem.*, **45**, 3531 (1981); G. A. Olah, Y. Vanker, and A. P. Fang, *Synthesis,* **1979**, 59; T. L. Ho, *Synth. Commun.*, **9**, 241 (1979).
5) Conventionally, HI was prepared by the use of excess KI and orthophosphoric acid at higher temperature (80 °C): H. Stone and H. Schecher, Org. Synth., Coll. Vol. IV, 543 (1963).
6) a) N. Kamiya, Y. Chikami, and Y.Ishii, *Synlett*, **1990**, 675; b) T.Kanai, Y. Kanagawa, Y. Ishii, and M. Ogawa, *J. Org. Chem.*, **55**, 3274 (1990); c) S. Irifune, T. kibayashi, Y. Ishii, and M. Ogawa, *Synthesis*, **1988**, 366; d) T. Kanai, Y. kanagawa, Y. Ishii, and M. Ogawa, *ibid.*, **1989**, 283.
7) E. Sonnet, *Synthesis*, **1980**, 828.
8) Ph_3PHI was easily prepared as follows: To a solution of NaI (1.8 g, 12 mmol) and Me_3SiCl (1.54 ml, 12 mmol) in CH_3CN (20 ml) was added H_2O (0.1 ml, 6 mmol). After evaporation of CH_3CN under reduced pressure, the resulting product was dissolved in $CHCl_3$ to remove impurities such as NaCl. After filtration, the solution was concentrated to form a white solid. Washing with ether followed by drying *in vacuo* gave Ph_3PHI (4.42 g, 94%): m p 169-170 °C .

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