Tetrahedron Letters,Vol.27,No.33,pp 3891-3894,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

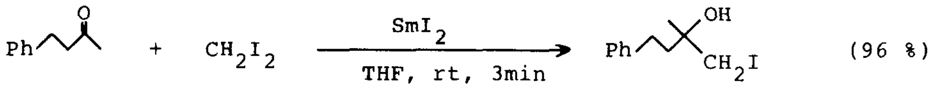
SmI_2-INDUCED IODOMETHYLATION OF CARBONYL COMPOUNDS(1)

Takanori Tabuchi, Junji Inanaga,* and Masaru Yamaguchi
Department of Chemistry, Kyushu University 33,
Hakozaki, Higashi-ku, Fukuoka 812, Japan

Summary: Carbonyl compounds were readily coupled with diiodomethane or dibromomethane at room temperature affording iodohydrins in high yields by the aid of SmI_2.

Although (monohalomethyl)lithiums have been known as monohalomethylating agents, their synthetic utility has been severely limited because of their extreme thermal instability.(2a,b) Recently two improved monochloromethylations of carbonyl compounds have been reported; (1) generation of (chloromethyl)lithium stabilized by the addition of lithium bromide at -115°C followed by its coupling with carbonyl compounds,(2b) and (2) in-situ generation of (chloromethyl)lithium from chloroiodomethane and alkyllithium in the presence of carbonyl compounds at -78°C.(3) But, in both cases, the operation at low temperature was still required. Fujita and Hiyama have successfully carried out dihalo- or trihalomethylation of carbonyl compounds at room temperature by using a combination of polyhaloorganosilanes and a sulfonium fluoride as reagents but they could not generate monohalomethyl anions by this procedure.(4)

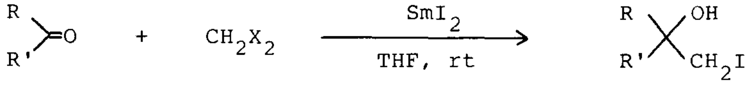
We report herein a very mild and practically useful iodomethylation(5) by using SmI_2 and diiodomethane at room temperature, though carbanion species may not be involved in the reaction.

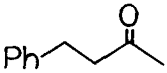
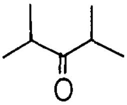
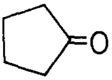
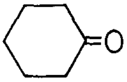
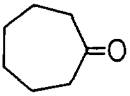
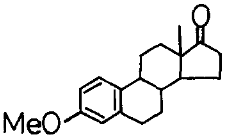


In a typical experiment, a SmI_2-THF solution(6) (0.1 mol dm^{-3}, 2.5 ml) was added to a solution of 4-phenyl-2-butanone (14.8 mg, 0.1 mmol) and diiodomethane (53.6 mg, 0.2 mmol) in dry THF (1 ml) and the mixture was stirred at room temperature for 3 min, at which time blue-green color had turned yellow. Usual workup followed by chromatographic purification (silica gel) gave 1-iodo-2-methyl-4-phenyl-2-butanol (27.8 mg, 96 %) (Entry 2).

Some of the results are summarized in the Table. An aldehyde and ketones, including easily enolizable ones, were readily iodomethylated at room temperature in very good yields. It is noteworthy that dibromomethane was also effective for the formation of iodohydrins but no trace of

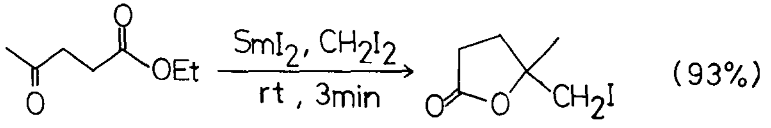
Table. Iodomethylation of Carbonyl Compounds at Room Temperature$^{a)}$



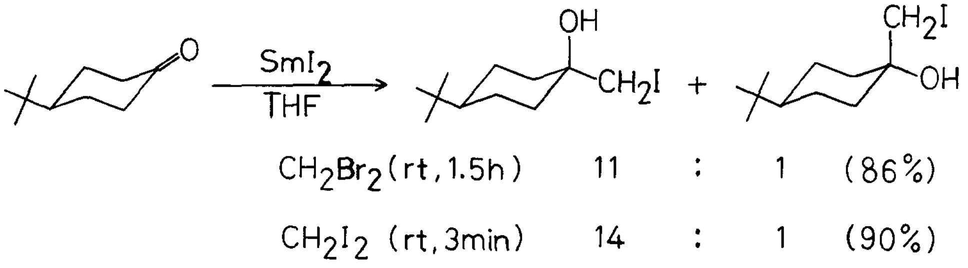
Entry	Carbonyl compound RCOR'	CH_2X_2 $^{b)}$	Reaction time	Iodohydrin Yield (%)$^{c)}$
1		A$^{d)}$	3 min	83
2		A	3 min	96
3	〃	B	1.5 h	93
4		A	3 min	86
5		A	3 min	82
6		A	3 min	90
7	〃	B	1.5 h	88
8		A	3 min	95
9	 e)	A$^{f)}$	4 min	87$^{g)}$

a) The reactions were carried out at room temperature by using carbonyl compound (0.1 mmol), CH_2X_2 (0.2 mmol), and SmI_2 (0.25 mmol) in THF (3.5 ml) unless otherwise mentioned. b) A: diiodomethane, B: dibromomethane. c) Isolated yield. The products gave satisfactory ^1H NMR spectra. d) Aldehyde (0.1 mmol), CH_2I_2 (0.3 mmol), and SmI_2 (0.3 mmol) were used. e) Estrone O-methyl ether. f) Ketone (0.1 mmol), CH_2I_2 (0.5 mmol), and SmI_2 (0.5 mmol) were used. g) A single compound, whose stereochemistry was not determined.

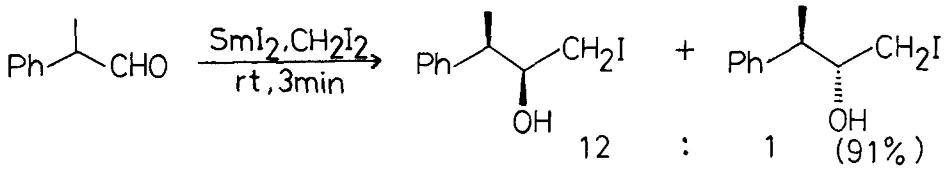
bromohydrins were detected in the reaction products (Entries 3 and 7).



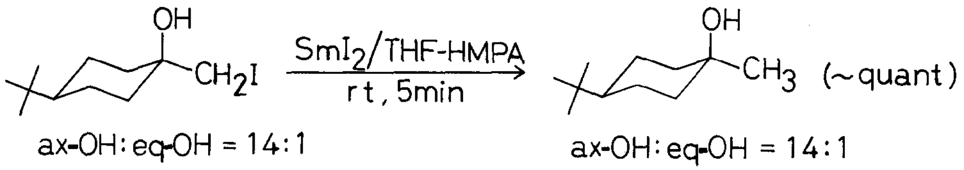
(1)



(2)



(3)

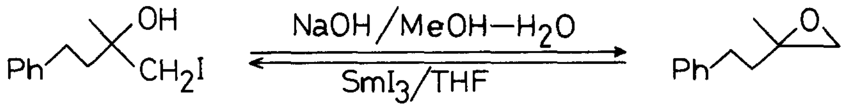


(4)

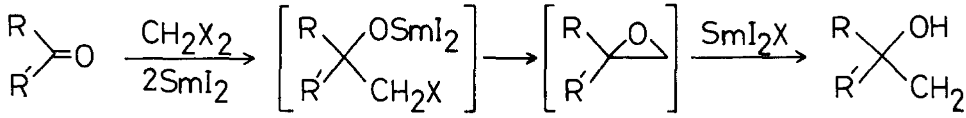
The ester group was not attacked by the reagent under the reaction conditions. Thus, an iodomethylated γ-lactone was obtained in high yield from ethyl levulinate (eq. 1).

Interestingly, high diastereoselectivity was observed in the reaction with 4-t-butylcyclohexanone or with 2-phenylpropionaldehyde, giving a product of equatorial-attack or an erythro-isomer, as a major compound, respectively (eq. 2 and 3)[7]. Since, the iodomethyl group was found to be cleanly converted to a methyl group by SmI_2 in a mixture of THF and HMPA,[8] the iodomethylation-reduction sequence will serve as an alternative way to the stereoselective methylation of carbony compounds (eq. 4)[9].

An iodohydrin was converted into the corresponding epoxide by conventional alkali treatment, and it was found that the epoxide was very rapidly cleaved by the treatment with SmI_3 regenerating the original iodohydrin (eq. 5). This fact and the observation that iodohydrins were exclusively formed even if dibromomethane was used in place of diiodomethane, indicate that the present iodomethylation reaction proceeds via an epoxide intermediate (eq. 6).



(5)



(6)

The present halomethylation reaction seems to proceed through radical process. Further investigation concerning the mechanism and stereochemical outcome is under way along with other general SmI_2-induced Barbier-type reactions.

References and Notes

1) Presented at the 52th National Meeting of the Chemical Society of Japan, Kyoto, Apr 1986. 2) For instance, $LiCH_2Cl$ decomposes even at -130°C. a) J.Villieras, M.Rambaud, R.Tarhouni, and B.Kirschleger, Synthesis, **1981**, 68. b) R.Tarhouni, B.Kirschleger, M.Rambaud, and J.Villieras, Tetrahedron Lett., **25**, 835 (1984). 3) K.M.Sadhu and D.S.Matteson, Tetrahedron Lett., **27**, 795 (1986). 4) M.Fujita and T.Hiyama, J. Am. Chem. Soc., **107**, 4085 (1985). 5) Iodomethylation of carbonyl compounds by using Sm metal and CH_2I_2 was reported at the same meeting as described in reference 1; see T.Imamoto, T.Takeyama, and M.Yokoyama, symposium paper II, 1480 (1986). A related hydroxymethylation using benzyl chloromethyl ether has also been reported: T.Imamoto, T.Takeyama, and M.Yokoyama, Tetrahedron Lett., **25**, 3225 (1984). 6) P.Girard, J.L.Namy, and H.B.Kagan, J. Am. Chem. Soc., **102**, 2693 (1980). 7) Stereochemistry of the products was determined, after conversion of iodomethyl groups to methyl groups, by comparing ^1H NMR (400 MHz) spectral data with the authentic ones. 4-t-Butyl-1-methylcyclohexanol: Y.Senda, J.Ishiyama, and S.Imaizumi, Tetrahedron, **31**, 1601 (1975). 3-Phenyl-2-butanol: T.Uzawa, S.Zushi, Y.Kodama, Y.Fukuda, K.Nishihata, K.Umemura, M.Nishio, and M.Hirota, Bull. Chem. Soc. Jpn., **53**, 3623 (1980). 8) A mild and very effective method for the reduction of organic halides by using SmI_2/THF-HMPA system has been developed and will be submitted for publication soon; cf. reference 1. 9) Isomeric ratios obtained in the present reaction are much higher than those obtained by simple methyl magnesium halide or methyllithium. For example, it has been reported that 4-t-butylcyclohexanone afforded a mixture of an axial- and an equatorial alcohol in a ratio of ca. 2.2:1 (MeMgX) and 1.9:1 (MeLi), respectively [for a review, see E.C.Ashby and J.T.Laemmle, Chem. Rev., **75**, 521 (1975)]. Higher selectivities have also been reported with more complex systems: For instance, 11.5:1 [MeLi + $LiClO_4$, E.C.Ashby and S.A.Noding, J. Org. Chem., **44**, 4371 (1979)], and 15.7:1 [Me_3CuLi_2, T.L.MacDonald and W.C.Still, J. Am. Chem. Soc., **97**, 5280 (1975); and $MeTi(OCHMe_2)_3$, M.T.Reetz, Top. Curr. Chem., **106**, 1 (1982)]. Recently, completely opposite selectivity (1:200) has been attained by using bulky aluminum reagent and MeLi [K.Maruoka, T.Itoh, and H.Yamamoto, J. Am. Chem. Soc., **107**, 4573 (1985)].

(Received in Japan 10 May 1986)