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THE REACTION OF CARBONYL COMPOUNDS WITH DIIODOMETHANE IN THE PRESENCE OF SAMARIUM: NOVEL SYNTHESES OF IODOHYDRINS AND CYCLOPROPANOLS

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Summary: The iodomethylation of carbonyl compounds giving iodohydrins has been achieved under ordinary conditions by the use of diiodomethane and samarium. A novel synthesis of cyclopropanols from α-haloketones or 1,2-dibenzoylethane is also described.

Nucleophilic halomethylations of carbonyl compounds provide synthetically useful halohydrins and related compounds. Several research groups have established di- and trihalomethylations which can be conducted at around room temperature.[1] In contrast, monohalomethylation is believed to be difficult to achieve under ordinary conditions.[2] Particularly, iodomethylation leading to iodohydrins has remained unsucceeded. We report herein a novel method for the iodomethylation of carbonyl compounds, and in addition wish to describe a new synthesis of cyclopropanols from α-haloketones or 1,2-dibenzoylethane.

Previously, we found that carbonyl compounds react with benzyl chloromethyl ether in the presence of divalent samarium to afford 2-benzyloxyethanol derivatives.[3,4] The results prompted us to investigate the direct iodomethylation of carbonyl compounds by the use of diiodomethane and samarium diiodide generated by the reaction of samarium metal with diiodoethane. A few preliminary experiments showed that the expected iodomethylation proceeded smoothly at room temperature, as is indicated in the following scheme.[5]

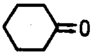
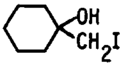
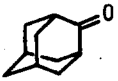
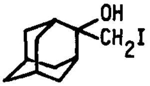
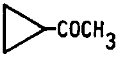
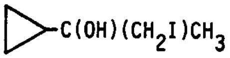
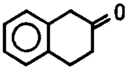
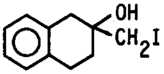
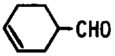
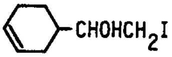
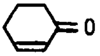
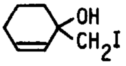
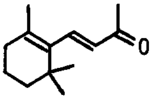
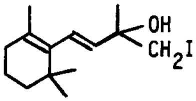
$$\mathrm{RCOR'} \quad + \quad \mathrm{CH_2I_2} \xrightarrow[<10\ \mathrm{min}]{2\ \mathrm{SmI_2}} \mathrm{RR'C(OH)CH_2I}$$

RCOR' : n-$C_6H_{13}COCH_3$ 73%
2-adamantanone 93%
$C_6H_5COCH_3$ 58%[6]

On the basis of this finding, we next developed a more convenient procedure using metallic samarium and diiodomethane. Thus, a solution of a carbonyl compound and diiodomethane in THF was added with stirring to samarium powder at 0 °C. The reaction was rapidly completed to yield the expected iodohydrin.[7,8] Some representative results are summarized in Table 1.

$$\mathrm{RCOR'} \xrightarrow[\mathrm{THF,\ 0\ ^\circ C}]{\mathrm{CH_2I_2\ /\ Sm}} \mathrm{RR'C(OH)CH_2I}$$

Table 1. Synthesis of Iodohydrins from Carbonyl Compounds[a]

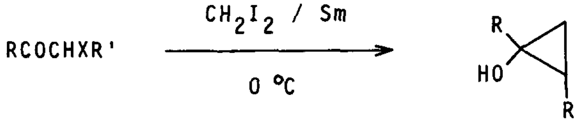
Entry	Carbonyl compound	Product	Yield (%)[b]
1	n-$C_6H_{13}COCH_3$	n-$C_6H_{13}C(OH)(CH_2I)CH_3$	93
2[c]	"	"	34[d]
3			81
4			84
5	$C_6H_5COCH_3$	$C_6H_5C(OH)(CH_2I)CH_3$	70
6			62
7			44
8	n-$C_{11}H_{23}CHO$	n-$C_{11}H_{23}CHOHCH_2I$	72
9			67
10	C_6H_5CHO	$C_6H_5CHOHCH_2I$	39
11			22
12[e]	"	"	55
13	$(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCHO$	$(CH_3)_2C{=}CH(CH_2)_2C(CH_3){=}CHCHOHCH_2I$	31
14		 [f]	53
15[g]	n-$C_6H_{13}CO(CH_2)_2COC_6H_{13}$-n	n-$C_6H_{13}C(OH)(CH_2I)(CH_2)_2C(OH)(CH_2I)C_6H_{13}$-n	47
16[g]	$CH_3CO(CH_2)_3COCH_3$	$CH_3C(OH)(CH_2I)(CH_2)_3C(OH)(CH_2I)CH_3$	68
17[g]	$C_6H_5CO(CH_2)_3COC_6H_5$	$C_6H_5C(OH)(CH_2I)(CH_2)_3C(OH)(CH_2I)C_6H_5$	68
18[g]	$C_6H_5CO(CH_2)_4COC_6H_5$	$C_6H_5C(OH)(CH_2I)(CH_2)_4C(OH)(CH_2I)C_6H_5$	59

a) All reactions were carried out at 0 °C with a molar ratio of 1:3:2 RCOR'/CH_2I_2/Sm, unless otherwise stated. General procedure is described in Ref. 7. b) Isolated yield. c) A molar ratio of 1:1:0.67 RCOR'/CH_2I_2/Sm was used. d) Starting ketone was recovered in 20% yield. e) A molar ratio of 1:6:4 RCOR'/CH_2I_2/Sm was used. f) This iodohydrin was extremely labile and decomposed to black tar within a few hours after isolation. g) A molar ratio of 1:6:4 diketone/CH_2I_2/Sm was employed.

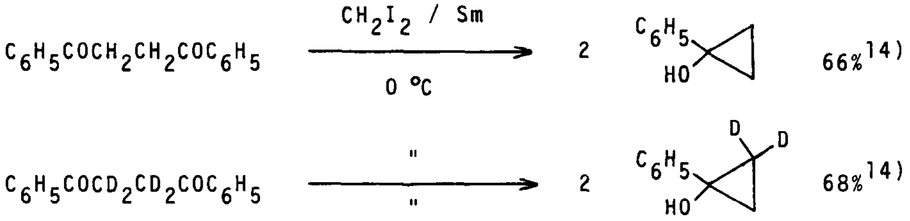
Simple ketones and aldehydes were converted to the corresponding iodohydrins in good to high yields. α,β-Unsaturated carbonyl compounds including aromatic aldehydes were also subjected to iodomethylation, although the yields were moderate. Several diketones except 1,2-dibenzoylethane (vide infra) underwent iodomethylation of both carbonyl groups to give compounds possessing two iodohydrin functions.

It is noted that this method is an approach to the preparation of various iodohydrins that have been inaccessible by the previously existing methods such as hydroxyiodonation of olefins.9) There are valuable functionalized products that can be directly utilized in further synthetic elaboration.10)

Another finding in this study is the formation of cyclopropanols. When α-haloketones were treated with diiodomethane and samarium at 0 °C, cyclopropanols were obtained in satisfactory yields.11) Surprisingly, the reaction of 1,2-dibenzoylethane under similar conditions also provided 1-phenylcyclopropanol instead of 1,6-diiodo-2,5-diphenylhexane-2,5-diol.12,13) The reaction of 1,2-dibenzoyl-1,1,2,2-tetradeuteroethane furnished 2,2-dideutero-1-phenylcyclopropanol. This result clearly indicates that the reaction proceeded through the cleavage of the carbon-carbon bond between two phenacyl groups.



R, R', X :	C_6H_5, H, Br	81%
	C_6H_5, H, I	88%
	p-BrC_6H_4, H, Br	67%
	-$(CH_2)_4$-, Br	81%



Further studies on mechanism and synthetic application are currently underway.

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3) T. Imamoto, T. Takeyama, and M. Yokoyama, Tetrahedron Lett., 25, 3225 (1984).

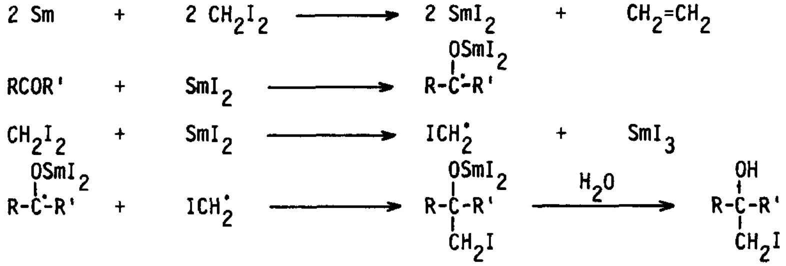
4) Kagan et al. initially demonstrated that divalent samarium is a powerful and unique single electron transfer reagent. a) P. Girard, J. L. Namy, and H. B. Kagan, J. Am. Chem. Soc., 102, 2693 (1980). b) H. B. Kagan, J. L. Namy, and P. Girard, Tetrahedron Supplement, 37, 175 (1981). c) H. B. Kagan in "Fundamental and Technological Aspects of Organo-f-Element Chemistry" T. J. Marks and I. L. Fragala ed., D. Reidel, 1985, pp. 49-76, and references cited therein.

5) Alkylations of ketones by alkyl halides mediated by SmI_2 were reported by Kagan et al. See Ref. 4a.

6) Pinacol coupling product, $C_6H_5C(OH)(CH_3)C(OH)(CH_3)C_6H_5$, was isolated in 16% yield.

7) General procedure: Freshly scraped samarium powder (50-200 mesh) (300 mg, 2 g atom) was placed in a two-necked flask fitted with a dropping funnel containing a carbonyl compound (1 mmol) and diiodomethane (803 mg, 3 mmol) in 6 mL of dry THF. The THF solution was slowly added at 0 °C under a nitrogen atmosphere. Usually, the reaction was initiated within a few minutes and the addition of the solution required about 20 min. After addition, stirring was continued for 20 min at the same temperature. The reaction mixture was treated with 1 N HCl and extracted with ether. The combined extracts were washed with $Na_2S_2O_3$ solution and brine, and dried over $MgSO_4$. Solvent was evaporated and product was isolated by preparative thin layer chromatography on silica gel.

8) The following reaction pathway may be conceivable. Direct electron transfer from samarium metal to carbonyl group and diiodomethane may also be involved.



$$2\ Sm + 2\ CH_2I_2 \longrightarrow 2\ SmI_2 + CH_2{=}CH_2$$

$$RCOR' + SmI_2 \longrightarrow R\text{-}\overset{OSmI_2}{\dot{C}}\text{-}R'$$

$$CH_2I_2 + SmI_2 \longrightarrow ICH_2^{\bullet} + SmI_3$$

$$R\text{-}\overset{OSmI_2}{\dot{C}}\text{-}R' + ICH_2^{\bullet} \longrightarrow R\text{-}\underset{CH_2I}{\overset{OSmI_2}{C}}\text{-}R' \xrightarrow{H_2O} R\text{-}\underset{CH_2I}{\overset{OH}{C}}\text{-}R'$$

9) G. Sumrell, B. M. Wyman, R. G. Howell, and M.C. Harvey, Can. J. Chem., 42, 2710 (1964); W. J. Cornforth and D. T. Green, J. Chem. Soc., C, 1970, 846; R. Antonioletti, M. D'Auria, A. D. Mico, G. Piancatelli, and A. Scettri, Tetrahedron, 39, 1765 (1983).

10) L. Schotte and G. Bergson, Svensk. Kem. Tidskr., 66, 179 (1954); J. Tsuji, H. Nagashima, and K. Sato, Chem. Lett., 1982, 3085.

11) The reaction was carried out with a molar ratio of 1:3:3 haloketone/CH_2I_2/Sm in the same procedure as in the preparation of iodohydrins.

12) The reaction was carried out with a molar ratio of 1:4:4 diketone/CH_2I_2/Sm.

13) In contrast, the reaction of aliphatic 1,4-diketone provided iodohydrin as a major product (entry 15 in Table 1).

14) The yield was calculated on the assumption that one mole of diketone affords two moles of cyclopropanol.

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