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A NOVEL SmI_2-INDUCED MASKED-FORMYLATION OF CARBONYL COMPOUNDS(1)

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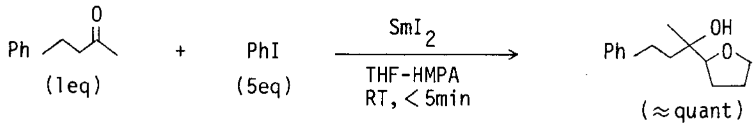
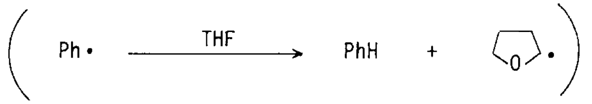
Summary: The reductive cross-coupling of 1,3-dioxolane with carbonyl compounds to yield α-hydroxy aldehyde derivatives was attained by the reduction of iodobenzene with a solution of SmI_2 in 1,3-dioxolane-CH_3CN-HMPA (20:2:1) in the presence of carbonyl compounds under extremely mild conditions. The process seems to involve 1,3-dioxolanyl radical intermediate.

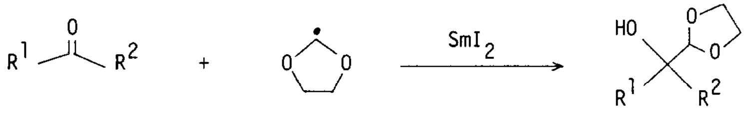
Formylation of carbonyl compounds sometimes provides quite a useful means in organic synthesis since it can directly introduce C_1-unit of an aldehydic oxidation level, and several methods have so far been developed for this reaction; (1) masked-formylation utilizing an anion derived from, e.g., 1,3-dithiane,(2) methyl methythiomethyl sulfoxide,(3) or methylenedioxy derivatives(4) or (2) cobalt-catalyzed direct formylation with carbon monoxide and hydrosilane.(5) However, the former requires the strongly basic conditions and the latter is not applicable to ketones. We report here a new method for the masked-formylation of aldehydes and ketones under extremely mild conditions.

Recently, we have found that the electron transfer system of SmI_2-THF-HMPA is highly efficient for the reduction of a variety of aliphatic and aromatic halides(6) and for the Barbier-type reaction of aliphatic halides with carbonyl compounds.(7) Aromatic halides, however, did not couple with carbonyl compounds at all but yielded the THF-adducts of carbonyl compounds (e.g., Eq 1).



(1)





(2)

The reaction may be explained as follows: Initially formed phenyl radical abstracted a hydrogen atom from THF(8) and a SmI_2-induced cross-coupling of the resulting THF radical with a ketone took place.(9) Based on the idea, THF was replaced by 1,3-dioxolane expecting that a masked-formylation would occur as shown in Eq 2. Thus, a SmI_2 solution in 1,3-dioxolane was prepared(10) and mixed with carbonyl compounds in the presence of iodobenzene (5 eq) and HMPA (ca. 5% of the solvent). The reaction completed within 5 min at room temperature affording 1,3-dioxolane adducts(11) in satisfactory yields (Table 1). The reaction with 4-tert-butylcyclohexanone did not show appreciable stereoselectivity while a high Cramselectivity was observed in the SmI$_2$-induced iodomethylation of the ketone.12)

Mechanistically, the reaction may proceed through radical coupling13) (route a) and/or via 1,3-dioxolanyl anion formation (route b).

Practically, the present masked-formylation may be useful especially for substrates having base-sensitive functionalities because of its extremely mild conditions.

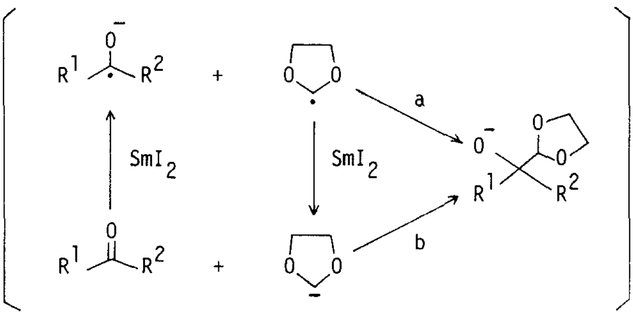
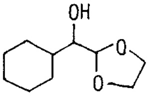
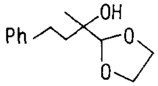
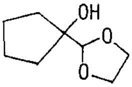
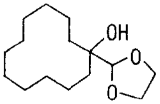
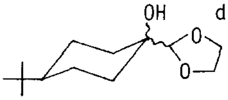


Table 1. Masked-Formylation by SmI$_2$ in 1,3-Dioxolane-CH$_3$CN-HMPA (20 : 2 : 1)a)

Productb) (% Yield)c)				
				 d)
(73)	(73)	(76)	(77)	(77)

a) The reactions were carried out by using carbonyl compounds (0.1—0.3 mmol), iodobenzene (5 eq), and a SmI$_2$ solution (0.1 mol dm^{-3}, 6 eq) under an atmosphere of nitrogen for 5 min at room temperature. b) Satisfactory ^{1}H NMR and analytical data were obtained. c) Isolated yield. d) A mixture of stereoisomers (ca. 1 : 1).

References and Notes

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7) K.Otsubo, K.Kawamura, J.Inanaga, and M.Yamaguchi, Chem. Lett., 1487 (1987).
8) The reduction of 2-bromonaphthalene by a solution of SmI$_2$-THF-HMPA in the presence of D$_2$O yielded non-deuterated naphthalene quantitatively, indicating that the reaction proceed through radical process: See ref. 6.
9) It has been reported that a small amount of THF-adduct of 2-octanone was isolated in the SmI$_2$-promoted Barbier-type reaction with 1-iodododecane: See H.B.Kagan, J.L.Namy, and P.Girard, Tetrahedron, **37**, Suppl. No 1, 175 (1981).
10) Prepared in a similar way to the preparation of a THF solution of SmI$_2$ [P.Girard, J.L.Namy, and H.B.Kagan, J. Am. Chem. Soc., **102**, 2693 (1984)]. Addition of CH$_3$CN (ca. 10 % in 1,3-dioxolane) was necessary to produce a nice clear solution.
11) The use of dimethoxymethane or 1,3,5-trioxane in place of 1,3-dioxolane produced the corresponding adducts but in poor yields; e.g., cyclohexanecarboxaldehyde gave the 1,3,5-trioxane-adduct in 36% yield.
12) T.Tabuchi, J.Inanaga, and M.Yamaguchi, Tetrahedron Lett., **27**, 3891 (1986).
13) The generation of 1,3-dioxolanyl radical and its use for the masked-formylation of heteroaromatic compounds under oxidation conditions has been reported: See C.Giordano, F.Minisci, E.Vismara, and S.Levi, J. Org. Chem., **51**, 536 (1986) and references cited therein.

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