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A DIRECT PREPARATION OF 1,2-DIACETATES FROM ALDEHYDES AND KETONES PROMOTED BY SAMARIUM DIIODIDE

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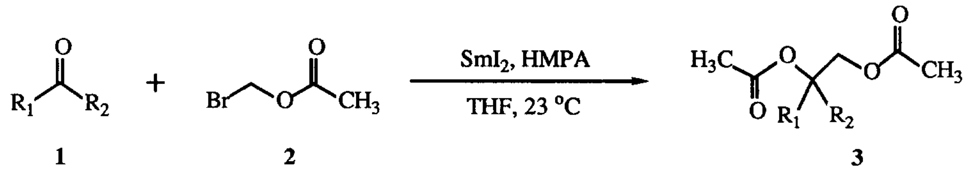
Abstract: In a mild reaction mediated by samarium diiodide, ketones and aldehydes have been converted into 1,2-diacetates from commercially available bromomethyl acetate in a single synthetic transformation.

The hydroxymethylation of ketones and aldehydes to prepare a 1,2-diol has been vigorously investigated by organic chemists for the last two decades.[1] Since the direct generation of a methanol dianion is not a feasible process, a plethora of masked synthetic equivalents have been devised.[1(b)] Nearly all of these currently available methods require multi-step preparations of the noncommercial reagents[1(a-e)] and the employment of harshly basic reaction conditions such as with the use of organolithium or Grignard reagents.[1(f-j)] In addition, there is often a potential need for additional protection steps of one or both alcohols after the hydroxymethylation transformation which must be done prior to persuing further synthetic manipulations. A general solution to these problems would combine a mild hydroxymethylation reaction with a concomitant protection of both alcohols achieved in a single reaction. Such synthetic methods which produce a bisprotected 1,2-diol directly from a ketone or aldehyde have not been examined in detail.[2] In this Letter we report the first method to convert a ketone or aldehyde directly into a 1,2-diacetate (a bisprotected 1,2-diol) from the commercially available[3] reagents bromomethyl acetate (2), HMPA and samarium diiodide,[4-6] in a single synthetic transformation.



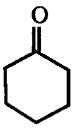
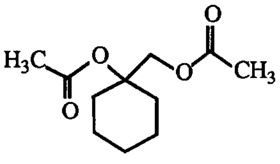
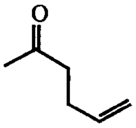
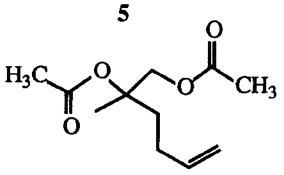
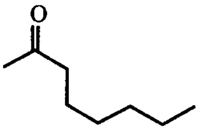
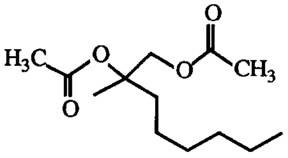
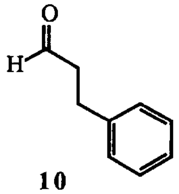
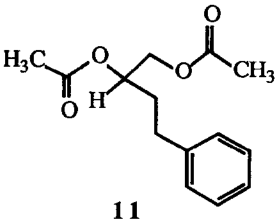
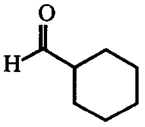
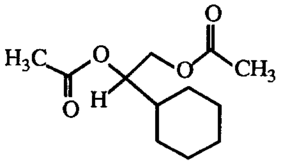
1 2 3

R_1 = H, alkyl; R_2 = alkyl

Several ketone and aldehyde substrates were examined and the results have been summarized in Table 1. Overall, the one-electron transfer reagent, SmI_2, provided reaction conditions which smoothly afforded the desired 1,2-diacetates in good (68-88%) yields. These mild conditions avoid the strongly basic or carbanionic conditions normally employed to prepare 1,2-diols and circumvent the need for additional alcohol protection step(s). It should be noted that during the course of these studies, we observed only pinacol (1,2-diol) products when HMPA was absent from the reaction mixture,[7] which result from simple dimerization of the ketone or aldehyde.

Table 1

1,2-Diacetates From Aldehydes and Ketones

Entry	Starting Substrate[a]	1,2-Diacetate	Yield[b]
1.	 **4**	 **5**	86%
2.	 **6**	 **7**	68%
3.	 **8**	 **9**	86%
4.	 **10**	 **11**	75%
5.	 **12**	 **13**	88%

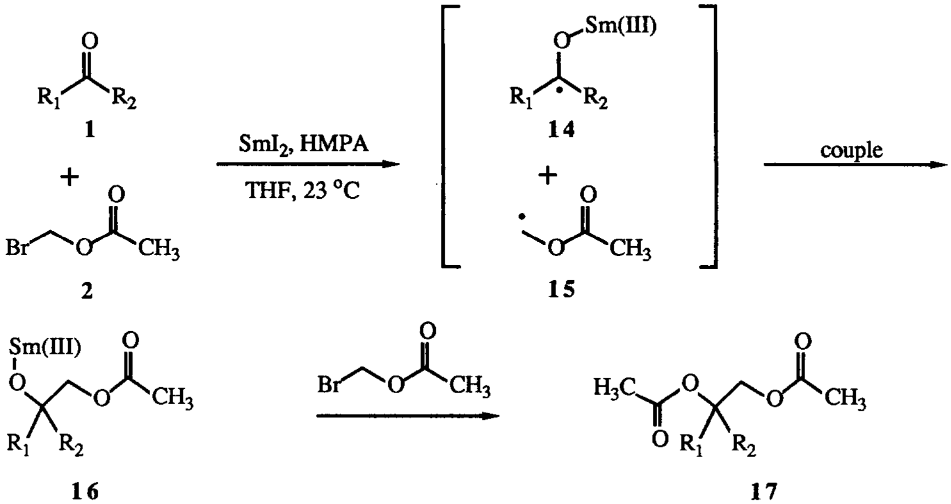
[a]All new compounds gave ^{1}H NMR, IR, ^{13}C NMR and accurate MS consistent with the structure shown; [b]yield data is for chromatographically homogeneous material.

Even with HMPA present, the reaction was unsuccessful with aromatic aldehydes and ketones such as benzaldehyde and acetophenone, producing either pinacol or pinacol diacetate products in these cases. In most examples the reaction was complete in 12-36 hours at 23 °C.

In a general precedure, SmI_2 (0.1M in THF, 3.0 mmol), HMPA (3.0 mmol), bromomethyl acetate (2.5 mmol) and an aldehyde or a ketone (0.5 mmol) were stirred at 23 °C. Small amounts of SmI_2 (ca. 1.0 mL) were periodically added in some reactions to maintain the deep blue-green color for extended periods. When the starting substrate was consumed, the reaction was quenched with aq. sat. NH_4Cl solution. Ethyl acetate and water were added and the mixture was stirred for 1 hour. The solution was extracted with ethyl acetate and the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Purification by flash chromatography gave the 1,2-diacetates.

Vicinal diols can be easily recovered directly from the diacetates shown in Table 1. The 1,2-diacetates **4**, **6**, **8**, **10**, and **12** each produced their corresponding 1,2-diols in 88%, 96%, 90%, 97%, and 84% yields respectively when treated with methanol and excess K_2CO_3.

A formalism of the reaction involves the formation of samarium ketyl **14**, by one-electron reduction of ketone (or aldehyde) **1**. Radical species **15** arises from bromomethyl acetate (**2**) after reaction with samarium diiodide and elimination of the halide, probably as SmI_2Br. The driving force to form both radical species **14** and **15** is the transformation of SmI_2 to the stabler Sm(III) species.



Coupling of the radicals produces **16**. The reaction of the ketyl oxygen with additional bromomethyl acetate affords the 1,2-diacetate product **17**.[8]

In summary, this reaction provides a direct one-step method to produce 1,2-diacetates from ketones and aldehydes from commercially available reagents. The mild reaction conditions utilizing the one-electron reducing agent, samarium diiodide, provide a unique alternative to the current technologies for hydroxymethylation of a carbonyl functionality by affording simultaneous protection of the 1,2-diol.

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(2) A global search of the databases of REACCS v. 7.1 produced by Molecular Design Limited could not produce a single example of this type of reaction from the literature.

(3) Bromomethyl acetate, HMPA, and 0.10 M solutions of SmI_2 in THF are available from Aldrich Chemical Company.

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(7) Kusuda, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett*. **1989**, 2945.

(8) A detailed mechanism of the reaction is unknown. An alternative possibility involves the Sm(III)-chelation of species **14** and **15** and subsequent coupling. It is also not unreasonable to have intramolecular transfer of the acetate in **16** to the samarium alkoxide prior to reaction with additional bromomethyl acetate.

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