

Oxidative methyl esterification of aldehydes promoted by molecular and hypervalent (III) iodine

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Abstract

A simple and mild new procedure for the facile direct oxidative methyl esterification of aldehydes using molecular iodine in combination with (diacetoxyiodo)benzene in methanol is described. Oxidative esterification is induced by iodonium ion generated *in situ* by the chemical oxidation of molecular iodine with (diacetoxyiodo)benzene.

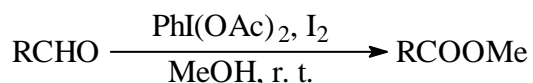
Keywords: Molecular iodine, (diacetoxyiodo)benzene, oxidation, ester, acetylhypiodite

Introduction

The direct oxidative transformation of aldehydes to esters in an extremely useful and selective functional group interconversion in organic synthesis.¹ A two-step reaction sequence involving the oxidation of hemiacetal,² acetal³ or cyanohydrin⁴ can bring about this conversion. Several one-pot conversions using different transition metal oxidants such as pyridinium dichromate,⁵ MnO₂,⁶ methyltrioxorhenium,⁷ rhodium⁸ or expensive silver⁹ have been reported. The efficiency of this strategy has been improved by including hydrogen peroxide¹⁰ as the principal oxidant coupled with a catalytic quantity of V₂O₅¹¹ and titanasilicate.¹² The other oxidative esterification protocol uses halogen derived oxidants such as *N*-halosuccinimide,¹³ hypochlorites,¹⁴ pyridiniumhydrobromide perbromide¹⁵ and molecular bromine.¹⁶ Despite these intensive efforts for oxidative esterification of aldehydes, the development of a more effective and mild method still remains interesting since many of the known methods require toxic heavy metal oxidants, dry reaction conditions, longer reaction time and poor yields of the products.

In the past decade, there has been increasing interest by organic chemists in the oxidizing properties of hypervalent iodine compounds.¹⁷ (Diacetoxyiodo)benzene (DIB), is the most extensively utilised hypervalent iodine (III) reagent, which is easy to handle, non-toxic, commercially available and is similar in reactivity to heavy metal oxidants.¹⁸ The oxidizing capacity of this versatile class of hypervalent iodine reagents is extensively investigated for the

oxidation of alcohols but there is hardly any report on the direct oxidative esterification of aldehydes. Recently, we have revealed that DIB combined with a catalytic quantity of molecular iodine can oxidize alcohols to ketones, acids and esters under mild reaction conditions.¹⁹ In continuation of this work, we wish to report herein the use of DIB combined with molecular iodine in the facile and direct oxidative methyl esterification of aldehydes (Scheme 1).



Scheme 1

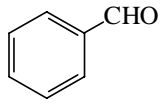
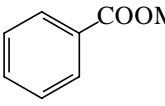
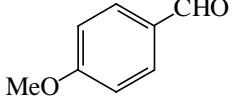
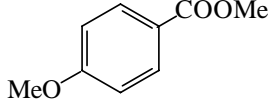
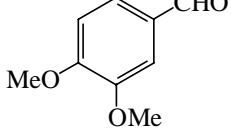
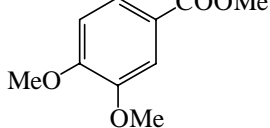
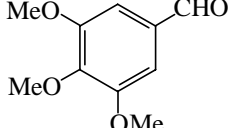
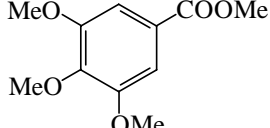
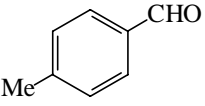
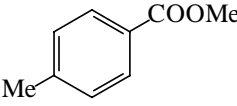
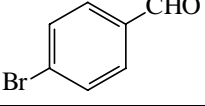
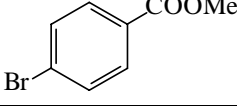
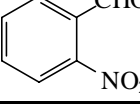
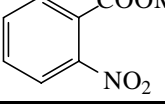
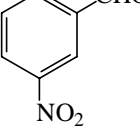
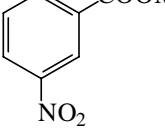
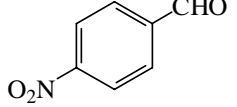
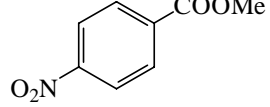
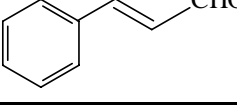
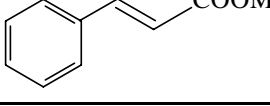
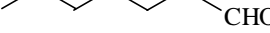

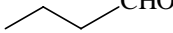

Results and Discussion

To study this process, we have examined the model reaction of benzaldehyde (1 mmol) with molecular iodine (0.5 mmol) in methanol (10 ml). When DIB (1.1 mmol) was added to the above stirred reaction mixture at room temperature, the red brown colour of iodine almost disappeared initially and again reappeared as the reaction progressed towards completion. After stirring above reaction mixture for 13 hours at room temperature, the corresponding methyl benzoate was obtained in 71% yield. However, the enhancement in the yield (83%) of methyl benzoate can remarkably be achieved by adding 1.7 equivalents of DIB with respect to the substrate aldehydes. In the above reaction, DIB does not bring about esterification without the molecular iodine and the molecular iodine alone fails to bring about esterification. The optimum yield of the product is obtained when a molar ratio of DIB to molecular iodine of 1.7 : 0.5 is used. Having succeeded with methylbenzoate formation, attempts were made at forming the ethyl or isopropyl esters of benzaldehyde by using ethanol or isopropanol as solvents. In this case, ethyl benzoate and isopropylbenzoate were formed in poor yields of 48% and 32% yields respectively. However, the formation of t-butyl ester of benzaldehyde was not observed under similar experimental conditions using t-BuOH as reaction solvent.

It is important to note that iodination product of any aromatic aldehydes was not observed under the above reaction conditions as well as in acetonitrile as reaction solvent. When aromatic aldehydes were treated with DIB/I₂ in acetonitrile medium at room temperature stirring for 24 hours, the starting aldehydes were found to be recovered in quantitative amount.

The potential scope of this oxidative esterification was then extended to a range of various aromatic and aliphatic aldehydes (Table 1). Thus the methoxy substituted aromatic aldehydes (entries b-d) underwent a clean oxidative esterification to form corresponding methyl esters. This is in contrast to the formation of Dakin reaction product using the oxone²⁰ or titanosilicates / H₂O₂¹² combination.

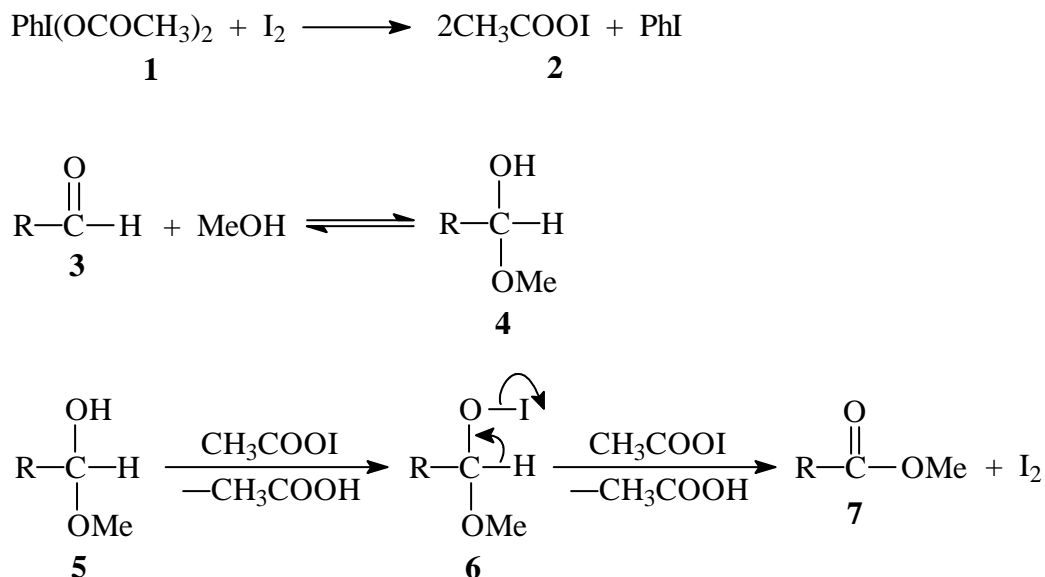
Table 1. Oxidative methyl esterification of aldehydes using DIB/I₂^a

Entry	Substrate	Product	Time (hr)	Yield (%) ^b	M.P. (Lit.) ²¹ /°C
a			13	83	liquid
b			13	85	49 (49-51)
c			14	83	60 (59-62)
d			12	84	82 (82-84)
e			13	80	34 (33-36)
f			10	82	79 (77-81)
g			15	67	liquid
h			13	89	78 (78-80)
i			14	88	96 (94-96)
j			11	83	35 (33-36)
k			10	74	liquid
l			10	67	liquid

^a All the reactions were carried out in methanol at room temperature stirring.^b Isolated yields.

Similarly, other aromatic aldehydes (entries e-i) with electron releasing and withdrawing substituents underwent oxidative methyl esterification in excellent yields. The reaction of cinnamaldehyde (entry j) with DIB / I₂ in methanol produces exclusively methyl cinnamate in 83% yield, without any observable reaction at the double bond functionality. Finally, the aliphatic aldehydes (entries k-l) also gave the corresponding methyl esters in good yields.

The reasonable mechanism for oxidative methyl esterification of aldehydes using DIB / I₂ in methanol is shown in Scheme 2. There is evidence in literature that iodonium ion generated by electrochemical oxidation of iodide anion can induce oxidative esterification of aldehydes.²² Recently, it has also been proposed that (diacetoxyiodo)benzene oxidizes molecular iodine to iodonium ion via acetylhypoiodite as putative intermediate, which is subsequently exploited in the iodohydroxylation of olefins²³ as well as nuclear iodination of electron rich arenes.²⁴ As a logical consequence of these two facts, we believe that the oxidative esterification of aldehydes is induced by iodonium ion generated by the chemical oxidation of molecular iodine with (diacetoxyiodo)benzene. Thus, the initially formed methyl hemiacetal **4** is oxidized by acetylhypoiodite **2** to the corresponding hemiacetal hypoiodite **6**. Another equivalent of acetyl hypoiodite will promote the concomitant oxidation of hemiacetal hypoiodite to methyl esters **7**.



Scheme 2

In conclusion, a transition metal-free protocol for oxidative esterification of aldehydes has been developed using (diacetoxyiodo)benzene in combination with molecular iodine. Although the literature enumerates a number of procedures for conversion of aldehydes to esters, the environmentally benign nature of DIB and I₂, mild reaction conditions, high yields of the products and experimental simplicity makes it a practical alternative.

Experimental Section

To a magnetically stirred solution of aldehyde (1 mmol), iodine (0.5 mmol) in MeOH (15 ml) was added (diacetoxyiodo)benzene (1.7 mmol). The resulting red brown solution was stirred in an open vessel for the time as mentioned in Table 1. Progress of the reaction was monitored by TLC. The red brown colour of iodine almost disappeared within half an hour and again reappeared as the reaction progressed towards completion. After completion of reaction, the mixture was washed with $\text{Na}_2\text{S}_2\text{O}_3$ and extracted with CH_2Cl_2 (2 x 10 ml). The organic extract was dried over anhydrous Na_2SO_4 . Removal of the solvent and subsequent silica gel chromatography (petroleum ether and EtOAc) afforded the corresponding methyl esters in the pure form.

Acknowledgement

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References

1. (a) Larock, R. C. In *Comprehensive Organic Transformations*; VCH: New York, 1989, pp 840. (b) March, J. *Advanced Organic Chemistry*, John Wiley and Sons, New York, 1992, pp 1196.
2. Craig, J. C.; Harning, E. C. *J. Org. Chem.* **1960**, 25, 2098.
3. Mavel, E. N.; Jonicich, M. J. *J. Am. Chem. Soc.* **1951**, 73, 973.
4. (a) Adams, A. D.; Schlessinger, R. H.; Tata, J. R.; Venit, J. J. *J. Org. Chem.* **1986**, 51, 3070. (b) Corey, E. J.; Gilman, M. W.; Granem, B. E. *J. Am. Chem. Soc.* **1968**, 90, 5616.
5. O'Conner, B.; Just, G. *Tetrahedron Lett.* **1987**, 28, 3235.
6. Bal, B. S.; Childers, Y. W.; Pinnick, H. W. *Tetrahedron* **1981**, 37, 2091.
7. Espenson, J. H.; Zhu, Z.; Zauche, T. H. *J. Org. Chem.* **1999**, 64, 1191.
8. Grigg, R.; Mitchell, T. R. B.; Sutthivaiyakit, S. *Tetrahedron* **1981**, 37, 4313.
9. Thomason, S. C.; Kubler, D. G. *J. Chem. Educ.* **1968**, 45, 546.
10. Sato, K.; Hyodo, M.; Takagi, J.; Aok, M.; Noyori, R. *Tetrahedron Lett.* **2000**, 41, 1439.
11. Gopinath, R.; Patel, B. K. *Org. Lett.* **2000**, 5, 577.
12. Chavan, S. P.; Danatle, S. W.; Gavande, C. A.; Venkataraman, M. S.; Praveen, C. *Synlett* **2002**, 2, 267.
13. (a) Ogawa, T.; Matsui, M. *J. Am. Chem. Soc.* **1976**, 98, 1629. (b) McDonald, C.; Holcomb, H.; Kennedy, K.; Kirkpatrick, E.; Leathers, T.; Veneman, P. *J. Org. Chem.* **1989**, 54, 1213.

14. Stevens, R. V.; Champman, K. T.; Stubbs, C. A.; Tam, W. W.; Albizati, K. F. *Tetrahedron Lett.* **1982**, 23, 4647.
15. Sayama, S.; Onami, T. *Synlett* **2004**, 2739.
16. Venkataramy, S. D.; Cleveland, J. H.; Pearson, D. E. *J. Org. Chem.* **1979**, 44, 3082.
17. (a) Moriatry, R. M. *J. Org. Chem.* **2005**, 70, 2893. (b) Stang, P. J. *J. Org. Chem.* **2003**, 68, 2997. (c) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, 102, 2523. (d) Moriatry, R. M.; Prakash, O. *Org. React.* **2002**, 57, 327.
18. Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: London, 1997; Chapter 3, p19.
19. Karade, N. N.; Tiwari, G. B.; Huple, D. B. *Synlett* **2005**, 2039.
20. Travis, B. R.; Sivakumar, M.; Hollist, G. O.; Barhan, B. *Org. Lett.* **2003**, 5(7), 1031.
21. Shono, T.; Matsumura, Y.; Hayashi, J.; Inoue, K.; Iwasaki, F.; Itoh, T. *J. Org. Chem.* **1985**, 50, 4967.
22. Corso, A. R. D.; Panunzi, B.; Tingoli, M. *Tetrahedron Lett.* **2001**, 42, 7245.
23. (a) Panunzi, B.; Ritiroti, L.; Tingoli, M. *Tetrahedron Lett.* **2003**, 44, 8753. (b) D'Auria, M.; Mauriello, G. *Tetrahedron Lett.* **1995**, 36, 4883. (c) Merkushev, E. B.; Simakhina, N. D.; Kovesnikova, G. M. *Synthesis* **1980**, 486.
24. (a) *Dictionary of Organic Compounds*, Chapman and Hall: London, 6th Edn., 1996. (b) *Aldrich Catalogue of Chemicals*, 2003.