

Chemistry Chat

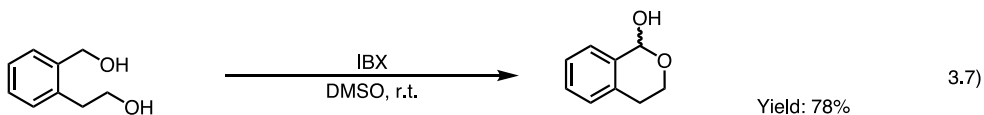
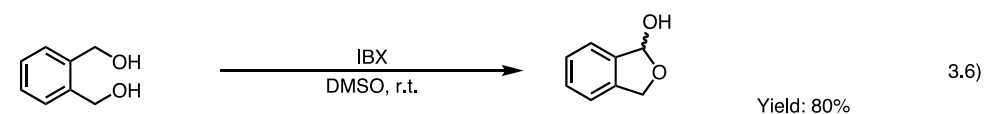
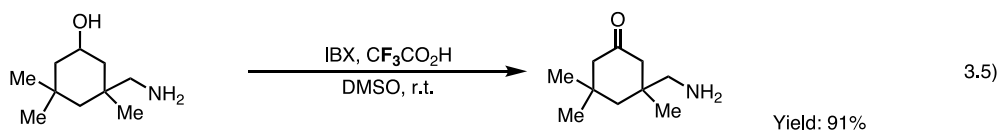
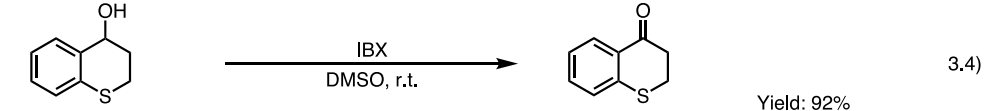
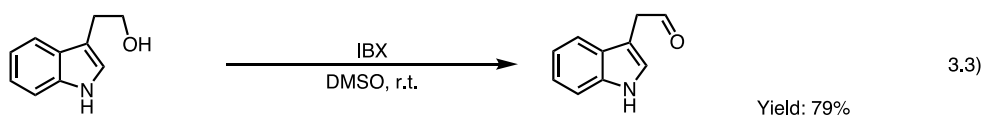
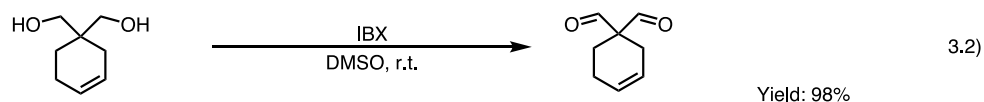
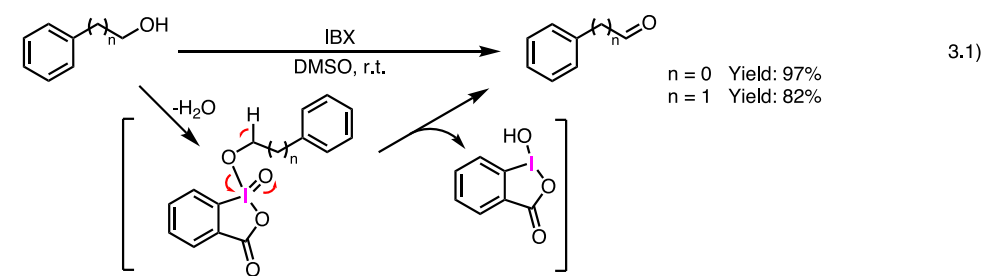
Oxidation of Alcohols with Hypervalent Iodines

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Hideo Togo

Organic hypervalent iodine [I(V), I(III)] compounds and inorganic hypervalent iodine [I(V)] compounds have high oxidizing ability, and therefore, they can be used for the oxidation of alcohols to aldehydes and ketones. 2-Iodoxybenzoic acid (IBX) is insoluble in organic solvents, such as diethyl ether and chloroform, but

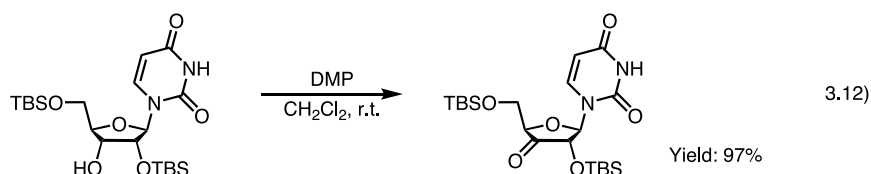
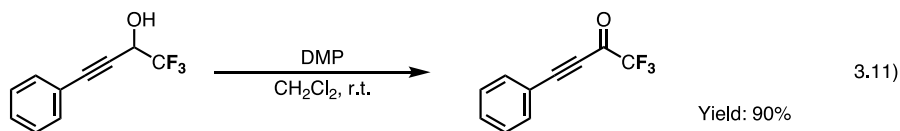
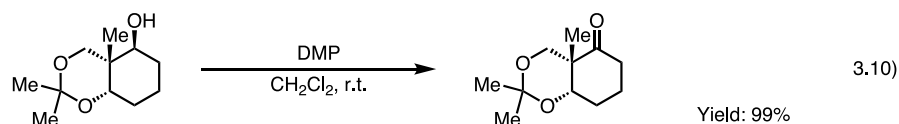
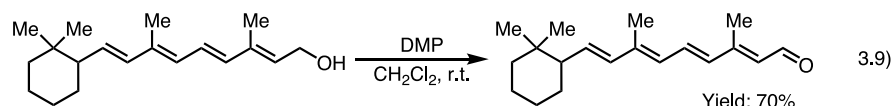
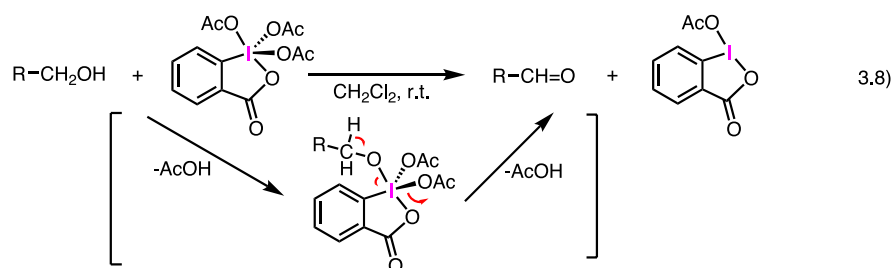
slightly soluble in DMSO. Treatment of *primary* alcohols with IBX in DMSO at room temperature generates the corresponding aldehydes in good yields, as shown in Eq. 3.1 and Eq. 3.2.¹⁾ Here, the olefin group is not oxidized by IBX.

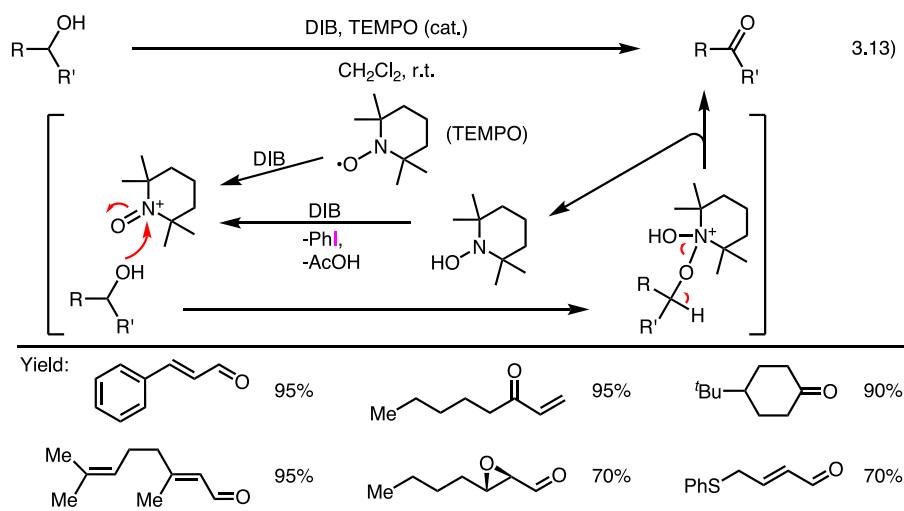


Treatment of a *primary* alcohol bearing an indole group and a *secondary* alcohol bearing a sulfide group with IBX in DMSO at room temperature also generates the corresponding aldehydes, as shown in Eq. 3.3 and Eq. 3.4, respectively.²⁾ Treatment of a *secondary* alcohol bearing a *primary* amine group with IBX in the presence of trifluoroacetic acid (1.0 eq.) in DMSO at room temperature generates the corresponding ketone bearing a *primary* amine group, as shown in Eq. 3.5.²⁾ Here, oxidation of the amine group does not occur because it is protonated by trifluoroacetic acid. Moreover, treatment of a 1,4-diol and 1,5-diol with IBX (1.2 eq.) in DMSO at room temperature generates the corresponding γ -lactol and δ -lactol, respectively, as shown in Eq. 3.6 and Eq. 3.7.³⁾ These lactols are formed from generated γ -(hydroxy)aldehyde and δ -(hydroxy)aldehyde,

respectively.

Treatment of *primary* alcohols with Dess-Martin periodinane (DMP) in dichloromethane at room temperature smoothly generates the corresponding aldehydes, as shown in Eq. 3.8. Eq. 3.9 shows the oxidation of retinol (vitamin A) to the corresponding aldehyde (retinal),⁴⁾ and Eq. 3.10 shows the oxidation of a cyclohexanol derivative bearing an acetal group to the corresponding cyclohexanone derivative.⁵⁾ Thus, DMP can be used for the oxidation of alcohols bearing olefinic and acetal groups at room temperature. Moreover, DMP can be used for oxidation of alcohols bearing strong electron-withdrawing groups, such as trifluoromethyl and 1-alkynyl groups, as shown in Eq. 3.11,⁶⁾ and for oxidation of a 2,5-*O*-protected *N*-nucleoside, *i.e.*, uridine, to generate the corresponding ketone in good yield, as shown in Eq. 3.12.⁷⁾

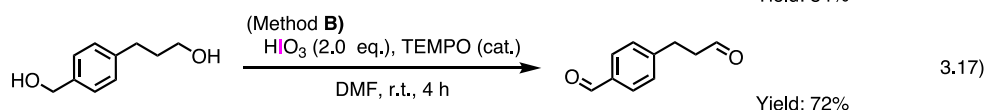
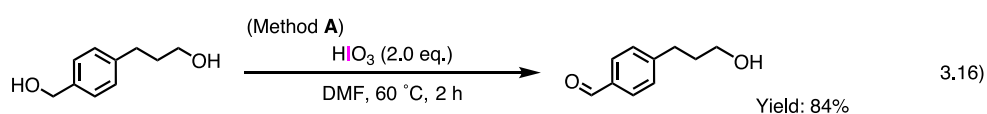
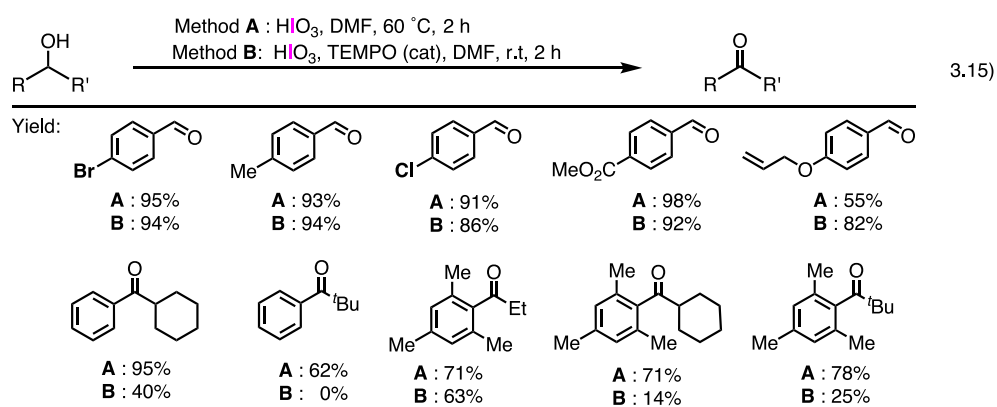
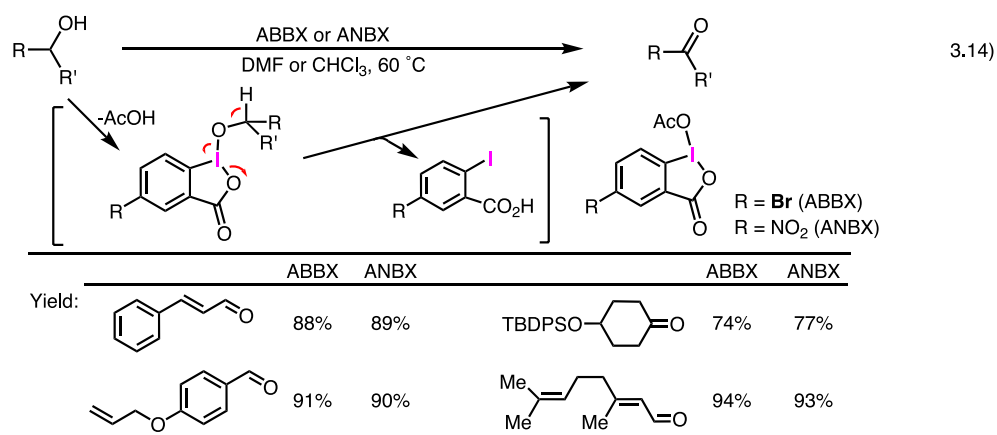




IBX and DMP have been used for the oxidation of alcohols in the total syntheses of many natural products. However, IBX and DMP are potentially explosive. Therefore, synthetic use of IBX and DMP in large-scale oxidation of alcohols and large-scale use in chemical factories is quite dangerous and unsuitable. The author has had one experience of violent explosion during the preparation of DMP in a draft chamber. On the other hand, oxidation of alcohols with (diacetoxyiodo)benzene (DIB) in the presence of 2,2,6,6-tetramethylpiperidine 1-oxyl radical (TEMPO, cat.) at room temperature is quite useful, since DIB does not have such an explosive character. Therefore, the large-scale oxidation of alcohols with DIB in the presence of TEMPO (cat.) can be carried out smoothly. Treatment of *primary* alcohols and *secondary* alcohols with DIB in the presence of TEMPO (10 mol%) in dichloromethane at room temperature efficiently generates the corresponding aldehydes and ketones in good yields, respectively, as shown in Eq. 3.13.⁸⁾ This reaction proceeds through formation of an oxo-ammonium

salt from TEMPO with DIB, addition of the alcohol to the oxo-ammonium salt to form an adduct, and β -elimination of the adduct to form an aldehyde or ketone, together with generation of *N*-hydroxy-2,2,6,6-(tetramethyl)piperidine. The generated *N*-hydroxy-2,2,6,6-(tetramethyl)piperidine is oxidized to the oxo-ammonium salt again by DIB and works as a catalyst. This method can be used for oxidation of alcohols bearing various kinds of functional groups, such as C-C double bonds, C-C triple bonds, epoxides, and sulfides.

On the other hand, warming treatment of *primary* alcohols and *secondary* alcohols with 1-acetoxy-5-bromo-1,2-benziodoxol-3(1*H*)-one (ABBX) and 1-acetoxy-5-nitro-1,2-benziodoxol-3(1*H*)-one (ANBX) in the absence of TEMPO in DMF or chloroform smoothly generates the corresponding aldehydes and ketones, respectively, as shown in Eq. 3.14.⁹⁾ However, this method cannot be used for preparation of aliphatic aldehydes bearing α -hydrogen atoms, such as acetaldehyde and propionaldehyde, from *primary* alcohols.



Iodic acid (HIO_3) has a strong oxidation ability. However, it is expensive and insoluble in typical organic solvents, such as ethers and chloroform. Therefore, synthetic uses of HIO_3 are quite limited, e.g., the oxidation of benzylic alcohols to aromatic aldehydes and aromatic ketones as shown in Eq. 3.15.¹⁰⁾ There are two methods for the oxidation of benzylic alcohols with HIO_3 . One is oxidation of benzylic alcohols to the corresponding aromatic aldehydes and ketones, except benzylic alcohol bearing an olefinic group, with HIO_3 in DMF at 60 °C (Method A). With this method, sterically hindered *secondary* benzylic alcohols bearing *tert*-butyl or 2,4,6-(trimethyl)phenyl (mesityl) groups can be smoothly oxidized to the corresponding aromatic ketones in good yields. The other is oxidation of benzylic alcohols to the corresponding aromatic aldehydes and ketones, except sterically hindered *secondary* benzylic alcohols, with

HIO_3 in the presence of TEMPO (cat.) in DMF at room temperature (Method B). With this method, benzylic alcohols bearing olefinic groups can be smoothly oxidized to the corresponding aromatic aldehydes in good yields. However, oxidation of sterically hindered *secondary* benzylic alcohols does not proceed smoothly. When 3-[*p*-(hydroxymethyl)phenyl]propan-1-ol, which has two kinds of hydroxy groups, is treated with Method A (HIO_3 alone) and Method B [HIO_3 in the presence of TEMPO (5 mmol%)], reaction with Method A generates *p*-(3-hydroxypropyl)benzaldehyde in good yield, as shown in Eq. 3.16, and reaction with Method B generates *p*-[2-(formyl)ethyl]benzaldehyde, as shown in Eq. 3.17. Thus, oxidation of alcohols to aldehydes and ketones with IBX, DMP, DIB-TEMPO (cat.), ABBX, ANBX, HIO_3 , and HIO_3 -TEMPO (cat.) can be carried out smoothly under mild conditions and transition metal free conditions.¹¹⁾

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Author Information

Hideo Togo was born in 1956 in Ibaraki prefecture of Japan. He completed his doctoral thesis in 1983 at University of Tsukuba. Then, he became a post-doctoral fellow at University of Lausanne in Switzerland (1983–1984) and at CNRS (Professor Sir Derek H. R. Barton) in France (1984–1985). Then, he became a research associate at University of Tsukuba in 1987 and then moved to Chiba University as a research associate in 1989. He became an associate professor in 1994, and a full professor in 2005. He retired from Chiba University in 2021, and became an emeritus professor in Chiba University and a research advisor in research center of technology of Godo Shigen Co. LTD.

Related Products

2-Iodoxybenzoic Acid (= IBX) (stabilized with Benzoic Acid + Isophthalic Acid)		5g	25g	I0791
Dess-Martin Periodinane	1g	5g	25g	D2045
2,2,6,6-Tetramethylpiperidine 1-Oxyl Free Radical (= TEMPO)		5g	25g	T1560
(Diacetoxyiodo)benzene (= DIB)	10g	25g	100g	I0330
1-Acetoxy-5-bromo-1,2-benziodoxol-3(1H)-one (= ABBX)			1g	A2678