

# Mesityltriphenylbismuthonium tetrafluoroborate as an efficient bismuth(V) oxidant: remarkable steric effects on reaction rates and chemoselectivities in alcohol oxidation

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**Abstract**—In the presence of *N,N,N',N'*-tetramethylguanidine, mesityltriphenylbismuthonium tetrafluoroborate oxidizes primary and secondary alcohols to aldehydes and ketones, respectively, under mild conditions. In this reaction, the mesityl ligand exclusively abstracts an  $\alpha$ -hydrogen to afford mesitylene and triphenylbismuthane as side products. A remarkable steric effect has also been exhibited in the chemoselective oxidation between primary and secondary alcohols.  
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Pentavalent arylbismuth compounds of the type  $\text{Ar}_3\text{-BiX}_2$  ( $\text{X}$  = anionic ligands) are known to be versatile oxidants for converting alcohols to carbonyl compounds by taking advantage of the facile  $\text{Bi}^{\text{V}}/\text{Bi}^{\text{III}}$  redox process.<sup>1,2</sup> In the oxidation of simple alcohols, the reaction is believed to proceed through two main steps; formation of an alkoxybismuth(V) intermediate and the following  $\alpha$ -hydrogen abstraction by the aryl ligand. Recently, we have revealed that the oxidizing ability of  $\text{Ar}_3\text{BiX}_2$  strongly depends on the substituents of the aryl ligands.<sup>3</sup> In particular, *ortho*-methyl groups have proved to accelerate the hydrogen abstraction step due to steric reasons, enhancing the overall rate of the oxidation. This finding led us to examine the effects of substituents of other classes of arylbismuth(V) compounds on their oxidizing ability. In 1987, Barton et al. reported that 3 $\beta$ -cholestanol and neopentyl alcohol were oxidized by using tetraphenylbismuth esters ( $\text{Ph}_4\text{BiX}$ ;  $\text{X}$  = OTs,  $\text{OCOCF}_3$ ) under basic conditions.<sup>4</sup> However, their pioneering work has apparently received little attention. We expected that highly reactive tetraaryl bismuth(V) oxidants would be provided by suitably choosing the substituents on their aryl ligands.

Herein, we report a new efficient bismuth(V) oxidant, mesityltriphenylbismuthonium tetrafluoroborate (mesit-

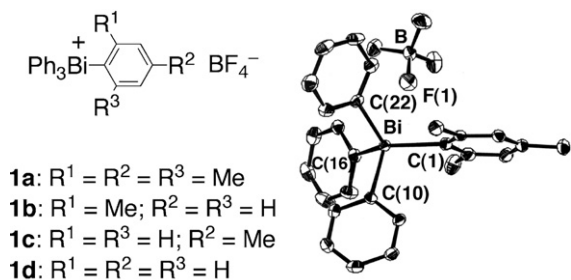
yl = 2,4,6-trimethylphenyl), which converts primary and secondary alcohols to aldehydes and ketones, respectively, in the presence of TMG (*N,N,N',N'*-tetramethylguanidine) under mild conditions. Remarkable steric effects of the mesityl group on the reaction rates and chemoselectivities of alcohol oxidation have been exhibited.

Tetraaryl bismuthonium tetrafluoroborates **1a–d** were prepared from triphenylbismuth difluoride,  $\text{BF}_3\cdot\text{OEt}_2$ , and the corresponding arylboronic acids, according to the reported procedure.<sup>5</sup> The structure of mesityltriphenylbismuthonium salt **1a** was further characterized by X-ray crystallography.<sup>6</sup> As shown in Figure 1, the bismuth center adopts a distorted tetrahedral geometry, which clearly endorses the onium nature of **1a**. The Bi–F(1) bond distance of 3.005(2) Å implies a weak electrostatic interaction between the cationic bismuth center and the counter anion. Due to this interaction, the C(1)–Bi–C(16) bond angle open to the anion side [125.26(14)°] is appreciably larger than the expected value (109.28°) for a tetrahedron, whereas the C(10)–Bi–C(16) bond angle [97.35(14)°] is smaller.

To compare the oxidizing abilities of **1a–d** as well as to examine the effect of base, we performed oxidation of benzyl alcohol in  $\text{CDCl}_3$  at room temperature (Table 1). In the presence of TMG, mesitylbismuthonium salt **1a** oxidized the alcohol to benzaldehyde much more rapidly than the other bismuthonium salts **1b–d**. The relative reaction rates were found to be in the order

**Keywords:** Bismuthonium salts; Alcohol; Carbonyl compounds; Oxidation; Chemoselectivity.

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**Figure 1.** Tetraarylbismuthonium salts **1a–d** (left) and ORTEP diagram of **1a** (right; 50% probability ellipsoids). Selected bond lengths (Å) and angles (deg): Bi–C(1), 2.207(4); Bi–C(10), 2.208(4); Bi–C(16), 2.202(4); Bi–C(22), 2.212(4); Bi–F(1), 3.005(2); C(1)–Bi–C(10), 102.13(13); C(1)–Bi–C(16), 125.26(14); C(1)–Bi–C(22), 112.88(14); C(10)–Bi–C(16), 97.35(14); C(10)–Bi–C(22), 107.33(14); C(16)–Bi–C(22), 108.94(14).

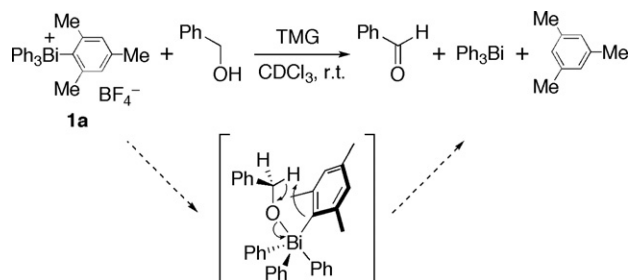
**Table 1.** Oxidation of benzyl alcohol with **1a–d** in CDCl<sub>3</sub>

Entry	<b>1</b>	Base	Time (h)	Yield <sup>a</sup> (%)
1	<b>1a</b>	TMG	1.5	>99
2	<b>1b</b>	TMG	1.5 (5)	77 (89 <sup>b</sup> )
3	<b>1c</b>	TMG	1.5 (10)	65 (85 <sup>b</sup> )
4	<b>1d</b>	TMG	1.5 (7)	75 (90 <sup>b</sup> )
5	<b>1a</b>	DBU	1.5	>99
6	<b>1a</b>	Et <sub>3</sub> N	20	31
7	<b>1a</b>	K <sub>2</sub> CO <sub>3</sub>	1.5	66
8	<b>1a</b>	Pyridine	4	0

<sup>a</sup> Determined by <sup>1</sup>H NMR using DMF as an internal standard.

<sup>b</sup> Yield after the reaction time indicated in parentheses.

**1a** ≫ **1b** > **1d** > **1c** (entries 1–4), suggesting that the introduction of methyl groups at both of the *ortho* positions significantly enhances the overall rate. Among the bases examined, TMG and DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) gave satisfactory results, whereas Et<sub>3</sub>N and K<sub>2</sub>CO<sub>3</sub> were found to be less effective. No oxidation took place with pyridine even after 4 h. In entries 1–7, equimolar amounts of arene(s) and triaryl-bismuthane(s) were formed as side products. This indicates that an  $\alpha$ -hydrogen of the alcohol is abstracted by the aryl ligand attached to the bismuth. Scheme 1 depicts a plausible reaction pathway for the oxidation with **1a**, which is essentially the same as that proposed by Barton and co-workers.<sup>7</sup> The first step is formation of the alkoxybismuth(V) intermediate, and the second step is  $\alpha$ -hydrogen abstraction by the mesityl ligand. It should



**Scheme 1.**

be noted that, in the oxidation with **1a**, triphenylbismuthane and mesitylene were formed in >99% yield.<sup>8</sup> Thus, the mesityl group abstracts the  $\alpha$ -hydrogen much more rapidly than the phenyl groups. Presumably, the Bi–C<sub>mesityl</sub> bond of the alkoxybismuth(V) intermediate is weakened due to steric congestion around the bismuth center, and, as a result, the rate of the second step is accelerated considerably. A similar steric effect of the *ortho*-substituents was observed for the alcohol oxidation with Ar<sub>3</sub>BiX<sub>2</sub>.<sup>3</sup>

With a new efficient bismuth(V) oxidant **1a** in hand, we examined the oxidation of several kinds of alcohols (Table 2).<sup>9</sup> Primary alcohols were converted to aldehydes, without any noticeable overoxidation to carboxylic acids (entries 1–8, 12, 13). In particular, benzylic and allylic alcohols were rapidly and selectively oxidized to benzaldehydes and  $\alpha,\beta$ -unsaturated aldehydes, respectively. Secondary alcohols were oxidized to ketones in good yields (entries 9–11, 14), but the reaction rates were much slower than those observed for similar primary alcohols. For instance, in chlorinated solvents, benzyl alcohol was quantitatively converted to benzaldehyde within 1.5 h, whereas the complete conversion of 1-phenyl-1-propanol to propiophenone required over 40 h (entries 1 vs 11). The rate of oxidation was found to be accelerated by changing the solvent to toluene.<sup>10</sup> Thus, the oxidations of 1-dodecanol and 3-pentanol proceeded more rapidly than those in chloroform (entries 12 and 14). Furthermore, the use of toluene was effective for the selective conversion of nonconjugated alcohols to their corresponding carbonyl compounds. For instance, treatment of 1-dodecanol with **1a**/TMG in toluene gave dodecanal as the sole oxidized product in quantitative yield, whereas a similar treatment in chloroform gave a mixture of dodecanal and 2-mesityldodecanal in 40% and 20% yields, respectively, after 2 h (entry 12).<sup>11</sup> 1-Pentanol was also oxidized by **1a**/TMG in toluene to afford pentanal quantitatively (entry 13).

To shed light on the relative reactivities of benzylic, allylic, and nonconjugated alcohols toward **1a**, intermolecular competitive oxidations were performed. As shown in Table 3, both benzylic and allylic alcohols were oxidized selectively in the presence of nonconjugated alcohols.

High chemoselectivities were also attained in the competitive oxidations between primary (1°) and secondary (2°) alcohols (Table 4). It should be emphasized that all of the alcohols themselves are oxidized efficiently by **1a**/TMG under mild conditions. When a mixture of equimolar amounts of benzyl alcohol and  $\alpha$ -substituted benzyl alcohols was reacted with **1a**/TMG in CDCl<sub>3</sub>, benzaldehyde was formed predominantly over phenyl alkyl ketones (entries 1–3). The 1°/2° selectivity of 92/8, obtained from the competitive reaction between benzyl alcohol and 1-phenyl-1-propanol (entries 2, 4–7), is much higher than those observed for **1b,d**/TMG (77/23 and 74/26), tri(*o*-tolyl)bismuth dichloride/TMG (63/37), and Dess–Martin periodinane (DMP) (67/33). In the competitive oxidation between 1-pentanol and 3-pentanol in toluene-*d*<sub>8</sub> (entries 8–10), the 1°/2° selectivity

**Table 2.** Oxidation of alcohols with **1a**

$\text{R}^1\text{R}^2\text{CHOH} \xrightarrow[\text{solvent, r.t.}]{\text{1a (1.1 equiv), TMG (1.1 equiv)}} \text{R}^1\text{R}^2\text{C=O}$				
Entry	Alcohol	Solvent	Time (h)	Yield <sup>a</sup> (%)
1		CDCl <sub>3</sub>	1.5	99 <sup>b</sup>
2		CH <sub>2</sub> Cl <sub>2</sub>	1.0	95
3		CH <sub>2</sub> Cl <sub>2</sub>	0.5	95
4		CH <sub>2</sub> Cl <sub>2</sub>	1.0	99
5		CH <sub>2</sub> Cl <sub>2</sub>	1.0	99
6		CDCl <sub>3</sub>	0.5	94 <sup>b</sup>
7		CH <sub>2</sub> Cl <sub>2</sub>	1.0	99
8		CH <sub>2</sub> Cl <sub>2</sub>	0.5	98
9		CH <sub>2</sub> Cl <sub>2</sub>	0.5	98
10		CH <sub>2</sub> Cl <sub>2</sub>	4.0	91
11		CDCl <sub>3</sub> Toluene- <i>d</i> <sub>8</sub>	40 3.0	88 <sup>b</sup> 98 <sup>b</sup>
12		CDCl <sub>3</sub> Toluene- <i>d</i> <sub>8</sub>	2.0 0.5	40 <sup>b,c</sup> 98 <sup>b</sup>
13		Toluene- <i>d</i> <sub>8</sub>	1.5	99 <sup>b</sup>
14		CDCl <sub>3</sub> Toluene- <i>d</i> <sub>8</sub>	3.0 3.0	7 <sup>b</sup> 99 <sup>b</sup>

<sup>a</sup> Isolated yield unless otherwise noted.<sup>b</sup> NMR yield.<sup>c</sup> 2-Mesityldodecanal was formed in 20% yield.**Table 3.** Competitive oxidations of benzylic, allylic, and nonconjugated alcohols with **1a**/TMG

$\text{R}^1\text{R}^2\text{CHOH} + \text{R}^3\text{R}^4\text{CHOH} \xrightarrow[\text{CDCl}_3, \text{r.t.}]{\text{1a (0.9 equiv), TMG (1.0 equiv)}} \text{R}^1\text{R}^2\text{C=O} + \text{R}^3\text{R}^4\text{C=O}$		
R <sup>1</sup> R <sup>2</sup> CHOH	R <sup>3</sup> R <sup>4</sup> CHOH	R <sup>1</sup> R <sup>2</sup> CO/R <sup>3</sup> R <sup>4</sup> CO <sup>a</sup>
		93/7
		97/3
		95/5

<sup>a</sup> Determined by <sup>1</sup>H NMR.**Table 4.** Competitive oxidations of primary versus secondary alcohols

$\text{PhCHOH} + \text{PhCHOH} \xrightarrow[\text{CDCl}_3, \text{r.t.}]{\text{oxidant (0.9 equiv), TMG (1.0 equiv)}} \text{PhCHO} + \text{PhC(O)R}$				
Entry	Oxidant	Time (h)	R	PhCHO/PhC(O)R <sup>a</sup>
1	<b>1a</b>	1	Me	81/19
2	<b>1a</b>	1	Et	92/8
3	<b>1a</b>	1	<i>i</i> -Pr	94/6
4	<b>1b</b>	7	Et	77/23
5	<b>1d</b>	7	Et	74/26
6	<i>o</i> -Tol <sub>3</sub> BiCl <sub>2</sub>	3	Et	63/37
7	DMP <sup>b</sup>	2	Et	67/33

${}^n\text{BuCHOH} + \text{EtCHOH} \xrightarrow[\text{toluene-}d_8, \text{r.t.}]{\text{oxidant (0.9 equiv), TMG (1.0 equiv)}} {}^n\text{BuCHO} + \text{EtCOEt}$				
Entry	Oxidant	Time (h)	<sup>n</sup> BuCHO/Et <sub>2</sub> CO <sup>a</sup>	
8	<b>1a</b>	1	89/11	
9	<b>1d</b>	3	52/48	
10	DMP <sup>b</sup>	3	67/33	

<sup>a</sup> Determined by <sup>1</sup>H NMR.<sup>b</sup> TMG was not added.

observed for **1a**/TMG (89/11) is appreciably higher than those observed for **1d**/TMG (52/48) and DMP (67/33). It is apparent that **1a** discriminates between steric bulkiness of the  $\alpha$ -substituents (H vs Et) of the alcohols more efficiently than other arylbismuth(V) oxidants and DMP. Nucleophilic addition to tetraarylbismuthonium salts seems to be sensitive to the steric environment around the cationic bismuth center as well as the bulkiness of the nucleophiles. In this regard, the mesityl ligand is more effective at discriminating between primary and secondary alcohols than tolyl and phenyl ligands are. Although the literature contains more selective oxidation methods,<sup>12</sup> **1a** constitutes a useful addition to the existing efficient oxidants.

In summary, we have demonstrated for the first time that mesityltriphenylbismuthonium tetrafluoroborate oxidizes primary and secondary alcohols to aldehydes and ketones, respectively, with high efficiency. The remarkable steric effects of the mesityl ligand on the reaction rates and chemoselectivities are of particular interest, as they exemplify that the oxidizing ability of tetraarylbismuthonium salts is controllable by suitable choice of the aryl ligands attached to the bismuth.

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### Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.02.085.

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- Barton, D. H. R.; Finet, J.-P.; Motherwell, W. B.; Pichon, C. *J. Chem. Soc., Perkin Trans. 1* **1987**, 251. In the presence of *N*-butyl-*N'*,*N'*,*N''*,*N''*-tetramethylguanidine, these alcohols were oxidized to the corresponding carbonyl compounds in 78–92% yields after 7.5–12 h.
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- Formula C<sub>27</sub>H<sub>26</sub>BBiF<sub>4</sub>, monoclinic, *P*2<sub>1</sub>/*n*, *a* = 10.206(2) Å, *b* = 17.488(4) Å, *c* = 13.798(3) Å, β = 91.0880(10)°, *V* = 2462.1(9) Å<sup>3</sup>, *Z* = 4, *D*<sub>c</sub> = 1.743 g cm<sup>-3</sup>, 5432 obsd, 299 variables, *R*<sub>w</sub> = 0.0526, *R* = 0.0254 (*I* > 2.00σ(*I*)), GOF = 1.029. Crystallographic data for the structure of **1a** have been deposited with the Cambridge Crystallographic Data Centre as Supplementary Publication No. CCDC 635005. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).
- In the oxidation of alcohols with Ph<sub>4</sub>BiX (X = OTs, OCOF<sub>3</sub>), triphenylbismuthane and benzene were formed. See Ref. 4.
- Formation of these products was confirmed by <sup>1</sup>H NMR and GC.
- Typical procedure: TMG (38 mg, 0.33 mmol) was added to a mixture of **1a** (213 mg, 0.33 mmol), alcohol (0.30 mmol), and CH<sub>2</sub>Cl<sub>2</sub> (10 mL), and the resulting mixture was stirred at room temperature. After the alcohol had been consumed (checked by TLC), the reaction mixture was concentrated under reduced pressure to leave an oily residue, which was then subjected on a short silica gel column (hexane ~ hexane/EtOAc or CH<sub>2</sub>Cl<sub>2</sub>). The carbonyl compounds were easily separated from triphenylbismuthane and could be isolated in a pure form.
- At present, we assume that the ground state of **1a**/TMG/alcohol is destabilized compared to the alkoxybismuth(V) intermediate in a nonpolar solvent such as toluene. The solvent effect will be investigated systematically in the future work.
- The formation of 2-mesityldodecanal was suggested by the <sup>1</sup>H NMR spectrum of the reaction mixture. This byproduct was presumably formed by C-arylation of the initial product, dodecanal, with **1a**/TMG.
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