Facile Oxidation of Alcohols to Carbonyl Compounds Using a Tris(2-methylphenyl)bismuth Dichloride–DBU Binary System**

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Various methods for the oxidation of alcohols to carbonyl compounds, one of the most important organic transformations, are available.[1] Although individually having some synthetic advantages, most conventional methods suffer from one or more experimental drawbacks, such as severe or delicate reaction conditions, complicated reaction procedures, and the need to use toxic, unstable, or potentially explosive reagents. Therefore, the search for a mild but efficient oxidation method with easy handling, nontoxicity, and reasonably stable oxidants is still the subject of numerous studies on organic synthesis.[2]

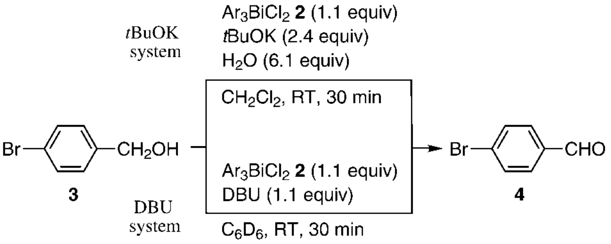
Pentavalent organobismuth compounds are attractive oxidants because of their inherent oxidizing ability derived from the facile Bi^V/Bi^{III} redox process[3] and due to the low toxicity of bismuth.[4] In 1934 Challenger and Richards reported that ethanol, *n*-propanol, and 2-propanol were oxidized by triphenylbismuth dihydroxide to acetaldehyde, propionaldehyde, and acetone, respectively.[5] Several decades later Barton et al. and Dodonov et al. independently developed a new oxidation method using polyphenylbismuth(v) reagents such as $(Ph_3BiCl)_2O$, Ph_3BiCO_3, and $Ph_3Bi(OAc)_2$,[6,7] in which a variety of alcohols are oxidized to the corresponding carbonyl compounds under neutral or basic conditions. However, their method often requires a long reaction time and/or a high reaction temperature to attain good results,[8] and so there is still room for practical improvement in the Bi^V-based oxidation systems.

Recently, we found that dimeric tris(2-methoxyphenyl)bismuthane oxide (**1**)[9] oxidizes alcohols to carbonyl compounds more rapidly (within 10 min) and under milder conditions (at room temperature) than the known organobismuth(v) reagents[6,7,10] or polymeric tris(4-methylphenyl)bismuthane oxide.[11] Although the bismuthane oxide **1** itself is thermally unstable and does not have the prerequisites for a practically usable oxidant, this finding suggested to us that the aryl ligands on the Bi^V center play an important role in alcohol oxidation. Thus, we set out to develop a one-pot oxidation system by the direct use of triarylbismuth dichlorides bearing suitable substituents, since this class of compounds are thermally stable and easy to handle.

Here we report a new, practical oxidation method using a binary system made up of tris(2-methylphenyl)bismuth dichloride and 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU), which converts primary alcohols to aldehydes and secondary alcohols to ketones with high efficiency and chemoselectivity under mild conditions. In this system, the *ortho*-tolyl groups on the Bi^V center give rise to a remarkable oxidizing ability, one which is difficult to attain with the *para*- and nonsubstituted phenyl groups. An additional improvement upon previous systems is that the carbonyl products can be easily isolated by simple work-up procedures.

To determine the effect of the substituent, we first compared oxidizing abilities among five triarylbismuth dichlorides **2a**–**e** in a reaction with *p*-bromobenzyl alcohol (**3**) (Table 1). In the presence of 2.2 equiv of *t*BuOK and 6.1 equiv of water, the *ortho*-substituted derivatives **2a** and **2b** oxidized **3** to *p*-bromobenzaldehyde (**4**) much more rapidly than the *para*- and nonsubstituted derivatives **2c**–**e**. When the reaction was performed in the absence of water or in the presence of only 1.2 equiv of *t*BuOK, the conversion of **3** into **4** was dramatically depressed. During these oxidations, equimolar amounts of arene (ArH) and Bi^{III} compounds of the types $[Ar_3Bi]$ and $[Ar_2BiOBiAr_2]$[12] were formed as by-products. These outcomes indicated that the triarylbismuth(v)-oxo or -hydroxo species is the active oxidant generated in situ. Actually, the independently prepared **1** showed almost the same efficiency as the **2b**/*t*BuOK/H_2O system.

Table 1. Oxidation of alcohol **3** using Ar_3BiCl_2 (**2**) and a base.



Compd **2**	Ar	Conversion of **3** [%][a] *t*BuOK system	DBU system
2a	*o*-MeC_6H_4	> 99 (62)[b] (15)[c]	98 (> 99)[d]
2b	*o*-$MeOC_6H_4$	94 (55)[b] (17)[c]	78
2c	*p*-MeC_6H_4	38	19
2d	*p*-$MeOC_6H_4$	28	5
2e	Ph	52	43

[a] Determined by ^1H NMR spectroscopy. Compound **3** was converted quantitatively into **4**. [b] Only 1.2 equiv of *t*BuOK was used. [c] Water was not added. [d] Toluene was used as the solvent.

We next examined the one-pot oxidation using DBU instead of *t*BuOK (Table 1). The best result was again obtained with the *ortho*-tolyl derivative **2a**, which quantitatively converted **3** into **4** in the presence of one equivalent of DBU. In this system, the reaction proceeded efficiently without water, and the Bi^{III} by-product was a crystalline complex, $[o\text{-}Tol_2BiCl_2^-][DBUH^+]$ (**5**), which was characterized by spectroscopy as well as by X-ray crystallography.[13]

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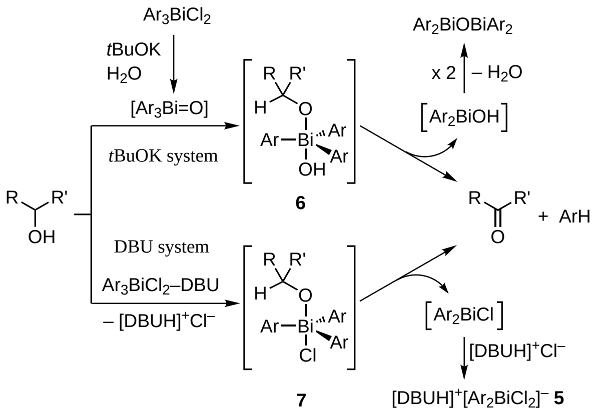
Owing to its ionic character, complex **5** is insoluble in nonpolar solvents. Thus, when the reaction was carried out in benzene or toluene, **5** was deposited from the reaction medium and could be removed by filtration. This brought a practical advantage over the *t*BuOK system in that the carbonyl product could be purified by passing it through a short silica gel bed with a small amount of eluent (hexane/EtOAc).[14]

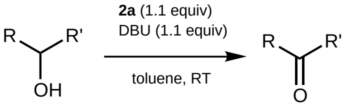
It has been confirmed that, in both systems, the steric environment around the Bi^V center plays an important role in the alcohol oxidation. Plausible reaction mechanisms of these oxidations are depicted in Scheme 1. Apparently, the α-hydrogen atom of the alcohol is abstracted by the aryl group via alkoxybismuth(v) intermediates **6** and **7**.[15] The kinetic isotope effects observed in the oxidation of p-$BrC_6H_4CH(D)OH$ by **2a** ($k_H/k_D = 3.3$ for *t*BuOK/$H_2O/CDCl_3$ and 3.4 for DBU/toluene at 25 °C, estimated by ^1H NMR spectroscopy) suggested that the rate-determining steps involved α-hydrogen abstraction from **6** and **7**. Presumably, the *ortho*-substituted aryl groups accelerated these Bi^V/Bi^{III} redox processes for steric reasons.

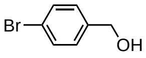
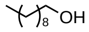
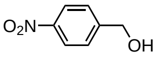
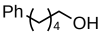
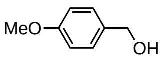
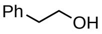
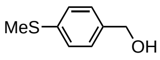
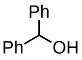
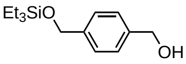
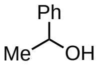
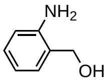
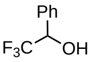
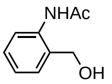
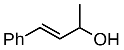
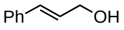
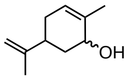
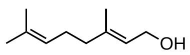
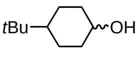
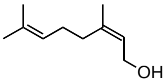
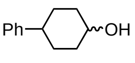


Scheme 1. Plausible reaction mechanisms for the oxidation of alcohols by the *t*BuOK and DBU systems.

With the availability of a mild and efficient oxidation system, **2a**/DBU, we examined the oxidation of various primary and secondary alcohols in toluene at room temperature (Table 2). The *para*- and *ortho*-substituted benzyl

Table 2. Oxidation of alcohols using the **2a**/DBU system in toluene.



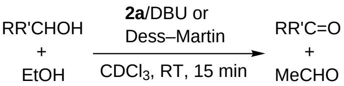
Entry	Alcohol	*t* [h]	Yield [%][a]	Entry	Alcohol	*t* [h]	Yield [%][a]
1		0.5	94	11		2.0	94
2		0.5	95	12		2.0	90[c]
3		0.5	99	13		0.5	–[d]
4		0.5	98	14		0.5	99
5		0.5	98	15		0.5	89
6		0.5	> 99	16		32	98[e]
7		0.5	95	17		0.5	> 99
8		0.5	> 99	18		1.0	93
9		0.5	94	19		2.0	93
10		0.5	> 99[b]	20		2.0	> 99

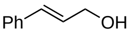
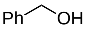
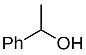
[a] Yield of isolated carbonyl compound unless otherwise noted. [b] Neral and geranial compounds were obtained in a 98:2 ratio. [c] 2-(*o*-Tolyl)-5-phenylpentanal was obtained in 5 % yield. [d] A complex mixture was formed and the alcohol was recovered in moderate yield. [e] Yield determined by NMR spectroscopy. The reaction was carried out in C_6D_6.

alcohols were oxidized to the corresponding substituted benzaldehydes in excellent yields (entries 1–7). Thiomethyl, triethysiloxy, amino, and amido groups remained intact under the present reaction conditions. Allylic and nonconjugated aliphatic alcohols were also oxidized in high yields to α,β-unsaturated aldehydes and nonconjugated aliphatic aldehydes, respectively (entries 8–12). Complete stereochemical retention was observed for geraniol (entry 9), whereas a slight isomerization was observed for nerol (entry 10). In these reactions, the aldehydes produced were not oxidized further to carboxylic acids, thus indicating the potential utility of the **2a**/DBU system as a selective oxidant. A limitation was observed in the oxidation with 2-phenylethanol, which could not be efficiently converted into phenylacetaldehyde (entry 13). In this reaction, a complex mixture was formed with only moderate recovery of the starting alcohol. It seems that the acidic α-proton of the initially formed phenylacetaldehyde is readily abstracted by DBU, causing undesired reactions.[16] Secondary alcohols were oxidized to the corresponding ketones in high yields (entries 14–20). It is worth noting that 2,2,2-trifluoro-1-phenylethanol could be cleanly oxidized to α,α,α-trifluoroacetophenone, though a longer reaction time was necessary (entry 16).[17] When **2c** (Ar = *p*-Tol) was used in place of **2a**, the trifluoromethyl ketone was not formed under all the same conditions.

To estimate the relative reactivity of allylic, benzylic, and nonconjugated alcohols toward the **2a**/DBU system, both intermolecular and intramolecular competitive oxidations were examined. As summarized in Table 3, the **2a**/DBU system oxidized cinnamyl and benzylic alcohols preferentially in the presence of ethyl alcohol, and their selectivities were found to be much higher than those attained by Dess–Martin periodinane.[18] The high chemoselectivity of benzylic versus nonconjugated aliphatic alcohols was also observed in the reaction of 1-phenyl-1,4-butanediol (**8**): When treated with 0.9 equiv of **2a**/DBU, **8** was converted exclusively into 4-hydroxy-1-phenylbutan-1-one (**9**) in 98% yield based on **2a** (Scheme 2). These results clearly demonstrate the synthetic utility of the **2a**/DBU system as a chemoselective oxidant.

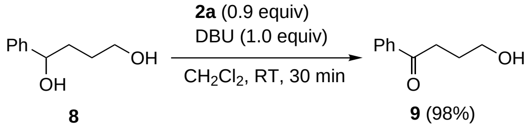
Table 3. Competitive oxidation of alcohols by **2a** and Dess–Martin periodinane.[a]



RR′CHOH	Ratio of RR′=O to MeCHO[b]	
	2a/DBU	Dess–Martin
	98:2	91:9
	96:4	90:10
	95:5	75:25

[a] Three equivalents each of RR′CHOH and ethanol were used. [b] Determined by ^{1}H NMR spectroscopy.

In summary, we have established a new practical oxidation method using the $(o\text{-Tol})_3BiCl_2$/DBU binary system, which promises facile conversion of alcohols into carbonyl compounds with high efficiency and selectivity under mild conditions. The remarkable oxidizing ability of this new system is derived from the steric effect of the *ortho*-tolyl groups attached to the Bi^V center. The present system also has a practical advantage over the previously reported Bi^V-based oxidation systems in that the carbonyl products can be easily isolated by simple filtration following treatment on a short column. Further studies on the use of this method in other organic transformations are currently in progress.



Scheme 2. The intramolecular competitive oxidation of alcohol **8** by the **2a**/DBU system.

Experimental Section

Oxidation of alcohol: DBU (46 mg, 0.30 mmol) was added to a stirred suspension of tris(2-methylphenyl)bismuth dichloride (**2a**;[19] 166 mg, 0.30 mmol) and alcohol (0.27 mmol) in toluene (3 mL) at room temperature, and the resulting mixture was monitored by TLC at several intervals. After the alcohol was consumed, the precipitated complex **5** was filtered off through a thin celite bed. The filtrate was concentrated under reduced pressure to leave an oily residue, which contained the desired carbonyl product in a high state of purity (> 90%). The residue was then passed through a short silica gel column (710 mm^2 × 18–45 mm of Wako-gel C-200, about 50 mL of hexane/EtOAc (5/1) as eluent) to afford the carbonyl compound in the yields listed in Table 2. Complex **5** was recovered quantitatively and could be converted into tris(2-methylphenyl)bismuthane by treatment with 2.5 equiv of *o*-TolMgBr in THF.

5: M.p. 181–184 °C (decomp); ^{1}H NMR (400 MHz, CDCl$_3$, TMS): $\delta = 1.63$–1.74 (m, 6H), 1.92 (tt, $J = 5.9$, 5.9 Hz, 2H), 2.58 (s, 6H), 2.76–2.79 (m, 2H), 3.19 (t, $J = 5.9$ Hz, 2H), 3.39 (t, $J = 5.9$ Hz, 2H), 3.43–3.45 (m, 2H), 7.31 (dd, $J = 7.6$, 7.3 Hz, 2H), 7.44 (dd, $J = 7.6$, 7.3 Hz, 2H), 7.48 (d, $J = 7.6$ Hz, 2H), 8.49 (d, $J = 7.6$ Hz, 2H), 10.84 ppm (brs, 1H); IR (KBr): $\tilde{\nu} = 3217$, 3126, 3038, 2980, 2937, 2856, 1651, 1589, 1470, 1448, 1383, 1323, 1292, 1271, 1207, 1159, 1109, 984, 845, 756, 743, 706, 606, 536, 436, 430 cm^{-1}; elemental analysis (%) calcd for $C_{23}H_{31}BiCl_2N_2$: C 44.89, H 5.08, N 4.55; found: C 44.85, H 4.99, N, 4.51.

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[8] For instance, the reaction conditions for the oxidations of cinnamyl alcohol and 1-pentanol with a $(Ph_3BiCl)_2O$/base system were reported to be 15 h at 21 °C and 6 h at 60 °C, respectively.[6a]

[9] Y. Matano, H. Nomura, *J. Am. Chem. Soc.* **2001**, *123*, 6443–6444. Compound **1** was prepared by the reaction of tris(2-methoxyphenyl)-bismuth dichloride with 2 equiv of *t*BuOK in the presence of 5 equiv of water.

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[11] H. Suzuki, T. Ikegami, Y. Matano, *Tetrahedron Lett.* **1994**, *35*, 8197–8200.

[12] The initially formed $Ar_2BiOBiAr_2$ disproportionated in solution to give Ar_3Bi.

[13] CCDC-182209 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

[14] In the *t*BuOK system, a long column was necessary to completely remove the Bi^{III} by-product (Ar_3Bi) from the carbonyl products in cases where their R_f values are similar.

[15] A similar mechanism was proposed by Barton et al. for the Ph_3BiX_2-based oxidation of alcohol.[6c]

[16] J. Matsuo, H. Kitagawa, D. Iida, T. Mukaiyama, *Chem. Lett.* **2001**, 150–151.

[17] Trifluoromethyl carbinols are known to resist oxidation and, at present, only a few methods are available for their conversion into the corresponding trifluoromethyl ketones; see a) R. J. Linderman, D. M. Graves, *J. Org. Chem.* **1989**, *54*, 661–668; b) I. E. Markó, P. R. Giles, M. Tsukazaki, I. Chellé-Regnaut, A. Gautier, S. M. Brown, C. J. Urch, *J. Org. Chem.* **1999**, *64*, 2433–2439; c) V. Kesavan, D. Bonnet-Delpon, J.-P. Bégué, A. Srikanth, S. Chandrasekaran, *Tetrahedron Lett.* **2000**, *41*, 3327–3330.

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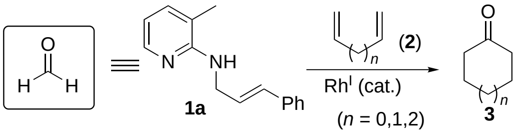
[19] A. Gillmeister, *Chem. Ber.* **1897**, *30*, 2843–2850. In this work, **2a** was prepared by oxidative chlorination of tris(2-methylphenyl)bismuthane with sulfuryl chloride.

Synthesis of Cycloalkanones from Dienes and Allylamines through C–H and C–C Bond Activation Catalyzed by a Rhodium(I) Complex**

Dae-Yon Lee, In-Jung Kim, and Chul-Ho Jun*

Among numerous examples of transition-metal-mediated cyclization to obtain medium-sized ring compounds,[1] intramolecular hydroacylation provides the most promising way to prepare cyclopentanones from 4-pentenal through the C–H-bond activation of an aldehyde.[2,3] However, its application has been limited to the synthesis of five-membered rings with a few exceptions,[3] because the competing decarbonylation of the acyl metal hydride intermediate prevails during the formation of the larger ring. In the course of our studies into chelation-assisted C–H- and C–C-bond activation,[4] allylic amine **1a**, which bears a coordination site, was devised and used as a masked form of formaldehyde in the hydroacylation of 1-alkenes to synthesize dialkyl ketones.[4d] We envisaged a cyclization of dienes **2**[5–7] with **1a** to furnish cycloalkanones **3** with various sizes, since decarbonylation cannot occur in the reaction of **1a** (Scheme 1). Herein we present a facile synthesis of various cycloalkanones from the reaction of allylic amines with dienes through chelation-assisted C–H- and C–C-bond activation.



Scheme 1. Formation of cycloalkanone **3** from the reaction of allylamine **1a** and diene **2**.

The reactions of **1a** with various dienes (**2**) are summarized in Table 1. For example, when **1a** was allowed to react with 1,4-pentadiene (**2a**) in the presence of $[\{(C_8H_{14})_2RhCl\}_2]$ (**4**, 5 mol%) and PCy_3 (**5**, 15 mol%) at 150 °C for 2 h, cyclohexanone (**3a**) and 2-methylcyclopentanone (**3b**) were obtained in 87% and 13% yield, respectively, after hydrolysis (Table 1, entry 1). Furthermore, the reaction with 1,5-hexadiene (**2b**) provided cycloheptanone (**3c**), 2-methylcyclohexanone (**3d**), and 2-ethylcyclopentanone (**3e**) in a ratio of 38:40:22 (Table 1, entry 2).[8]

The mechanism for this reaction is depicted in Scheme 2. Aldimine **6a** is generated by Rh-catalyzed isomerization of **1a**. Subsequent intermolecular hydroiminoacylation[9] of **2b**

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