### COMMUNICATION

# Synthesis of Alkylbismuths by Regiodivergent Carbobismuthination of Simple Alkenes

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Organobismuth compounds have recently attracted much attention because they show remarkably characteristic reactivities including highly effective initiation of living radical polymerization,<sup>[1]</sup> para C-H activation of phenol derivatives,<sup>[2]</sup> direct allyl transfer to carbonyls,<sup>[1c]</sup>  $\alpha$ -phenylation of carbonyls,<sup>[3]</sup> and other traditional reactions such as crosscoupling and addition reactions to carbonyl compounds.<sup>[4]</sup> However, most of the practical syntheses of organobismuths involve transmetalation between a bismuth halide and an organometallic compound, which has limited the number of compatible functional groups and constricted the development of organobismuth chemistry.<sup>[4]</sup> Therefore, a new method for the synthesis of organobismuth reagents is highly desirable. Of the options, the carbobismuthination of alkenes represents a powerful tool for the synthesis of alkylbismuth compounds because carbon-carbon and carbon-bismuth bonds can be simultaneously formed to easily give a complex alkylbismuth, but this has never been reported.<sup>[5]</sup> Recently, our group studied regio- and stereoselective carbometalation by activation of the carbon-carbon multiple bond by a metal halide toward external nucleophilic attack, in which the separate introduction of a carbon nucleophile and a metal into the carbon-carbon unsaturated bond in an anti-addition manner.<sup>[6]</sup> In this reaction system, carbometalation is caused simply by mixing a metal salt, a carbon nucleophile, and an unsaturated hydrocarbon without the preparation of organometallic nucleophiles in contrast to general carbometalation. Under this concept, we wish to report a novel synthetic method for alkylbismuths by the carbobismuthination of alkenes that directly utilizes bismuth trihalides and ketene silyl acetals. The present carbobismuthination is not only remarkable as a synthetic method of alkylmetals with an ester moiety,<sup>[6b,7]</sup> but also has the notable feature whereby a change in the type of halogen on the bismuth atom switches the regioselectivity, which differs from our previously reported version of the carbometalation.<sup>[6d]</sup> Until now, it has been difficult to realize an efficient switchable regioselectivity in the carbometalation of one alkene,

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although many highly regioselective reactions have been developed.<sup>[8]</sup> As far as we could ascertain, this is the first example in which the regioselectivity has been switched by the counter anion on a metal in the carbometalation of an alkene (Figure 1).



Figure 1. Switchable-regioselective carbobismuthination of alkenes.

First, we examined the reaction between styrene (1a, 1 mmol),  $BiBr_3$  (1.5 mmol), and dimethylketene *tert*-butyldimethylsilyl methyl acetal (2a, 1.5 mmol; Scheme 1). After this reaction was carried out in  $CH_2Cl_2$  (1 mL) at room tem-



Scheme 1. Carbobismuthination of styrene (1a) using BiBr<sub>3</sub> and ketene silyl acetal 2a. 1a (1 mmol), BiBr<sub>3</sub> (1.5 mmol), 2a (1.5 mmol),  $CH_2Cl_2$  (1 mL).

perature, treatment with 30 wt % HBr of a CH<sub>3</sub>COOH solution gave the corresponding  $\alpha$ -alkylated esters **5aa** and **6aa** in 77 and 5% yields, respectively. This result indicated that carbobismuthination among **1a**, BiBr<sub>3</sub>, and **2a** mainly afforded alkylbismuth **3** along with a small amount of **4**. Performing the reaction in the dark exclusively gave **5aa** in 94% yield. X-ray crystallographic analysis successively revealed the structure of **3**; the bismuth atom was bound to the external carbon of the double bond in **1a**, and the nucle-

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ophilic carbon of 2a was bound to the internal one (Figure 2a). The dimer of 3 was formed by a bromine bridge, as shown in Figure 2b. The geometry around the bismuth atom in 3 was a distorted square-pyramidal, and three bromines and a carbonyl oxygen formed a square plane. In <sup>1</sup>H and



Figure 2. X-ray crystallographic analysis and selected chemical shift of  $^1\!H$  and  $^{13}\!C$  NMR of alkylbismuth dibromide 3.

<sup>13</sup>C NMR spectra of **3**, signals of  $\alpha$ - and  $\beta$ -protons, and the  $\alpha$ -carbon of the bismuth atom are significantly downfield shifted due to electron-withdrawing ability of BiBr<sub>2</sub> group.<sup>[9]</sup>

Various types of alkenes and ketene silyl acetals were investigated in the carbobismuthination using BiBr<sub>3</sub> (Table 1). Trimethylsilyl ketene acetal 2b as well as 2a were found to afford the desired product 5aa in 86% yield (Table 1, entry 1). Dialkylketene silyl acetals 2c and d were applicable to give the corresponding ester products in high yields (Table 1, entries 2 and 3). The reaction using phenylmethylketene silyl acetal 2e also afforded ester 5ae (Table 1, entry 4). Carbobismuthination using monoalkylketene silyl acetal 2f smoothly took place (Table 1, entry 5). Optimized conditions were employed with aromatic alkenes bearing electron-donating and -withdrawing groups, giving the desired products 5ba, ca, and da in 99, 92 and 76% yields, respectively (Table 1, entries 6-8). In particular, the reaction of *p*-methoxystyrene (1b) gave an excellent yield in a shorter time. Aliphatic alkene 1e was applicable and afforded good results (Table 1, entry 9). This carbobismuthination was extended to a 1,1-disubstituted alkene, producing the desired ester 5 fb in the reaction using alkene 1f (Table 1, entry 10). Unfortunately, other types of multi-substituted alkenes such as stilbene and cyclohexene were not applicable.

Next, we examined the oxidative transformation of alkylbismuth **3** (Scheme 2). *N*bromosuccinimide (NBS) smoothly transformed alkylbismuth **3** to  $\gamma$ -bromo ester **7aa** in a one-pot manner. The treatment of **3** with diphenyl disulfide in the presence of azobisisobutyronitrile (AIBN) gave  $\gamma$ -phenylthio ester **8aa** in 74% yield.<sup>[6d,10]</sup>

After the investigation of various bismuth(III) salts, the use of  $BiCl_3$  inverted the regioselectivity, affording only the corresponding ester **6ab** in 47% yield [Eq. (1)].



It is noteworthy that UV irradiation increased the yield of **6ab** to 71% in the presence of  $BiCl_3$ . In contrast, performing the reaction in the dark retarded the reaction. These re-



[a] (1) **1** (1 equiv),  $BiBr_3$  (1.5 equiv), **2** (1.5 equiv),  $CH_2Cl_2$ , RT. (2) 30 wt % HBr in AcOH (1 mL). [b] Yields were determined by <sup>1</sup>H NMR analysis using an internal standard. Values in parentheses are isolated yields. [c]  $BiBr_3$  (1 equiv).



Scheme 2. Transformation of alkylbismuth **3**. [a] NBS (2.5 equiv), THF, 0°C to RT. [b] PhSSPh (4.5 equiv), AIBN (2 equiv), DMF, 100 °C.

sults suggested that UV irradiation accelerates the carbobismuthination using BiCl<sub>3</sub>. Radical initiators such as AIBN and Et<sub>3</sub>B were ineffective.<sup>[11]</sup> Radical scavenger, 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) did not stop the carbobismuthination.<sup>[11]</sup> Other bismuth(III) salts such as BiI<sub>3</sub> and  $Bi(OTf)_3$  were ineffective and gave no product (Tf=triflate).<sup>[10]</sup> The structure of alkylbismuth product 9 from the reaction of styrene (1a) with diethylketene ethyl trimethylsilyl acetal (2c) was revealed by X-ray crystallographic analysis, and clearly showed a regioselectivity that was opposite to carbobismuthination using BiBr<sub>3</sub> (Scheme 3). Like alkyl-(dibromo)bismuth 3, alkylbismuth 9 dimerized through a chloride bridge, and a distorted square-pyramidal. In <sup>1</sup>H and <sup>13</sup>C NMR spectra, 9 showed considerable downfield shifts of  $\alpha$ - and  $\beta$ -protons, and the  $\alpha$ -carbon of the bismuth atom as in the case of alkylbismuth 3.

Table 2 shows the scope of carbobismuthination using BiCl<sub>3</sub>. Various types of dialkylketene silyl acetals 2c, g, and h smoothly gave the corresponding esters 6ac, ag, and ah, respectively (Table 2, entries 1–3). Aromatic alkenes pos-

CI

9

3.82 ppm (<sup>1</sup>H NMR)

Ph

CI

106.4 ppm (<sup>13</sup>C NMR)

(<sup>1</sup>H NMR)

Et OEt

6.78 and 5.81 ppm



Diagram of 9

sessing electron-withdrawing and -donating groups were suitable substrates (Table 2, entries 4–6). A phthalimide moiety tolerated these conditions (Table 2, entry 7). However, aliphatic alkenes, such as 1-hexene, were unsuitable for

After the investigation of the oxidative transformation of

an alkyl(dichloro)bismuth, PhI(OAc)<sub>2</sub> as an oxidant in the presence of Me<sub>3</sub>SiOAc was found to transform alkylbismuth **9** to  $\gamma$ -acetoxy ester **10ac** in a one-pot procedure [Eq. (2)].



To gain insight into the carbobismuthination process, we determined the relative configuration of the deuterated carbon center of the alkylbismuth product given by the reaction using monodeuterated styrene **1a**-*d*. In the carbobismuthination using BiBr<sub>3</sub>, the corresponding alkylbismuth **3**-*d* was obtained stereoselectively, which indicated that the addition of BiBr<sub>3</sub> and **2a** to **1a**-*d* occurred stereoselectively in an *anti*-fashion [Eq. (3)]. BiCl<sub>3</sub>, however, showed no stereoselectivity [Eq. (4)].



Control experiments using isolated  $\alpha$ -bismuthino esters **11** were performed. We previously reported that the transmetalation between a bismuth trihalide and a ketene silyl acetal occurred to afford an  $\alpha$ -dihalobismuthino ester and a silyl halide at room temperature: 1) The transmetalation between BiBr<sub>3</sub> and **2b** was in equilibrium [Eq. (5)], and 2) the transmetalation between BiCl<sub>3</sub> and **2b** took place completely [Eq. (6)]. Isolated  $\alpha$ -dibromobismuthino ester **11a** did not

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BiCl<sub>3</sub>

Ph

1a

**OTMS** 

CI1

Bi

Ėt 2c

OEt

 $CH_2CI_2$ 

UV, 2 h

CI2

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this reaction system.

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Table 2. Scope of alkene 1 and ketene silyl acetal 2 in carbobismuthination using  ${\rm BiCl}_{3^{\rm , [a]}}$ 



[a] (1) **1** (1 mmol), BiBr<sub>3</sub> (1.5 mmol), **2** (1.5 mmol), CH<sub>2</sub>Cl<sub>2</sub> (2 mL), RT, 2 h. UV = 300 W high-pressure mercury lamp. (2) 30 wt % HBr in AcOH (1 mL). [b] Yields were determined by <sup>1</sup>H NMR analysis using an internal standard. Values in parentheses are isolated yields.

react with styrene (1a), even in the presence of equimolar amounts of BiBr<sub>3</sub> [Eq. (7)]. The addition of Me<sub>3</sub>SiBr (TMSBr) promoted the carbobismuthination to furnish the corresponding ester **5aa** in 41% yield. This result indicated that  $\alpha$ -dibromobismuthino ester **11a** is unreactive and that BiBr<sub>3</sub> and **2** generated by the transmetalation between **11a** and Me<sub>3</sub>SiBr caused the carbobismuthination. It is noteworthy that the reaction of isolated  $\alpha$ -dichlorobismuthino ester **11b** with styrene (1a) under UV irradiation occurred in the absence of additives, which indicated that **11b** is an active intermediate in contrast to **11a** [Eq. (8)].

$$BiBr_{3} + \underbrace{\bigcirc}_{OMe} \underbrace{\bigcirc}_{CH_{2}Cl_{2}} \\ 2b \\ RT \\ 11a \\ 0Me \\ 10Me \\ 10M$$

$$BiCl_3 + \underbrace{\bigcirc}_{\mathbf{2b}}^{OTMS} \xrightarrow{CH_2Cl_2, RT} Cl_2Bi \underbrace{\bigcirc}_{\mathbf{0Me}}^{O} + TMSCI \quad (6)$$

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A plausible reaction mechanism is illustrated in Scheme 4. Path A shows the carbobismuthination using  $BiBr_3$ . The coordination of alkene 1 to  $BiBr_3$ causes a positive charge at the internal carbon of the double bond, which is stabilized by an  $R^1$ group.<sup>[12]</sup> Then, the nucleophilic attack of ketene silyl acetal 2 occurs at the internal carbon atom from the opposite side of BiBr<sub>3</sub>, and then alkylbismuth product 12 and Me<sub>3</sub>SiBr are generated. In the carbobismuthination using BiCl<sub>3</sub>, the fast transmetalation irreversibly occurs and the resultant  $\alpha$ bismuthino ester 11 is likely to be a reaction species (Path B). Single-electron transfer from UV irradiation-excited alkene 1\* to bismuthino ester 11 generates radical cation 13 and anion 14. The enolate anion derived from radical anion 14 nucleophilically adds to radical cation 13 to produce 15. Finally, the BiCl<sub>2</sub> radical couples with radical 15, affording alkylbismuth 16. The effect of UV irradiation and no effect of both radical initiator and scavenger support this reaction mechanism although other radical mechanism cannot be excluded in this stage. The following factors would determine the reaction path: 1) A soft Lewis acid, BiBr<sub>3</sub>, sufficiently interacts with an alkene moiety to generate a positive charge; and, 2) A hard Lewis acid, BiCl<sub>3</sub>, does not sufficiently interact with an alkene, and so after transmetalation the reaction of the  $\alpha$ -bismuthino ester **11** with alkene 1 takes place by UV irradiation.<sup>[13]</sup>

In summary, we accomplished the first carbobismuthination of alkenes by bismuth trihalides and ketene silyl acetals in which the regioselectivity





was inverted by changing  $BiBr_3$  to  $BiCl_3$  to furnish two types of alkylbismuth compounds possessing an ester moiety. In addition, we found that the X<sub>2</sub>Bi groups in the resultant alkylbismuths could be substituted for by H, Br, SPh, and OAc groups. Applications to other nucleophiles are currently being tested.

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Scheme 4. Plausible reaction mechanisms.

#### **Experimental Section**

Typical procedure for carbobismuthination using BiBr<sub>3</sub> followed by protonolysis (Table 1, Entry 4) To a suspension of BiBr<sub>3</sub> (0.75 mmol, 0.337 g) and methylphenylketene methyl trimethylsilyl acetal (**2e**; 0.76 mmol, 0.180 g) in dichloromethane (2 mL) was added styrene (**1a**; 0.51 mmol, 0.053 g). The mixture was stirred for 4 h at room temperature in a dark. Then, 30 wt% HBr in CH<sub>3</sub>COOH (1 mL) was added, and the mixture was stirred at room temperature for 30 min. The reaction was then quenched with NaHCO<sub>3</sub> (10 mL) and extracted with diethyl ether (3× 15 mL). The combined organic layers were dried over MgSO<sub>4</sub>. The evaporation of the volatiles gave the crude product which was analyzed by <sup>1</sup>H NMR. Further purification was carried out by column chromatography and distillation with glass tube oven under reduced pressure to give the product **3ae** (0.13 g, d.r. 1.2:1, 55%).

Typical procedure for carbobismuthination using BiCl<sub>3</sub> followed by plotonolysis (Table 2, Entry 1) To a suspension of BiCl<sub>3</sub> (0.74 mmol, 0.234 g) and diethylketene ethyl trimethylsilyl acetal (2c; 0.74 mmol, 0.160 g) in dichloromethane (1 mL) was added styrene (1a; 0.53 mmol, 0.0553 g). The mixture was stirred and was irradiated with ultraviolet (300 W high-pressure mercury lamp). for 2 h at room temperature. Then, 30 wt % HBr in CH<sub>3</sub>COOH (1 mL) was added, and the mixture was stirred at room temperature for 30 min. The reaction was then quenched with NaHCO<sub>3</sub> (10 mL) and extracted with diethyl ether ( $3 \times 15$  mL). The organic layer was dried over MgSO<sub>4</sub>. The evaporation of the volatiles gave the crude product which was analyzed by <sup>1</sup>H NMR spectroscopy. Further purification was carried out by column chromatography and distillation with glass tube oven under reduced pressure to give the product **6ac** (0.061 g, 46%).

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