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Bi(III) carboxylates as efficient reagents for preparation of esters under mild conditions. A new method for the protection of carboxylic acids

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Abstract—Bi(III) carboxylates have been obtained by reaction of triphenylbismuth with various monocarboxylic acids. By a ligand-exchange reaction, these Bi(III) carboxylates react with tertiary or benzylic-type bromides and afford esters. This reaction sequence constitutes a new efficient way for the temporary protection of carboxylic acids under mild conditions. © 2001 Elsevier Science Ltd. All rights reserved.

In a series of preliminary studies, we have established the general usefulness of bismuth(III) reagents for the halogenation of alcohols,[1] the halogen exchange reactions[2] and the protection of aliphatic alcohols as benzyl ethers.[3] More recently, we showed that the behaviour of bismuth(III) halides (BiX_3; X = Cl, Br and I) is totally different according to the nature of the halide bonded to the bismuth atom[4] and proposed a mechanism to explain such behaviour. We noted that bismuth(III) derivatives acting as reagent, react according to a general ligand-exchange mechanism. Their reactivities agree with the Hard and Soft Acids and Bases (HSAB) Pearson's principle. Referring to the bismuth atom, ligand exchange occurs if the entering group is a softer base than the leaving one (Scheme 1).

On this basis we thought that it would be possible to achieve ligand exchange between a bismuth carboxylate and an alkyl bromide, as the bromide ion is a softer base than carboxylate,[5] the result being an ester (Scheme 2).

$$3\ \mathrm{R\text{-}Y} + \mathrm{BiX_3} \longrightarrow 3\ \mathrm{R\text{-}X} + \mathrm{BiY_3}$$

$$\text{Y}^- \text{ being a softer base than X}^-$$

Scheme 1.

To check this new way to access ester function, we first prepared bismuth(III) acetate and benzoate by reacting the commercially available triphenylbismuth with the corresponding carboxylic acid (Scheme 3). This exchange reaction took advantage of the very weak phenyl/bismuth bond which has one of the weakest aryl/element bond energies[6] and was achieved in good yield.[7] This reaction is all the easier as carboxylates are softer bases than phenyl anion. Only a stoichiometric amount of the carboxylic acid was required. Moreover, the by-product of the reaction was the volatile benzene.

Both bismuth acetate and benzoate were in turn reacted with a series of bromides in CCl_4 to promote exchange reaction under stoichiometric conditions (Scheme 2). This reaction was easy to monitor because the colour of the solid changed from white [$Bi(OCOCH_3)_3$ or $Bi(OCOC_6H_5)_3$] to yellow [like $BiBr_3$]. That colour

$$3\ \mathrm{R\text{-}Br} + \mathrm{Bi(OCOR')_3} \longrightarrow 3\ \mathrm{R'COOR} + \mathrm{BiBr_3}$$

Scheme 2.

$$3\ \mathrm{R'COOH} + \mathrm{Bi(C_6H_5)_3} \longrightarrow \mathrm{Bi(OCOR')_3} + \mathrm{C_6H_6}$$

Scheme 3.

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change proved that the ligand exchange reaction occurred. Table 1 summarises the results obtained.

The data reported in Table 1 call for the following comments:

(i) The primary bromides, 1-bromohexane and 1-bromooctane, did not react whatever the bismuth carboxylate. This agrees with results previously reported[2] dealing with the reaction involving bismuth(III) halides as a reagent. Therefore, this method is not applicable for the synthesis of esters of primary alcohols.

(ii) Secondary bromides afforded alkene formation simultaneously with the expected acetate or benzoate. The aliphatic 2-bromopentane led to ester as major product (75%). On the contrary, with cyclohexyl bromide, the alkene was the major product (70%).

(iii) Tertiary and benzylic bromides appeared to be the most reactive substrates, yielding exclusively the corresponding esters. Except for benzene, no other by-product was detected. Thus, bismuth(III) carboxylates acted as a reagent. It is worthwhile to remark that these two groups (*tert*-butyl and benzyl) are also common protecting groups for carboxylic acids.

Thus, it appears that carboxylic acids can be easily converted to their *tert*-butyl or benzyl esters via their reaction with triphenylbismuth, followed by *tert*-butyl or benzyl bromides.

The fact that primary bromides are unreactive affords an interesting functional group selectivity. Indeed, a specific exchange could be expected with primary/tertiary dibromides as previously observed for halogen exchange of alkyl halides in the presence of BiX_3.[2]

We have applied the same approach to prepare tosylates from bromides according to Scheme 4. Bismuth(III) tosylate was first obtained following the above described procedure.[7] Because of its high reactivity, *tert*-butyl bromide was then added.

The white solid [$Bi(OTs)_3$] became yellow [like $BiBr_3$] and the bromide disappeared within a few minutes from the liquid phase. Both observations agree with an exchange reaction between the bromide and tosylate groups. However, we did not detect any product in the organic phase. Moreover, during the reaction, the volume of the solid increased.

Recently,[4] we have shown that Bi(III) (a soft Lewis acid) can form intermediate complexes possessing several coordination-type around the bismuth atom. Besides, an example of intramolecular coordination of a sulfonyl group with a bismuth atom has previously been described.[8] So we suspected that when the tosylate (TsOtBu) was formed, it would give a complex with the Lewis acid $BiBr_3$ produced during the reaction. That could explain the swelling of the solid and the absence of the expected tosylate in the organic phase. To verify that point, we ran the following experiment: 3-tosylpentane and $BiBr_3$ in a 3:1 molar ratio were refluxed in CCl_4 for 1 h. We observed that the volume of the solid rapidly increased. At the same time, 3-tosylpentane disappeared from the solution while no other product was detected. This observation would seem to agree with our former assumption.

In conclusion, this study confirms that bismuth, acting as a reagent, reacts according to a general ligand-exchange mechanism in agreement with the HSAB principle.

Our procedure based on the use of bismuth(III) carboxylates in the presence of bromides provides a new simple, efficient and useful alternative for the preparation of tertiary and benzyl-type esters from bromides. Our results offer the possibility of using this method to protect carboxylic acids as *tert*-butyl, benzyl or 1-phenylethyl esters, which are largely used since they can

Table 1. Reaction of Bi(III) acetate and benzoate with various bromide derivatives in CCl_4[a]

RBr	T°C	Reaction times	Products with $Bi(OAc)_3$[b]	Products with $Bi(OBz)_3$
1-Bromohexane	Reflux	10 days	No reaction	No reaction
1-Bromooctane	Reflux	12 days	No reaction	No reaction
2-Bromopentane	Reflux	45 h	75% 2-Pentyl acetate+25% 2-pentene	75% 2-Pentyl benzoate+25% 2-pentene
Cyclohexyl bromide	Reflux	48 h	30% Cyclohexyl acetate+70% cyclohexene	30% Cyclohexyl benzoate+70% cyclohexene
tert-Butyl bromide	25°C	1 h	*tert*-Butyl acetate (100%)	*tert*-Butyl benzoate (100%)
Benzyl bromide	25°C	2 h	Benzyl acetate (100%)	Benzyl benzoate (100%)
1-Phenylethyl bromide	25°C	1 h	1-Phenylethyl acetate (100%)	1-Phenylethyl benzoate (100%)

[a] $Bi(OCOC_6H_5)_3$ or $Bi(OCOCH_3)_3$ (1.25 mmol) in CCl_4 (5 ml) at room temperature or at reflux was stirred vigorously (1200 rpm). To this stirred suspension, bromide derivative (R′Br, 3.75 mmol) was added and the stirring was continued. The reaction was followed by GC analysis of the liquid phase until complete bromide consumption. The mixture was filtered and the solvent evaporated under reduced pressure to provide the product (yield range 90–96%). The products were analysed by GC, ^1H NMR and their spectral data compared with those of authentic samples.

[b] Identical results were obtained with commercially available $Bi(OAc)_3$.

$$Bi(C_6H_5)_3 + 3\ TsOH \longrightarrow Bi(OTs)_3 \xrightarrow{3\ R\text{-}Br} R\text{-}OTs + BiBr_3$$

Scheme 4.

be easily removed.[9] The advantages of this procedure are mainly the mild conditions, easy work-up, good yields and short reaction times.

We are presently exploring the scope of this new reaction.

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7. **Preparation of bismuth(III) carboxylate**: In a 10 ml flask, triphenylbismuth (1.25 mmol) was dissolved in anhydrous CCl_4 (5 ml) under vigorous stirring (1200 rpm) at reflux. Then, benzoic or acetic acid (3.75 mmol) was introduced. The reaction was monitored by TLC. After 16 hours, the white solid formed was filtered and dried under reduced pressure (89% yield). The products were analysed by ^1H NMR and the data are consistent with its assigned structure. Furthermore, mass spectroscopy (FAB+) showed the characteristic signals of such products (e.g. *m*/*z* for $Bi(OCOC_6H_5)_3$: 473 $[M+H]^+$; 495 $[M+Na]^+$).
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