



Bis(*sym*-collidine)bromine(I) hexafluorophosphate as oxidant

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Abstract

Primary and secondary alcohols in solution in methylene chloride are oxidised with bis(*sym*-collidine)bromine(I) hexafluorophosphate in good yields to the carbonyl compounds. For secondary and tertiary alcohols in which one of the substituents is a 4-methoxyphenyl group the oxidation takes place by cleavage of the phenyl-*sp*³ carbon bond and formation of bromoanisole and carbonyl compounds.
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The search for non-metallic oxidation reagents is still a major goal in chemical synthesis. Numerous compounds have already been used such as the Dess–Martin periodinane.¹ However, in this field, the best known oxidation method is still the utilisation of dimethylsulfoxide in the presence of catalysts, such as the Moffatt and Swern oxidations. Among all these methods, the reactivity of positive halogen reagents such as sodium or calcium hypochlorite or NBS has been examined.¹ We can also cite bis(quinuclidine)bromine(I) reagents² used in the presence of additives.

During our studies concerning the reactivity of bis(collidine)bromine(I) hexafluorophosphate (BBH),³ we observed that this reagent could act as an oxidant. The simplicity of the reaction conditions used with BBH prompted us to examine this reaction in more detail. These oxidations were conducted in methylene chloride at room temperature in the presence of 1.7 equivalents of BBH.⁴ Our results are reported in Table 1. The reactions were monitored by TLC. The yields were calculated after purification of the products by liquid chromatography on silica gel. The structure of the products were determined in general by comparison with authentic samples and confirmed from their spectral data. With the exceptions of tetrahydropyran-2-

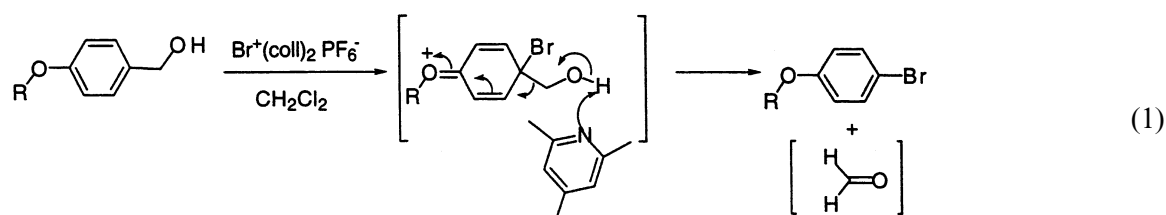
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Table 1
Oxidation of alcohols with BBH

Entry	Alcohol	Reaction time (h)	Products	(Yield, %)
a	R = H	2.5		(75)
b	R = Cl	2.5		(86)
c	R = NO ₂	3		(70)
d	R = OMe	3		(70) ^a
e	R = OCH ₂ Ph	2		(85) ^a
f		0.5		(96)
g		5		(95) ^b
h		10		(75)
i		5		(93)
j		24		(82)
k		2.5		(97)
l		48		(96)
m		4		(91)
n		15		(84)
o		12		(83)
p		48	N.R.	-

^a Acetaldehyde was not isolated. ^b Reaction conducted in the presence of 2.5 equiv. of BBH.

methanol (entry p) and the 4-alkoxybenzylalcohols (entries d and e), the carbonyl compounds were obtained in high yields. The fact that tetrahydropyran-2-methanol did not react is probably due to its higher oxidation potential compared with the other alcohols studied. With 4-alkoxybenzylalcohols we observed the formation of 4-alkoxy-1-bromobenzene. These latter reactions implied the cleavage of a C–C bond and formation of acetaldehyde, probably by the mechanism reported in Eq. (1). This cleavage was not observed when the benzylalcohol was substituted in the *ortho* position by an alkoxy group (entry g). In this case, bromination in the *para* position to the methoxy group was easier (entry f) than the oxidation of the primary alcohol which occurred only when an excess of BBH was used (entry g). Competition between oxidation of the benzyl alcohol and its cleavage was observed in one case (entry h). Except for these particular cases, BBH appears to be a good reagent for oxidising primary and secondary alcohols into carbonyl compounds.⁵



Even if there are some reports in the literature concerning the cleavage of benzyl alcohols using reagents which generate F^+ ,⁶ Cl^+ ,⁷ or Br^+ ,⁸ this reaction was not studied as a method to prepare carbonyl compounds. Reaction of 4-methoxybenzyl alcohols with BBH at room temperature led cleanly to a mixture of bromoanisole and carbonyl compounds.⁹ The products were purified by liquid chromatography over silica gel, and identified from their spectral data.¹⁰ Our results are reported in Table 2. This reaction occurred with secondary and tertiary alcohols leading to aldehydes and ketones, respectively. Bromoetherification was observed (entry e) when the alcohol was unsaturated. 6-Methoxy-1-tetralols (entries f and g) furnished interesting intermediates by a very simple method. 5-Methoxy-1-indanol only formed a mixture of unidentified products under the same conditions.

In conclusion, we have shown that bis(collidine)bromine(I) hexafluorophosphate is an interesting reagent for the oxidation of alcohols. It also allows the transformation of 4-methoxybenzylalcohols into carbonyl compounds. Since these alcohols can be prepared from 4-bromoanisole, this could also be a new method for protecting carbonyl compounds (Eq. (2)).

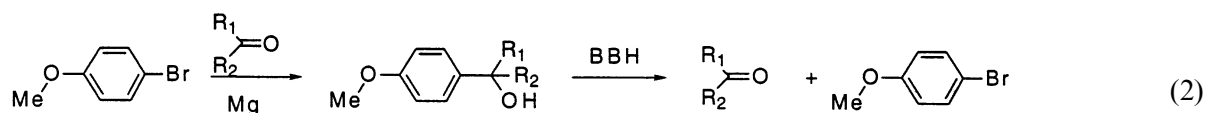


Table 2
Reaction of 4-methoxybenzylalcohols with BBH

entry	alcohol	product	(yield, %)
a		$C_8H_{17}-CHO$	(60) ^a
b		$C_8H_{17}-C(=O)Me$	(91) ^a
c			(60) ^a
d			(83) ^a
e			(79) ^b
f			(67)
g			(86)

^a 4-bromoanisole was also isolated (80-95%). ^b mixture (70-30) of two diastereoisomers.

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- Representative procedure:** To a solution of alcohol (2 mmol) in methylene chloride (20 mL) was added bis(collidine)bromine(I) hexafluorophosphate^{3c} (3.4 mmol, 1.64 g). After reaction of the alcohol (TLC) the solvent was removed and the residue purified by chromatography over silica gel (hexanes/ether).
- This reaction can be written as follows:
 $alcohol + Br^+(collidine)_2PF_6^- \rightarrow carbonyl\ compound + H-(collidine)^+Br^- + H-(collidine)^+PF_6^-$
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9. **Representative procedure:** To a solution of alcohol (2 mmol) in methylene chloride (10 mL) was added over 1 h a methylene chloride solution (10 mL) of bis(collidine)bromine(I) hexafluorophosphate^{3c} (2.4 mmol, 1.16 g). After stirring for 30 min at room temperature, the solvent was removed and the residue purified by chromatography over silica gel (hexanes/ether).
10. **Selected data.** **4-(2-Bromo-5-methoxyphenyl)butanal:** ¹H NMR (250 MHz, CDCl₃): 9.77 (m, 1H); 7.40 (d, *J*=11 Hz, 1H); 6.78 (d, *J*=4 Hz, 1H); 6.65 (dd, *J*=4 and 11 Hz, 1H); 3.80 (s, 3H); 2.75 (dd, *J*=7 and 11 Hz, 2H); 2.51 (dd, *J*=2 and 11 Hz, 2H); 2.00 (m, 2H). ¹³C NMR: 202.0; 158.9; 141.4; 133.3; 116.0; 113.9; 113.3; 55.3; 42.9; 35.3; 22.1. **8-(2-Bromo-5-methoxy-phenyl)octan-5-one:** ¹H NMR (250 MHz, CDCl₃): 7.42 (d, *J*=11 Hz, 1H); 6.78 (d, *J*=5 Hz, 1H); 6.65 (dd, *J*=5 and 11 Hz, 1H); 3.78 (s, 3H); 2.71 (dd, *J*=7 and 11 Hz, 2H); 2.45 (q, *J*=10 Hz, 4H); 1.92 (m, 2H); 1.57 (m, 2H); 1.34 (m, 2H); 0.92 (t, *J*=11 Hz, 3H). ¹³C NMR: 210.6; 158.8; 141.8; 133.0; 115.8; 114.7; 113.1; 55.2; 42.3; 41.6; 35.3; 25.7; 23.7; 22.2; 13.7.