



## Ferric Chloride: An Excellent Reagent for the Removal of Benzyl Ethers in the Presence of *p*-Bromobenzoate Esters

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**Abstract:** Anhydrous  $\text{FeCl}_3$  in dry  $\text{CH}_2\text{Cl}_2$  removed benzyl ethers from carbohydrates containing *p*-bromobenzoate esters, without hydrogenolysis of the bromine atoms. In addition, debenzylations of  $\beta$ -glycopyranosides occurred with simultaneous anomerization or retention of the anomeric configuration.

*p*-Bromobenzoate esters are suitable derivatives for stereochemical studies. Thus, on the one hand, the *p*-bromobenzoate group is probably the most commonly used chromophore ( $\lambda_{\text{max}}$  245 nm,  $\epsilon$  18500 in MeCN) for determining the absolute configurations and conformations of organic compounds by the circular dichroic exciton chirality method,<sup>1</sup> due to its excellent electronic properties ( $\lambda_{\text{max}}$ ,  $\epsilon$  value, and polarization). On the other hand, it is known, since the first successful experiment described by Bijvoet and co-workers,<sup>2</sup> that the presence in a molecule of an anomalous scatterer, such as the bromine atom, is important for determining absolute configurations by X-ray diffraction.

The facile cleavage of the benzyl oxygen bond has made the benzyl group a useful protecting group during multistep syntheses, several methods being available for this purpose.<sup>3</sup> In connection with our stereochemical studies, where both benzyl and *p*-bromobenzoyl groups are used to prepare model glycopyranosides, cleavage of alcohol-protecting benzyl groups under a variety of methods led in all cases to the simultaneous hydrogenolysis of the bromine atoms ( $\lambda_{\text{max}}$  230 nm).

The utilization of ferric chloride in  $\text{CH}_2\text{Cl}_2$  at room temperature is a suitable method to achieve selective debenzylations in carbohydrates,<sup>4</sup> as well as to anomerize  $\beta$ -glycopyranosides to their corresponding  $\alpha$ -anomers.<sup>5</sup>

We wish to report herein that the afore-mentioned method was highly suitable to achieve selective debenzylations without affecting the *p*-bromobenzoate esters. In addition, higher yields and retention of the anomeric configuration were achieved by lowering the temperature and using 3.0 equiv of  $\text{FeCl}_3$  per benzyl ether group.

These results can be observed in Table 1.<sup>6</sup> All model compounds led to the corresponding debenzylated compound, in moderate to excellent yields, without undergoing simultaneous hydrogenolysis of the bromine atoms.<sup>7</sup> Debonylation of  $\alpha$ -glycopyranosides was performed in higher yields when 3.0 equiv of  $\text{FeCl}_3$  per benzyl ether group was used (entries 1 and 2) or when the temperature was lowered (entries 8 and 9), entry 7 showing the high stability of the *p*-bromobenzoate group vs  $\text{FeCl}_3$ . In the case of  $\beta$ -glycopyranosides, debonylation occurred with simultaneous anomerization or retention of the anomeric configuration, depending on the reaction conditions. While anomerization was favoured by increasing the equiv of  $\text{FeCl}_3$  (compare entries 3 and 4, and 11 and 12), retention of the anomeric configuration was obtained by lowering the temperature, entries 6 and 11 showing high or complete stereoselectivity, respectively.

Table 1. Debenzylations of benzyl *p*-bromobenzoyl glycopyranosides with simultaneous anomerization or retention of the anomeric configuration.

Entry	Substrate	Product	Equiv	Time (min)	Yield <sup>a</sup> (%)	Ratio <sup>b</sup> α : β	T (°C)
1			3	60	68	100 : 0	25
2			9	30	92	100 : 0	25
3			3.3	45	83	40 : 60	25
4			9	30	92	100 : 0	25
5			9	60	92	40 : 60	0
6			9	60	96	15 : 85	-20
7			9	45	97	90 : 10	25
8 (α)			9	45	56	100 : 0	25
9 (α)			9	60	70	100 : 0	0
10 (β)			9	30	48	30 : 70	25
11 (β)			9	45	76	0 : 100	0
12 (β)			12	60	35	70 : 30	0

△ = *p*-BrBzO<sup>a</sup> Isolated yield (α + β). <sup>b</sup> <sup>1</sup>H NMR ratio.

**General Procedure.** To a stirred solution of the substrate (20 - 70 μmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (20 mL/mmol) at the selected temperature under Ar, anhydrous FeCl<sub>3</sub> was added (see Table), and the reaction left until the color of the reaction mixture changed to brown. The reaction was quenched by addition of water (1 mL) and diluted with CH<sub>2</sub>Cl<sub>2</sub> (25 mL). This mixture was stirred for 1 min and then extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic layers were dried over magnesium sulfate, and the solvent was removed under reduced pressure. This crude reaction mixture was purified by flash silica gel column chromatography (CHCl<sub>3</sub>/MeOH solvent systems).

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- Adequate characterization was obtained for all compounds.
- All reaction products exhibited UV maximum at the wavelength of *p*-bromobenzoate chromophore, λ<sub>max</sub> 245 nm.

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