

# SYNLETT Spotlight 199

## 2,2,2-Trichloroethyl Chloroformate (TrocCl)

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This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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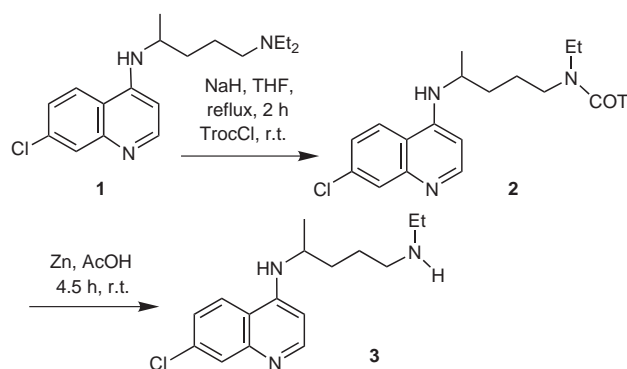
### Introduction

2,2,2-Trichloroethyl chloroformate (TrocCl,  $\text{CCl}_3\text{CH}_2\text{OCOCl}$ , bp 171–172 °C.) is a stable chloroformate which acylates aliphatic and aromatic hydroxyl and amino groups under mild conditions.<sup>1,2</sup> This reagent is commercially available and has been widely used in regio-, chemo-, and stereoselective syntheses. The Troc group shows a sharp and characteristic proton singlet at  $\delta = 4.68\text{--}4.89$  ppm, which makes its presence or absence easily detectable by  $^1\text{H}$  NMR spectroscopy.<sup>3–5</sup> TrocCl has

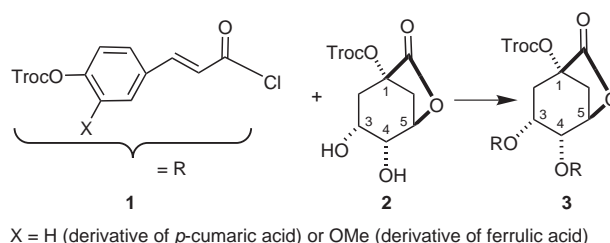
proved to be an excellent reagent for dealkylation of secondary or tertiary amines, with good selectivity, thus producing clean reaction products.<sup>1,3</sup> Moreover, TrocCl is a suitable substrate for Mitsunobu inversion reactions.<sup>6</sup> Recently, the total synthesis of Aprotaxin A with protection and deprotection of an allyl ester intermediate with TrocCl was described.<sup>7</sup> Several methods of Troc removal have been described, leaving a wide variety of other functional groups unaffected.<sup>7,8,10</sup> The following examples highlight the importance and early applicability of this reagent in organic chemistry.

### Abstracts

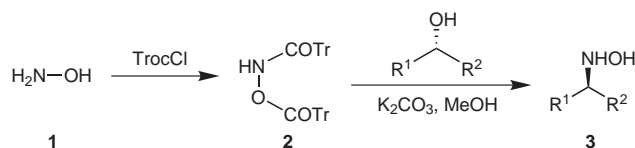
(A) Ansari and Craig<sup>3</sup> have described the use of TrocCl to achieve desethylchloroquine (**3**) in a short, efficient two-step synthesis. In the first step, an internal amide ion from the secondary nitrogen in chloroquine (**1**) is generated, followed by rapid elimination of an ethyl group. The carbamate **2** thus produced easily undergoes deprotection to the target compound at room temperature with zinc in acetic acid.



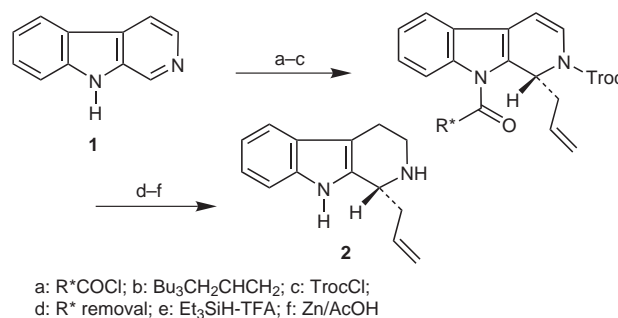
(B) TrocCl selectively acylates the aromatic hydroxyl group of ferrulic and *p*-cumaric acids (**1**). TrocCl is also used to protect the C-1 position of 3,4-isopropylidene-1,5-quinide (**2**) in the preparation of 3,4-disubstituted lactones **3**. It was shown that the use of TrocCl provides for regiospecificity of the esterification and impedes any degradation or isomerization.<sup>4,11</sup>



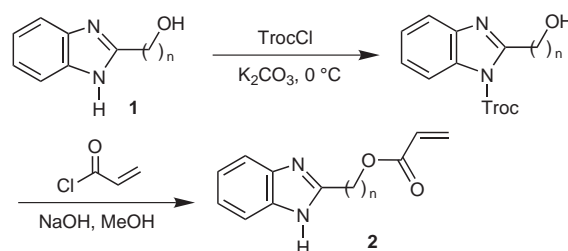
(C) Hydroxylamines **2** that are doubly N,O-protected with Troc are easily obtained from TrocCl and hydroxylamine (**1**). According to Knight and Leese,<sup>6</sup> these intermediates allow ready access to enantiopure hydroxylamines **3** starting from the corresponding secondary alcohols.



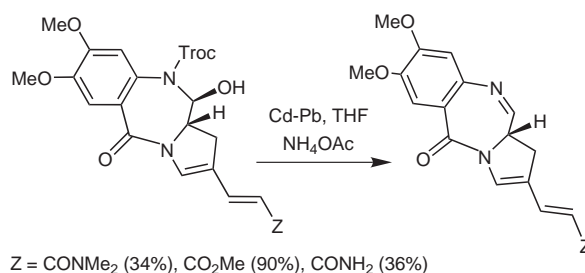
(D) The synthesis of an important chiral alkaloid, 1-allyl-1,2,3,4-tetrahydro- $\beta$ -carboline (**2**), from  $\beta$ -carboline (**1**) and a chiral auxiliary ( $R^*$ ) was successfully achieved when TrocCl was employed to protect the N-2 position.<sup>8</sup>



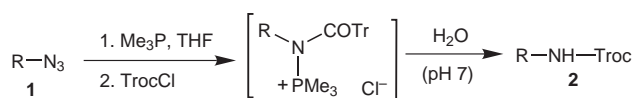
(E) Hydroxyalkylbenzimidazoles **1** with various alkyl chain lengths are selectively acylated with TrocCl in the preparation of benzimidazole functional acrylate monomers **2**.<sup>9</sup>



(F) TrocCl has recently been used in the synthesis of three novel C-2-C-3 unsaturated pyrrolo[2.1-c][1,4]benzodiazepine analogues containing conjugated acrylyl C-2 substituents.<sup>10</sup> According to the authors, this reagent was chosen for its compatibility with both palladium coupling chemistry and pyrrolobenzodiazepine N-10-C-11 imine formation.



(G) Direct conversion of azide **1** to carbamate **2** in high yields (92%) can be achieved via a phosphazene route with TrocCl.<sup>12</sup>



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