

# SYNLETT Spotlight 38

## Titanium Tetrachloride (TiCl<sub>4</sub>)

Compiled by Sariah Sana

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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

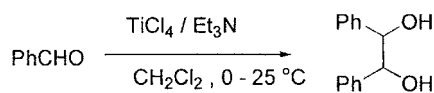
### Introduction

Titanium tetrachloride (TiCl<sub>4</sub>) is one of the most important and typical Lewis acids. Its strong affinity towards oxygenated organic compounds and powerful dehydrating action are manifested in various functional group transformations.<sup>1</sup> TiCl<sub>4</sub> has emerged as an efficient Lewis acid catalyst in organic chemistry. A number of reviews are available on the preparation and reactions of lower valent Ti.<sup>2</sup>

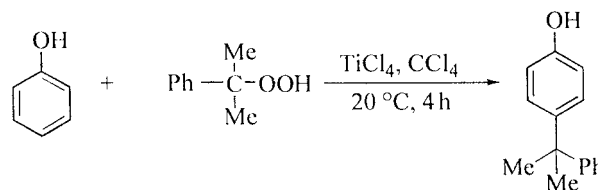
Recently TiCl<sub>4</sub> was efficiently used as a catalyst in various important reactions, which include the enantioselective synthesis of  $\gamma$ -amino acids and  $\gamma$ -lactones,<sup>3</sup> alkylation of carbonyl compounds,<sup>4</sup> pinacol coupling,<sup>5</sup> pyrrolidine synthesis,<sup>6</sup> Claisen rearrangement,<sup>7</sup> oxepene synthesis<sup>8</sup> and asymmetric aldol reaction,<sup>9</sup> etc.

### Abstract

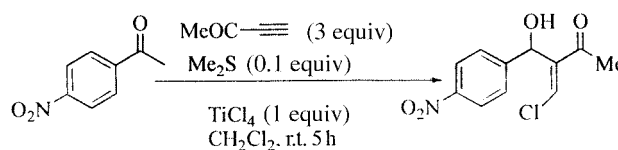
(A) TiCl<sub>4</sub> catalyzed the Pinacol coupling in the presence of triethylamine. During the pinacol coupling reaction aromatic aldehydes and imines are converted into corresponding diols and diamines in good yield. In this reaction low valent titanium species are formed in situ by the reaction of TiCl<sub>4</sub> with triethylamine. This low valent species later on catalyzed the pinacol coupling reaction.<sup>10</sup>



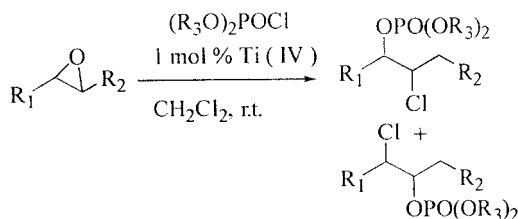
(B) The title reagent efficiently catalyzed the electrophilic alkylation of activated aromatic substrates in the presence of tertiary hydroperoxides. Phenols and phenol ethers are easily alkylated with tertiary hydroperoxides in the presence of a catalytic amount of TiCl<sub>4</sub> in good yield with high regioselectivity.<sup>11</sup>



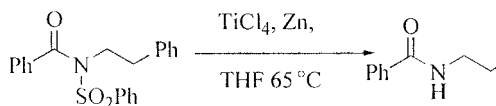
(C) TiCl<sub>4</sub> is used as a Lewis acid in the Baylis–Hilman reaction of  $\alpha$ -halomethylene aldols. Aromatic aldehydes under Chalcogeno–Baylis–Hilman conditions react with acetylenic ketones in the presence of dimethylsulphide and TiCl<sub>4</sub> in dichloromethane at r.t. to afford a halomethylenaldols and  $\beta$ -halo- $\alpha$ -(hydroxyalkyl)-acrylates in fair to good yield.<sup>12</sup>



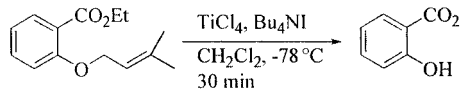
(D) Titanium (IV) reagent catalyzed the ring opening of epoxides by dialkyl halophosphate (formed in situ) under mild condition to give the corresponding vicinal halohydrin phosphate in good yields with high regioselectivity. The small amount of catalyst required and mild experimental conditions make the procedure useful for the synthesis of multifunctional systems.<sup>13</sup>



(E)  $\text{TiCl}_4$  catalyzed the deprotection of *N*-sulfonylated amides.  $\text{Bu}_2\text{Sn}$  and  $\text{SmI}_2$  are also effective in deprotection but yields are improved with  $\text{TiCl}_4$ . The reaction is chemoselective as *N*-benzoyl or acylated amides are selectively deprotected without affecting the *N*-benzoyl or acyl group to give *N*-acylated derivatives in the same reaction conditions.<sup>14</sup>



(F) Treatment of the prenyl ethers of ethyl salicylate with  $\text{TiCl}_4$ - $n\text{Bu}_4\text{NI}$  mixed reagent resulted in cleavage of the C–O bond to provide ethylsalicylate in quantitative yield. It is interesting to note that no cleavage was observed when ethyl-prenyloxybenzoate was used as a substrate. The cleavage reaction of ether proved to be accelerated by the chelating effect of a neighbouring group in the substrates.<sup>15</sup>



## References

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