

# SYNLETT Spotlight 336

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

## 2,2,2-Trifluoroethanol

Compiled by Hartmut Schwertfeger

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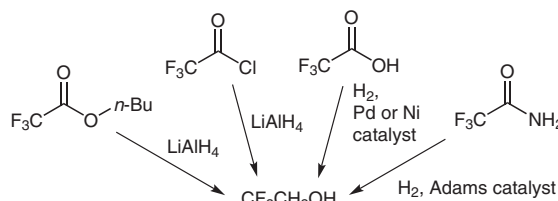
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### Introduction

2,2,2-Trifluoroethanol (TFE) is one of the most common used fluorinated alcohols that is available on large commercial scale. In contrast to its non-fluorinated analogue, TFE has a lower boiling point (74 °C) and is more acidic (pKa 12.4).<sup>1</sup> Due to its low boiling point TFE can easily be removed from reaction mixtures by distillation. TFE can be prepared by reduction of trifluoroacetamide<sup>2</sup> or trifluoroacetic acid<sup>3</sup> with H<sub>2</sub> and various catalysts. Another possibility is the treatment of trifluoroacetyl chloride<sup>4</sup> and *n*-butyl trifluoroacetate<sup>5</sup> using LiAlH<sub>4</sub> (Scheme 1). Owing

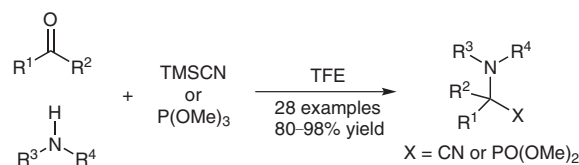
to its unique properties TFE has been used in a variety of reactions as a solvent, cosolvent or additive,<sup>1</sup> but it can also be utilized as a reagent for the introduction of a fluorine moiety.



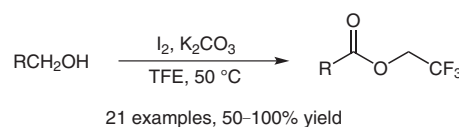
Scheme 1 Preparation of 2,2,2-trifluoroethanol

### Abstracts

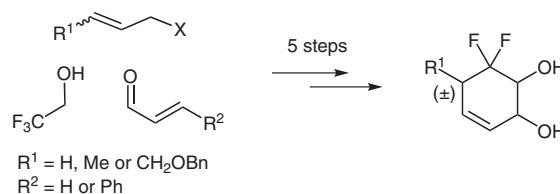
(A) TFE was used as a recyclable solvent for the one-pot, three component coupling of aldehydes or ketones, amines, and trimethylsilyl cyanide or trimethyl phosphite to give  $\alpha$ -amino phosphonates or  $\alpha$ -amino nitriles.<sup>6</sup>



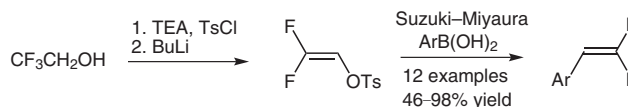
(B) Primary alcohols were converted into their corresponding 2,2,2-trifluoroethyl esters with iodine and K<sub>2</sub>CO<sub>3</sub> in TFE. In this reaction TFE acts as reagent and solvent.<sup>7</sup>



(C) TFE can also be used as a simple starting compound to generate precursors for fluorinated sugar structures. Thereby, TFE is firstly converted into an allyl ether that is further transformed into cyclohexene diols.<sup>8</sup>



(D) The difluorovinylations of arylboronic acids was achieved via the Suzuki–Miyaura cross-coupling. In this reaction, TFE was transferred into the 2,2-difluorovinyl tosylate, which was then utilized as a reagent in the coupling reaction.<sup>9</sup>



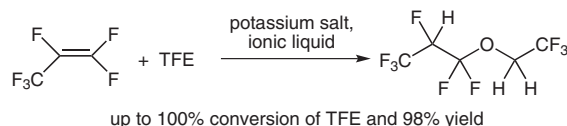
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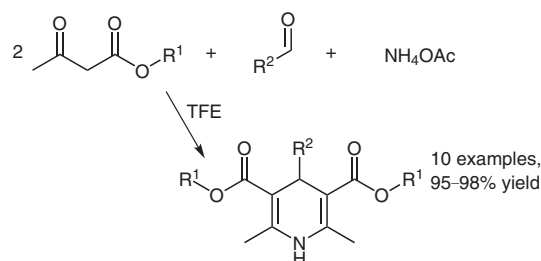
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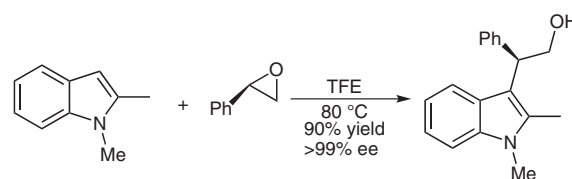
(E) The hydroalkoxylation of hexafluoropropene with TFE in the presence of a catalytic system consisting of a potassium salt and an ionic liquid leads to the formation of  $\text{CF}_3\text{CHF}(\text{CF}_2\text{OCH}_2\text{CF}_3)$ . This compound is one of the third generation chlorofluorocarbons (CFC) alternatives.<sup>10</sup>



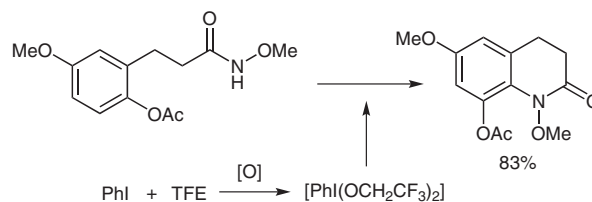
(F) Hantzsch 1,4-dihydropyridines (and also polyhydroquinolines) can be prepared in high yields by utilizing TFE as solvent. After the reaction the solvent is distilled off and can be reused in further reactions.<sup>11</sup>



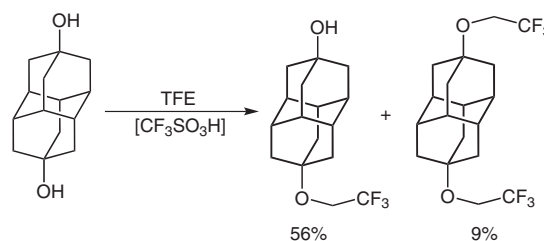
(G) Aliphatic and aromatic epoxides react with indoles and pyrroles in TFE without the use of a catalyst. In this reaction the ring opening is electrophilically assisted by TFE. The examples shown have high stereoselectivities (>99% ee) indicating an  $\text{S}_{\text{N}}2$ -type process.<sup>12</sup>



(H) Quinolinones can be obtained by oxidation of methoxyamides utilizing a hypervalent iodine reagent. This reagent is prepared electrochemically from iodobenzene and TFE.<sup>13</sup>



(I) The monoprotection (desymmetrization) of diamondoid, benzylic, and ethynyl diols has been achieved using TFE under acidic conditions. The obtained diamondoid monoethers can further be converted into unequally disubstituted diamondoid derivatives, such as amino acids or amino alcohols.<sup>14</sup>



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