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2,2,2-trifluoro-N-phenylacetamide using
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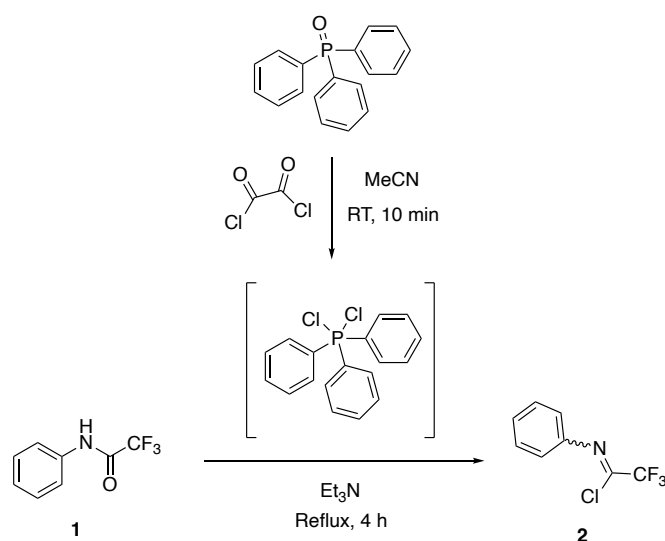
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Synthesis of N-phenyltrifluoroacetimidoyl chloride (CAS: 61881-19-4) via chlorination of 2,2,2-trifluoro-N-phenylacetamide using triphenylphosphine oxide/oxalyl chloride combination system

N-phenyltrifluoroacetimidoyl chloride (CAS: 61881-19-4) is a versatile fluorine-containing reagent that have find wide applications, especially in the synthesis of glycans¹. A recent report of its synthesis employing dichlorotriphenylphosphane instead of CCl₄/PPh₃ combination as the chlorinating reagent² attracted our attention. Inspired by this work, we further attempted using triphenylphosphine oxide/oxalyl chloride combination³ for the in-situ generation of dichlorotriphenylphosphane that serve as the chlorinating reagent. Under this condition, the chlorination reaction proceeds smoothly and N-phenyltrifluoroacetimidoyl chloride was formed in high yield as determined by ¹⁹F-NMR analysis. After the reaction, triphenylphosphine oxide can be quantitatively recovered from the reaction mixture.



Experimental Procedure

A 50 mL, three-necked, round-bottomed flask equipped with a teflon-coated magnetic stir bar and a reflux condenser was charged with triphenylphosphine oxide (2.00 g, 7.19 mmol) and a solution of **1** (1.00 g, 5.29 mmol in 10 mL MeCN) was slowly added under argon atmosphere. The mixture was stirred at RT and oxalyl chloride (1.00 mL, 11.8 mmol) was added dropwise. After the addition, the mixture was stirred for 10

min, then Et₃N (1.60 mL, 11 mmol) was added. The mixture was heated at reflux for 4 h, ¹⁹F NMR of the reaction mixture revealed that the reaction was complete and **2** was formed in high yield (-77.1 ppm in MeCN). The mixture was cooled to RT, filtered, washed with PE (20 mL) and evaporated under reduced pressure to afford a brown solid, which was extracted with PE (20 mL×3) and filtered. The filtrate was evaporated under reduced pressure to afford crude product, which was further purified by silica gel flash column chromatography (PE) to afford **2** as a colorless oil (280 mg, 25%). The NMR spectral data of **2** was identical with the literature data¹. The relatively lower yield was most likely due to the relatively low boiling point of the product.

In order to recover triphenylphosphine oxide from the reaction mixture, the above solid obtained after the filtration process was suspended in water (500 mL), filtered and dried to afford crude triphenylphosphine oxide (2.08 g) in essentially quantitative yield.

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