

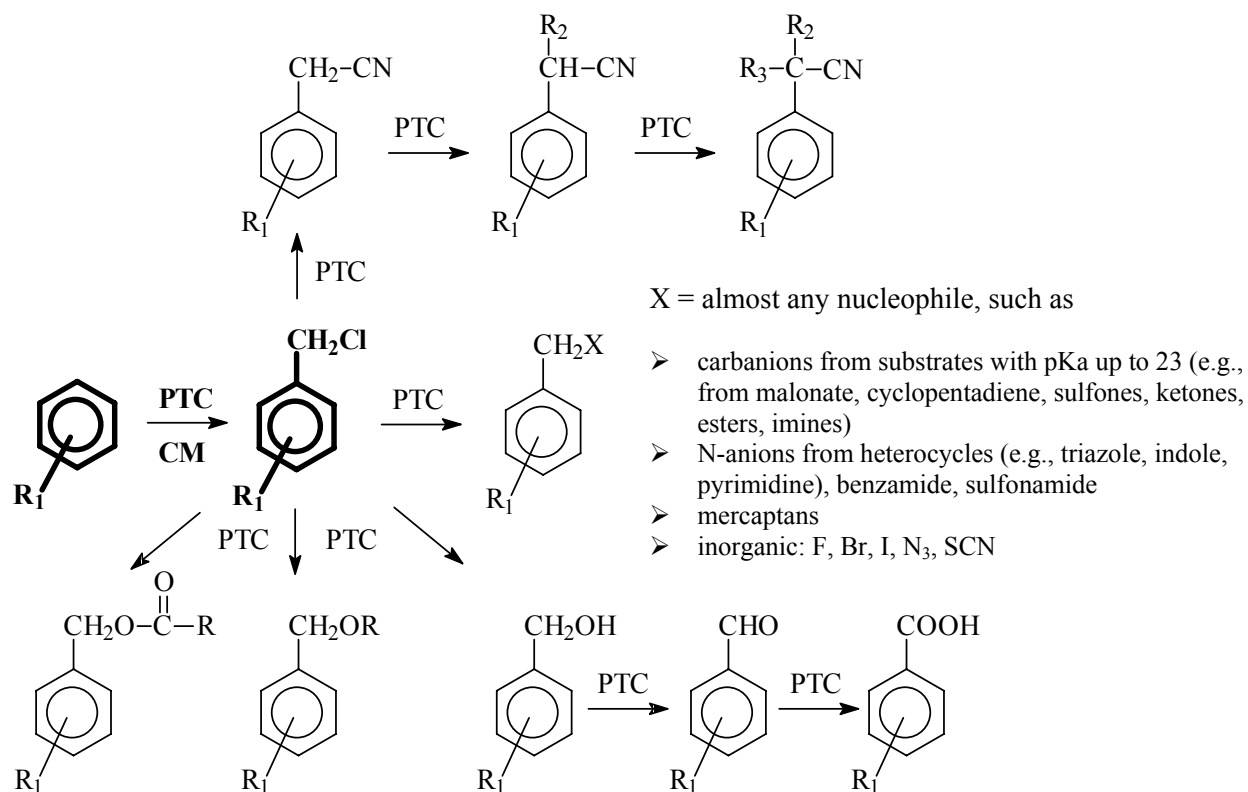
Chloromethylation

An Outstanding PTC Platform

Phase-transfer catalysis excels in nucleophilic substitution. The title “King of PTC S_N2 Substrates” belongs to benzyl chloride and benzyl chloride derivatives which react cleanly, rapidly and in high yield under PTC conditions. Nucleophilic substitution of the chloride of benzyl chloride derivatives provides a broad array of useful products and intermediates such as benzyl esters, ethers, nitriles, alkylated nitriles, alcohols, aldehydes, acids and much more (see Figure CM-1). Benzyl chloride derivatives are used commercially in the manufacture of pharmaceuticals, agrochemicals, dyes, flavors & fragrances, monomers, additives, modification of polymers and a wide range of specialty and fine organic chemicals.

PTC Organics developed PTC chloromethylation technology which provides access to these benzyl chloride derivatives and can be directly converted into valuable downstream products using other outstanding PTC reactions. This technology offers multiple advantages. The new PTC chloromethylation is emulsion-free, resulting in easy workup (separation achieved in < 1 min) and avoids the use, isolation and transfer of chloromethyl methyl ether or its regulated byproduct, bis-(chloromethyl)ether. Interestingly, careful choice of chloromethylation conditions leads to higher selectivity and higher reactivity simultaneously. **A great advantage of the new PTC chloromethylation is that it provides the first step for a variety of versatile multi-step high-yield PTC reaction sequences performed without isolation of intermediates.** The actual chloromethylation can be performed and treated in a sealed reactor system and the chloromethylated intermediate can be further reacted without isolation or handling. This reduces cycle time and reduces loss of intermediates and catalyst. The system can be designed to be performed using a single catalyst and either solvent-free PTC conditions or a single solvent PTC system.

Figure CM-1: Consecutive High-Yield PTC Reactions Starting with Chloromethylation
Avoiding Isolation of Intermediates



Given these advantages and the broad scope of utility of benzyl chloride derivatives and downstream products, PTC Organics and Single Site Catalysts (Chester, PA) are commercializing the chloromethylation and subsequent PTC reactions. SST Corporation (Clifton, NJ) is promoting chloromethylation sequences in the pharmaceutical industry.

Figure CM-2 shows some of the reactions in the benzyl chloride tree which have been successfully developed by PTC Organics. Figure CM-3 shows reaction sequences which may be able to benefit from consecutive PTC reactions in the chloromethylation platform. PTC Organics is aware of other reaction sequences (not shown) beginning with chloromethylation which have significant potential for improvement using PTC for pharmaceutical, agrochemical and monomer applications. Contact PTC Organics (tel: +1 856-222-1146) to inquire about your potential application.

Figure CM-2: PTC Applications Using Benzyl Chloride Derivatives Developed by PTC Organics

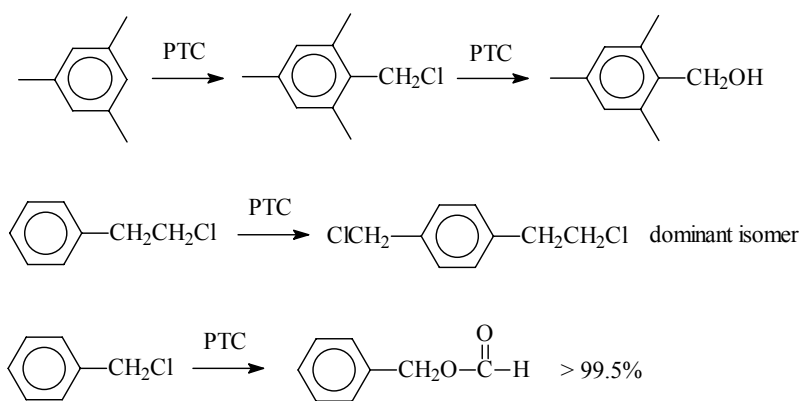


Figure CM-3: Potential Consecutive PTC Reaction Sequences

