SYNLETT
Spotlight 450

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

Hexachlorocyclohexa-2,5-dien-1-one

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Zahra was born in Tehran, Iran. She obtained her M.Sc. in organic chemistry from the Bu Ali Sina University, Hamedan (Iran) in 2005 under the supervision of Professors A. Khazaei and M. A. Zolfigol. She then joined the Arya Sasol Polymer Company until 2011. In 2012, she commenced her Ph.D. studies in the Catalysis and Peptide research Unit at the University of KwaZulu-Natal, Durban (South Africa) under the direction of Professors P. I. Arvidsson, T. Govender, H. G. Kruger, and Dr. G. E. M. Maguire. Her main research field involves organocatalytic methodology.

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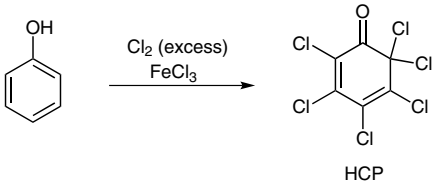
Introduction

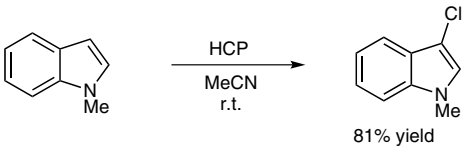
Hexachlorocyclohexa-2,5-dien-1-one is informally called hexachlorophenol (HCP). It is an efficient reagent for the chlorination of a wide variety of compounds and was used in several chiral organocatalytic reactions. HCP is a yellow to brown crystalline solid, which is usually prepared via electrophilic chlorination of phenol by chlorine gas in the presence of a metal chloride catalyst, such as iron(III) chloride.[1]



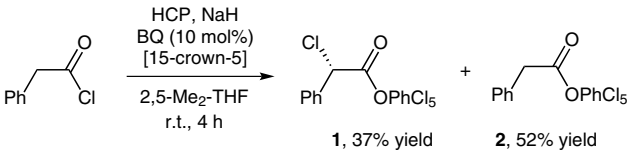
Scheme 1

Abstracts

(A) The application of HCP in the halogenation of aromatic heterocyclic compounds has been investigated.[2] For example, equimolar amounts of HCP convert *N*-methylindole into the corresponding 3-chloro-*N*-methylindole in 81% yield.[3]



(B) Lectka and co-workers have established a tandem catalytic asymmetric chlorination–esterification process using cinchona alkaloid derivatives as catalysts and polychlorinated quinones as the halogenating agents.[4] For instance, they reported the reaction of phenyl acetyl chloride in the presence of benzoyl quinine (BQ; chiral organocatalyst), sodium hydride, and HCP to form α-chloro ester **1** and ester **2** in 37% and 52% yield, respectively.[5]



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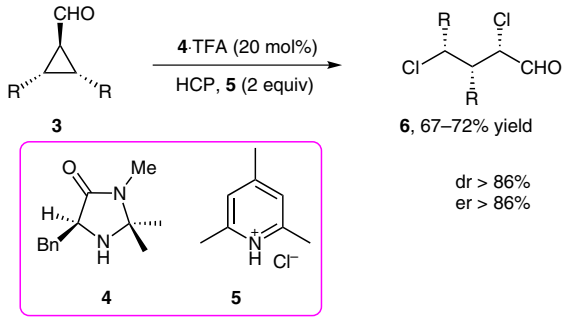
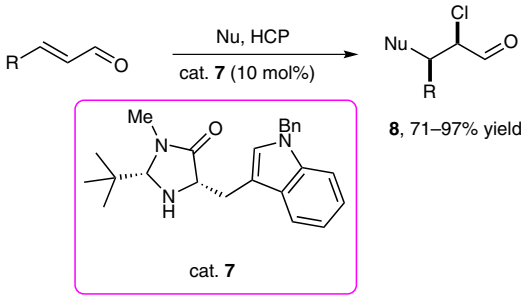
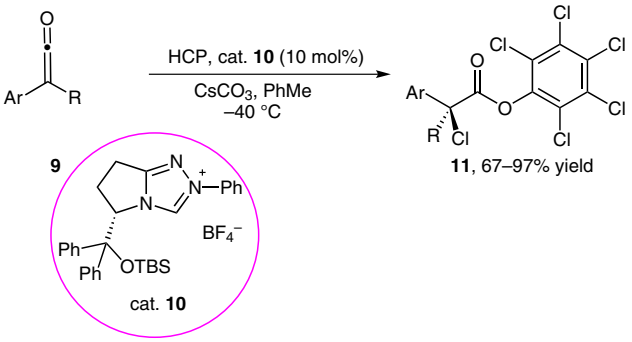
(D) Diastereo- and enantioselective synthesis of β,γ-dichloroaldehydes **6** derived from cyclopropylcarbaldehyde **3** was achieved using HCP, amine **4** (chiral organocatalyst), and 2,4,6-collidine **5**.[6] The aldehyde is activated via imine formation with **4**. Ring opening occurs by the attack of Cl^-. In the last step, the enamine functionality attacks Cl^+, which is followed by hydrolysis to give the product. MacMillan had previously reported the use of HCP for the synthesis of other α-chloroaldehydes.[7]



(E) Huang et al. developed an innovative strategy for the preparation of a series of asymmetric α-halo-β-aryl aldehydes from α,β-unsaturated aldehydes **8**.[8] In this enantioselective organocatalytic cascade reaction, amine **7** was employed as catalyst for the functionalization of enals in the presence of HCP as the chlorination agent. Activated heterocycles behave as nucleophiles in this reaction.



(F) The chiral N-heterocyclic carbene (NHC) percusor **10** efficiently promotes the organocatalytic chlorination and esterification of disubstituted ketenes **9**.[9] The corresponding tertiary α-halo esters **11** are isolated from ketenes **9** in the presence of HCP catalyzed by the NHC derived from **10** in good yield and promising levels of asymmetric induction (up to 61% ee).



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