Hexachlorocyclohexa-2,5-dien-1-one

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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

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
(D) Diastereo- and enantioselective synthesis of \(\beta,\gamma\)-dichloroaldehydes 6 derived from cyclopropylcarbalmdehyde 3 was achieved using HCP, amine 4 (chiral organocatalyst), and 2,4,6-collidine 5. The aldehyde is activated via imine formation with 4. Ring opening occurs by the attack of \(\text{Cl}^−\). In the last step, the enamine functionality attacks \(\text{Cl}^+\), which is followed by hydrolysis to give the product. MacMillan had previously reported the use of HCP for the synthesis of other \(\alpha\)-chloroaldehydes.  

(E) Huang et al. developed an innovative strategy for the preparation of a series of asymmetric \(\alpha\)-halo-\(\beta\)-aryl aldehydes from \(\alpha,\beta\)-unsaturated aldehydes 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) precusor 10 efficiently promotes the organocatalytic chlorination and esterification of disubstituted ketenes 9. The corresponding tertiary \(\alpha\)-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).

References