Introduction

1,3-Dichloroacetone (CAS: 534-07-6) is the simplest and most common example of the \( \alpha, \alpha' \)-dihaloketone derivatives. It is a crystalline solid (mp 39–41 °C), corrosive, toxic, and has to be handled in a fume hood. It shows a good solubility in organic solvents and a very high chemical reactivity, justified by the presence of three vicinal electrophilic carbons, which enables it to undergo several chemical transformations. Although it is commercially supplied, it may be prepared by chlorination of acetone in methanol as proposed by Gallucci.\(^1\) Alternatively, an expeditious synthesis has been reported by Barluenga via the in situ formation of a lithium carbenoid, such as chloromethylithium, which reacts with the ethyl ester of chloroacetic acid, as shown in Scheme 1.\(^2\)

Abstracts

(A) 1,3-Dichloroacetone has been extensively used as substrate to carry out Sn-type reactions with phosphorous nucleophiles (i.e., triphenylphosphine). The obtained ylide I represents an useful starting material for further functionalizations.\(^3\) It is the precursor of silyloxy butadienes that may undergo Diels–Alder reactions as reported by Alonso.\(^4\) Analogously, a second chloro displacement and a Wittig-type reaction on I lead to a series of \( \omega \)-unsaturated \( \alpha \)-alkoxy enones and \( \alpha \)-amino enones, suitable for ring-closing metathesis reactions.\(^5\)

(B) The \( \text{O}^5\) and \( \text{S}^6-8\) nucleophiles can perform nucleophilic displacement on 1,3-dichloroacetone, thus representing an useful technique to add a three-carbon unit to organic compounds. By choosing appropriately the stoichiometric ratio between 1,3-dichloroacetone and the nucleophile, it is possible to obtain the substitution of both chlorine atoms.\(^9,10\)
(C) The electrophilic behavior of the vicinal carbon atoms of this reagent is involved in reactions with ambident nucleophiles leading to cyclic systems characterized by the presence of a chloromethyl moiety suitable for further derivatizations.\(^{11-17}\) Significantly, the unique examples cited in literature of the use of 1,3-dichloroacetone with aromatic amines entail reactions with highly nucleophilic ambident amines (e.g., 2-aminopyridine).\(^{18-20}\)

(D) The activation of the carbonyl moiety by an acid allows the addition to the carbonyl carbon of a suitable nucleophile (hydroxylamine derivatives\(^{21}\) or diols).\(^{22}\) It seems that reactions carried out on carbonyl-protected 1,3-dichloroacetone result in better chemoselectivity compared to those conducted on the unprotected one, maybe because of the high acidity of the methilenic protons of the last one.

(E) 1,3-Dichloroacetone is useful as a starting material for a one-pot synthesis of several 1-substituted cyclopropanols.\(^{23,24}\) In this procedure, the initially formed 2-substituted 1,3-dichloro-isopropoxide is reduced to the desired compounds by using low-valent iron.\(^{25}\) Analogously, cyclopropenone derivatives are readily available from 1,3-dichloroacetone.\(^{22}\)

References