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CHLORINATION OF KETONES WITH TRICHLOROISOCYANURIC ACID

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ABSTRACT: Trichloroisocyanuric acid is an effective reagent for the chlorination of ketones in the alpha position.

Ketones can be chlorinated in the alpha position using chlorine,[1] N-chlorosuccinimide,[2] sulfuryl chloride,[3] selenium oxychloride,[4] and cupric chloride.[5] We wish to report that trichloroisocyanuric acid [1,3,5-trichloro-1,3,5-triazine-2,4,6-(1H,3H,5H)-trione (1)] can also be used to chlorinate ketones in the alpha position.

Trichloroisocyanuric acid is a stable, nonvolatile solid used commercially as a disinfectant and to a limited extent as a laboratory reagent. Previously reported reactions utilizing 1 include the chlorination of aromatic systems,[6] alkanes,[7] fatty acid esters,[8] allylic thioethers,[9] cyclic ethers[10] and cyclic

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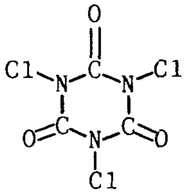
acetals,[11] the allylic chlorination of alkenes,[12] and the oxidation of ethers to esters.[13]



1

One, two, or three chlorine atoms can be selectively added to acetophenone with 1 in acetic acid by various combinations of reactants, time, temperature, and a catalyst. The results are summarized in Table I.

Table I

Chlorination of Acetophenone with Trichloroisocyanuric Acid

Mole Ratio Reactants 1 : Ketone : BF_3	Time, hr.-Temp.	Product	% Yield, Isolated
0.33 : 1 : 0.315	0.25-80°C	$C_6H_5COCH_2Cl$	50[a]
1.00 : 1 : 0.315	17-80°C	$C_6H_5COCHCl_2$	81[b]
2.00 : 1 : 0	5-reflux	$C_6H_5COCCl_3$	81[c]

[a] Mp 53.5-54.2°C (reported mp 54.0°C).[14]
[b] GC purity, 99%.
[c] GC purity, 98%.

Monochlorination of aliphatic ketones is readily accomplished using 1 in the presence of boron trifluoride etherate. The results are summarized in

Table II. For volatile ketones, like 2-propanone and 2-butanone, the reaction was carried out using excess ketone as the solvent. Acetic acid was the solvent for cyclohexanone and 2-methylcyclohexanone. With a high ratio of boron trifluoride unsymmetrical ketones gave chlorination preferentially at the more substituted position as do other chlorinating agents under acidic conditions.[16]

Addition of azobisisobutyronitrile to a reaction of acetophenone at 80°C did not increase the rate of reaction indicating that an ionic pathway is probably involved.

Trichloroisocyanuric acid is a safe, convenient, and selective chlorinating agent for ketones.

Experimental

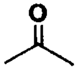
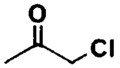
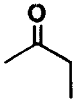
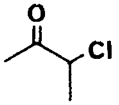
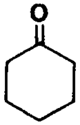
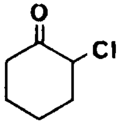
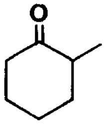
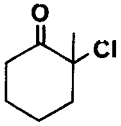
All products, except for trichloroacetophenone, were characterized by comparison of the IR and NMR spectra to those of authentic samples.

α-Chloroacetophenone

A solution of **1** (0.774 g, 3.33 mmol), acetophenone (1.20 g, 10.0 mmol), and boron trifluoride etherate (0.45 g, 3.15 mmol) in 20 mL acetic acid was stirred for 15 min. in an 80° oil bath. After cooling, the precipitate was filtered and washed with acetic acid, and the filtrate poured into 100 mL crushed ice and

Table II

Chlorination of Aliphatic Ketones with Trichloroisocyanuric Acid

Ketone	Mole Ratio Reactants **1** : Ketone : BF_3	Time, min - Temp	Major Product	Yield (bp)	GC Purity
	1 : 20.4 : 0.023	60 - reflux		88% (44-46°C, 40 torr)	96[a]
	1 : 17.4 : 2.40	90 - rm temp		58% (43-46°C, 40 torr)	93[b]
	1 : 2.40 : 0.0054	50 - 80°C		77% (104-107°C, 50 torr)	95[c]
	1 : 1.98 : 2.00	90 - rm temp		87% (89-90°C, 30 torr)	85[d]

[a] Also contains 4% 2-propanone and a trace of 1,1-dichloroacetone.

[b] Also contains 2% 2-butanone and 4% of an unidentified compound.

[c] Also contains a trace of cyclohexanone and two unidentified compounds of 2% each.

[d] Also contains four unidentified$_{15}$compounds from 1-7%. Chlorination with SO_2Cl_2 gave a similar mixture of products.

water. After the ice melted, the crystals were filtered, washed with water, and dissolved in pentane. The solution was dried over $MgSO_4$, filtered, and freed of solvent to give 0.798 g (50%); mp 53.8-54.8°C (reported mp 54.0°C).[14]

α,α,α-Trichloroacetophenone

A solution of **1** (4.686 g, 20.0 mmol) and acetophenone (1.20 g, 10.0 mmol) in 20 mL acetic acid was refluxed for 5 hr. After cooling, the precipitate was filtered and washed with acetic acid, the filtrate was diluted with water, and the mixture extracted with 4 x 20 mL pentane. The pentane solution was washed with 20 mL sat NaCl and dried over $MgSO_4$. After filtration, the pentane was removed *in vacuo* and the residue purified by Kugelrohr distillation (oil bath temp 150-170°C at 35 torr): 1.88 g (81%); IR (neat) 5.86, 11.75, 12.14, 12.84, 14.56 μ; NMR (CCl_4) δ 7.2-7.8 (m, 3H), 8.0-8.5 (m, 2H). The product was greater than 98% pure by GC analysis. A sample was converted into benzoic in 97% yield by treatment with 4 N NaOH for 15 min at 60°C followed by conc HCl: mp 121.4-121.9°C; mmp 121.6-122.1°C.

The procedures for preparation of α,α-dichloroacetophenone, 1-chloro-2-propanone, and 2-chlorocyclohexanone were similar.

3-Chloro-2-butanone

While stirring a solution of BF_3 etherate (2.840 g, 20 mmol) in 15 mL 2-butanone at room temp, a total of 1.936 g (8.33 mmol) of 1 was added in ca 0.1 g batches over 90 min. After an additional 15 min, the precipitate was removed by filtration and the filtrate diluted with 150 mL sat NaCl. The mixture was extracted with 4 x 20 mL ether and the ether dried, filtered, and removed *in vacuo*. Most of the 2-butanone was removed by distillation at atmospheric pressure and the residue fractionated using a concentric tube column: 1.066 g (58%; 93% pure by GC).

2-Chloro-2-methylcyclohexanone was prepared in a similar fashion by dropwise addition of an acetic acid solution of 1 over 90 min.

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