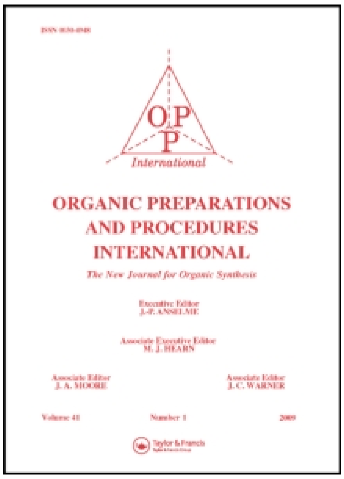


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

A CRITICAL EXAMINATION OF THE PREPARATION OF POLYCHLORINATED ACETONES

Baldur Föhlisch[a]; Hartmut Zinser[a]
[a] Institut für Organische Chemie der Universität Stuttgart, Stuttgart, GERMANY

To cite this Article Föhlisch, Baldur and Zinser, Hartmut(2004) 'A CRITICAL EXAMINATION OF THE PREPARATION OF POLYCHLORINATED ACETONES', Organic Preparations and Procedures International, 36: 6, 549 — 572
To link to this Article: DOI: 10.1080/00304940409355973
URL: http://dx.doi.org/10.1080/00304940409355973

ORGANIC PREPARATIONS AND PROCEDURES INT., 36 (6), 549-572 (2004)

A CRITICAL EXAMINATION OF THE PREPARATION OF POLYCHLORINATED ACETONES

Baldur Föhlisch* and Hartmut Zinser

Institut für Organische Chemie der Universität Stuttgart
Pfaffenwaldring 55, D-70569 Stuttgart, GERMANY
baldur.foehlisch@oc.uni-stuttgart.de

A CRITICAL EXAMINATION OF THE PREPARATION OF POLYCHLORINATED ACETONES

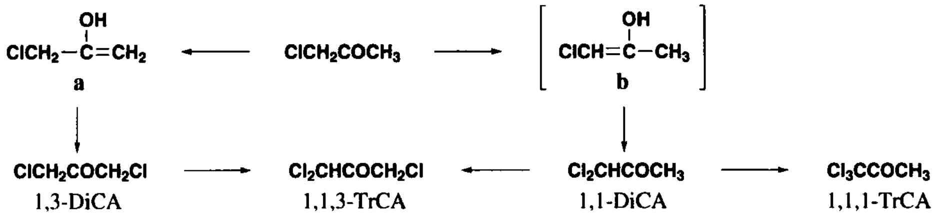
Baldur Föhlisch* and Hartmut Zinser

Institut für Organische Chemie der Universität Stuttgart
Pfaffenwaldring 55, D-70569 Stuttgart, GERMANY
baldur.foehlisch@oc.uni-stuttgart.de

INTRODUCTION

Over the last few years, 1,1,3-trichloroacetone, 1,1,3,3-tetrachloroacetone and pentachloroacetone have been used as starting materials for the generation of chloro substituted oxyallyl intermediates which are valuable as components for [4+3] cycloaddition reactions.[1-3] The names of chloroacetone, pentachloroacetone and hexachloroacetone will be used and the other compounds will be abbreviated as follows: 1,1-dichloroacetone (**1,1-DiCA**), 1,3-dichloroacetone (**1,3-DiCA**), 1,1,1-trichloroacetone (**1,1,1-TrCA**), 1,1,3-trichloroacetone (**1,1,3-TrCA**), 1,1,1,3-tetrachloroacetone (**1,1,1,3-TeCA**) and 1,1,3,3-tetrachloroacetone (**1,1,3,3-TeCA**). **1,1,3-TrCA** is a building block for a folic acid synthesis,[4] and hence, is produced in industrial scale (*vide infra*).[5] **1,1,3,3-TeCA** and pentachloroacetone have been also commercially available for a long time. However, as far as we are aware, these chemicals are no longer listed in laboratory chemicals suppliers' catalogues. Therefore, we believe it useful to disclose our results of these preparations that can be performed in a laboratory with standard equipment.[6] Moreover, we provide a survey of other relevant studies including the patent literature that may not be generally available to most readers.

Undoubtedly, the simplest and most straightforward preparation of these haloketones is by the action of molecular chlorine (dichlorine) on acetone. However, this process is unselective; substitution of hydrogen atoms in acetone by chlorine proceeds stepwise with the evolution of hydrogen chloride and formation of chloro derivatives of all degrees of substitution (*Schemes 1* & *3*). For example, reaction of acetone with two equivalents of dichlorine at 25-30°C is reported to furnish a mixture of the *gem*-disubstituted 1,1-dichloroacetone (**1,1-DiCA**, 14%), 1,1,1-trichloroacetone (**1,1,1-TrCA**, 26.3%), **1,1,3-TrCA** (20.4%), unspecified 'tetrachloroacetone' (35%), and pentachloroacetone (4.3%).[7] With one equiv. of chlorine, **1,1-DiCA** predominated, and no monochloroacetone could be isolated.[8]



Scheme 1

Sulfuryl chloride is also a well-known and inexpensive chlorinating agent that is expected to be more selective than dichlorine.[9a] Reaction of sulfuryl chloride with an equimolar amount of acetone at 30-40°C is reported to give a *ca.* 40:60 mixture of chloroacetone and **1,1-DiCA.**[10] With two equivalents of sulfuryl chloride, **1,1-DiCA, 1,3-DiCA,** and **1,1,3-TrCA** were isolated in a 72:6:20 ratio.[10] The principal problem is to arrest the reaction at the required stage of polychlorination. Moreover, due to the simultaneous formation of hydrogen chloride, condensation reactions of unreacted acetone or chlorinated ketones may occur. In attempt to achieve enhanced selectivity, the chlorination of acetone has been performed under a variety of reaction conditions.[9] Chlorinations in protic solvents may result in the formation of additional by-products.[9] To obtain dichloro- and trichloroacetones, it has been recommended that the chlorination be conducted with exclusion of water at temperatures up to 100°C, using the liquid reaction mixture consisting from di- and trichloroacetones as the 'solvent'.[11]

With the goal of obtaining **1,1,3-TrCA**, Bugrova *et al.* investigated the chlorination of acetone with dichlorine in the presence of several metal salt catalysts ($FeCl_3$, $CuCl_2$, FeS, CuS, CdS, Sb_2S_5), amines (diethylamine, triethylamine, *N,N*-dimethylaniline) and pyridine.[7] The best results were obtained when an equimolar amount of chlorine gas was passed slowly at 25-30°C in acetone in the presence of pyridine or diethylamine as catalyst. The mixture of chlorinated products contained 50-57% **1,1,3-TrCA**. However, a serious problem is the purification of **1,1,3-TrCA** by distillation since the by-products, **1,3-DiCA, 1,1,3,3-TeCA** and **1,1,1,3-TeCA**, have similar boiling points (see *Table 1* and *Experimental Section*). From the relative amounts of chlorination products in the mixture, the Russian workers[7] inferred that the rates of replacement of hydrogen atoms by chlorine is in the ratio $CH_2Cl:CH_3:CHCl_2$ = 100:10:1.

A patent application[5] claims that the use of iodine, monochloroiodo and trichloroiodo or iodo compounds -which are reported to have a catalytic effect upon the selectivity of the chlorination- led to increased proportions of **1,1,3-TrCA** in the chlorination mixtures.[5] In another patent, trialkyl- and triphenyl phosphites have been suggested as catalysts.[12]

Table 1. Boiling points of Chlorinated Acetones

Compound	bp. (°C/Torr) at atm. pressure	bp. (°C/Torr) at red. pressure	Reference
Chloroacetone	120/760	59/80	a
	119/763	41/24	b, c
1,1-Dichloroacetone	118/770	54/80	a
	120	----	d
1,3-Dichloroacetone	172	75-77/22	e, f
	173	58-62/10	d
	173/759	----	g, a
1,1,1-Trichloroacetone	134	56-58/40	d, h, i
	134/754	28/10	i, h
1,1,3-Trichloroacetone	172/760	83.8-84.6/30	a
	----	72-73/20	d
	----	67-68/14	e
	----	62-63/10	d
1,1,1,3-Tetrachloroacetone	183	89/30	d, e
	----	70.5-71/14	j
1,1,3,3-Tetrachloroacetone	171-181	82-83/22	d, a
	180-182/718	74-77/12	k, e
	184/760	69/11	l, a
Pentachloroacetone	191	97.5-98.5/40	l, b
	192/753	70-72/12	n, m
Hexachloroacetone	198-201/760	116-118/60	o, d
	202	110/40	l, b
	202-204	73-75/9	n, m

a) H. Gerding and H. G. Harding, *Rec. Trav. Chim Pays-Bas*, **74**, 1409 (1955). b) Ref. 46. c) R. Rittner, J. A. Vanin and B. Wladislaw, *Magn. Reson. Chem.* **26**, 51 (1988). d) Ref.7. e) Ref. 16. f) Ref. 14. g) T.Posner and K. Rohde, *Ber.*,**42**, 3233 (1909). h) Ref. 29. i) A. Winston, J. P. M. Bederka, W. G. Isner, P. C. Juliano and J. C. Sharp, *J. Org. Chem.* **30**, 2784 (1965). j) Ref. 35. k) S. Levy and K. Jedlicka, *Ann.*, **249**, 66 (1888). l) M. W. Wagner, H. Kloosterziel and A. F. Bickel, *Rec. Trav. Chim. Pays-Bas*, **81**, 933 (1962). m) V. P. Kukhar, I. V. Migaichuk, L. A. Lazukina, L. M. Trikleb and I. G. Khaskin, *Zh. Obsh. Khim.*, **53**, 1578 (1983); *J. Gen. Chem. USSR* (Engl. Transl.), **53**, 1424 (1983). n) Ref. 45. o) C. Bew, V. Otero de Joshi, J. Gray, P. T. Kaye and G. D. Meakins, *J. Chem. Soc. Perkin 1*, 945 (**1982**).

RESULTS AND DISCUSSION

1. Mechanistic Considerations

In spite of the fact that the papers cited above do not deal with mechanisms, there is little doubt that the reaction of acetone (and chloroacetones) with dichlorine, and sulfuryl chloride under the reported conditions proceeds *via* enol intermediates.[9a, 10] Since two enol forms (**a** and **b**) are possible from monochloroacetone, chlorination may lead to **1,1-DiCA** and **1,3-DiCA**, and the latter, on further chlorination, inevitably must give **1,1,3-TrCA**,[13] while the former may yield **1,1,1-TrCA** or **1,1,3-TrCA** (*Scheme 1*). The first step, necessary for polychlorination, is the rate of formation of the isomeric enol tautomers of monochloro-acetone. At sufficiently high concentrations of the halogenating agent, if that step is the rate-limiting one in dichlorination,[9a] the results indicate that 1-chloro-2-propenol (**b**) is formed faster than isomer **a** (3-chloro-2-propenol), consistent with the enhanced acidity of the α-CH_2 group bearing the chlorine substituent.[14] The formation of **1,1,3-TrCA** is slightly favored over that of **1,1,1-TrCA** from **1,1-DiCA**, as found for the chlorination in acidic protic solvents (ratio 1.6-3.8).[15,16] Whereas further chlorination of **1,1,1-TrCA** is retarded (*vide infra*), **1,1,3-TrCA** is expected to form two tetrachloroacetone isomers, and finally pentachloroacetone and hexachloroacetone.

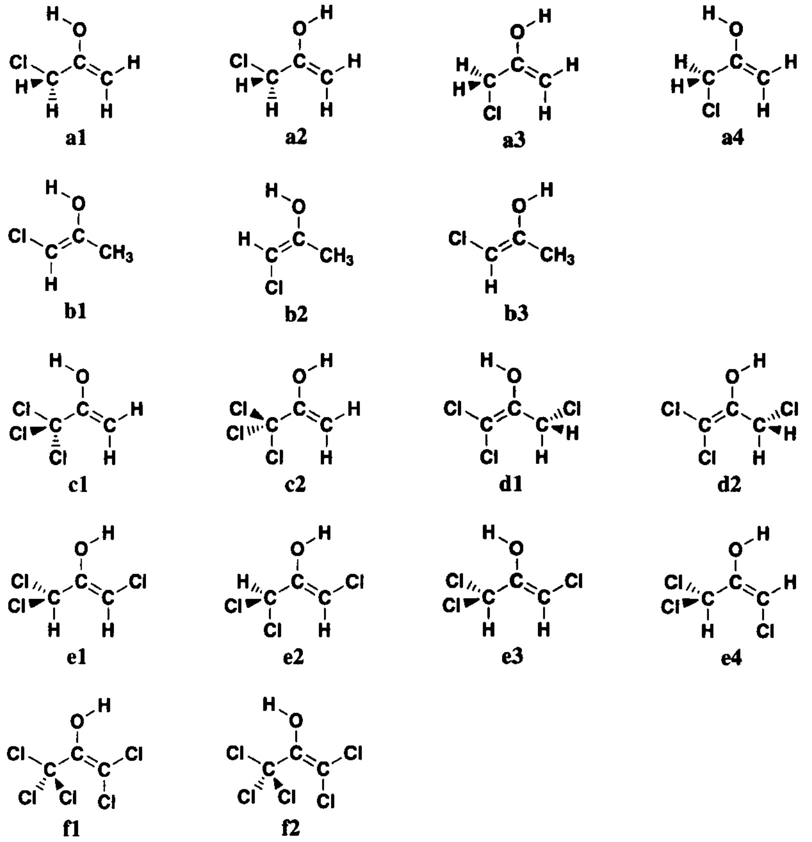
In the absence of added catalysts, the introduction of the first chlorine substituent in acetone is clearly acid-catalyzed (*auto-catalyzed*) by the hydrogen chloride generated simultaneously.[17] For the second, and subsequent chlorination(s), base catalysis or a combined acid-base catalysis might be expected.[18-20] Using amines or pyridine as catalysts,[7] it is safe to assume a base-catalysed enolization of acetone and of halogenated acetones respectively, as the first step of the chlorination reaction. However, the HCl evolved in the course of the reaction will immediately protonate these bases forming amine hydrochlorides.[21] In the case of pyridine, both a mono- and a *bis*-hydrochloride are known; the latter, however, decomposes[22,23] at ca. 55°C, a temperature that is lower than that which is used for the reaction. At that point, the chlorination will probably be governed by a 'cooperative catalysis by proton donors and acceptors', as suggested for 3-pentanone[19] and alkanals.[20] A second factor may be a transformation of dichlorine into a more selective reagent. Pyridinium trichloride ($C_5H_6N^+$ Cl_3^-) is well known and may act as the chlorinating species.[24]

It has been known for a long time[5] that iodine chloride is formed by reaction of chlorine with iodine. Normally ICl functions as a iodinating reagent, but can also act as a chlorinating agent.[25] In the present case, formation of iodoacetone should be favored. As reported in the patent application,[5] iodoacetone, just like 1-chloro-3-iodoacetone and 1,1-dichloro-3-iodoacetone, is also a promoter of the chlorination reaction.[5] 1,1-Dichloro-3-iodoacetone is the final product that can be isolated after the chlorination is complete, and used as a catalyst in a new batch.[5] Presumably, dichlorine is also transformed by these organoiodo compounds to give hypervalent iodine species, just as (dichloroiodo)benzene (iodobenzene dichloride) is formed from iodobenzene.[26]

The question is whether the rate of chlorination(s) of the *enols* is affected by the 'nature' (structure) of the chlorinating species and if so, how. We believe that, at present, no clear answer can be given and thus prefer not to speculate on that point.

2. Calculations

Quantum chemical calculations of relative rates and activation energies of the enolization of chloroacetones would be desirable. However, it will be expensive to carry out these calculations at a level sufficiently accurate to match the experimental results in solution. In order to gain a preliminary insight, calculations of the energies and dipole moments of several chloroacetones and their *enol* tautomers (*Scheme 2*) at the B3LYP/cc-pVDZ level were performed by



Scheme 2

Rauhut.[27] The results which, of course, correspond to energies in the gas phase are summarized in *Table 2*.

It has been concluded from spectroscopic evidence and dipole moment determinations that the prototypic α-haloketone, chloroacetone, exists in the liquid state as an equilibrium mixture of "*cis*-halogen-oxygen" (*i.e.* synperiplanar, *sp*) and "*gauche*" (*i.e.* anticlinal (*ac*) forms.[28,29] In the gas phase and in non-polar solvents, it was established that chloroacetone prefers the "*gauche*" conformation; however in more polar media, solvation effects lead to an increase of stability in the *sp* isomer and to its predominance (in agreement with the larger dipole moment of this species).[29] In order to avoid confusion by different conformation nomenclatures used in the literature,[28,29] we classify the species hereafter according to the Klyne-Prelog convention.

Table 2. Relative *ab initio* Energies for Chloroacetones and their *enol* Tautomers (in kcal/mol) and Calculated Dipole Moments (Debye units)

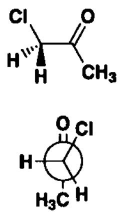
Species	Conformation	E_{rel}	Dipole Moment
Chloroacetone	*ap*	0.00[a]	1.2
Chloroacetone	*sp*	1.1	3.8
enol **a1**	*anti-sp*	12.9	1.3
enol **a2**	*syn-sp*	13.4	2.5
enol **a3**	*syn-ap*	14.1	2.1
enol **a4**	*anti-ap*	16.7	2.3
enol **b1**	*syn-(Z)*	8.0	1.2
enol **b2**	*syn-(E)*	12.0	1.6
enol **b3**	*anti-(Z)*	12.9	3.7
1,1,1-TrCA	*sp*	0.00[b]	2.2
enol **c1**	*anti-sc*	13.9	0.5
enol **c2**	*syn-sc*	15.0	2.8
1,1,3-TrCA	*sp-ac*	0.00[c]	1.9
1,1,3-TrCA	*sp-sp*	1.3	3.3
enol **d1**	*syn-sc*	6.6	1.7
enol **d2**	*anti-sc*	8.1	1.8
enol **e1**	*syn-sc-(Z)*	5.8	1.9
enol **e2**	*syn-ac-(Z)*	6.7	1.3
enol **e3**	*anti-sc-(Z)*	6.9	1.4
enol **e4**	*syn-sc-(E)*	10.3	2.8
Pentachloroacetone	*sp-sc*	0.00[d]	1.9
Pentachloroacetone	*sp-ac*	3.3	0.8
enol **f1**	*syn-sp*	12.2	1.6
enol **f2**	*anti-sp*	12.8	1.6

[a] $E_0 = -652.7760658$ hartree, ZVPE = 0.074702 hartree, $E_{tot} = -652.7013638$ hartree.

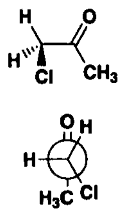
[b] $E_0 = -1571.98966600$ hartree, ZVPE = 0.05549 hartree , $E_{tot} = -1571.934176$ hartree.

[c] $E_0 = -1571.99280225$ hartree, ZVPE = 0.057354 hartree, $E_{tot} = -1571.93544825$ hartree.

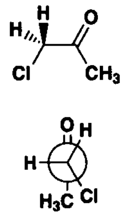
[d] $E_0 = -2491.20130695$ hartree, ZVPE = 0.037675 hartree, $E_{tot} = -2491.16363195$ hartree.



"cis" (sp)



"gauche" (ac)



(ap)

The result of the calculations for chloroacetone (*Table 2*) is that the conformation with opposite heteroatoms, *i.e.* antiperiplanar (*ap*), has the lowest energy (E_{tot} + ZPVE = -652.7013638 hartree), and thus is put as the reference energy (E_{rel} = 0.00 kcal/mol) to draw a comparison with isomeric species. The synperiplanar (*sp*) conformer is calculated to be of somewhat higher energy (E_{rel} = 1.1 kcal/mol). This is in agreement with calculations and spectroscopic investigations of fluoroacetone which was shown to exist in the vapor phase predominantly in the *ap* conformation.[30] In the liquid phase, however, the *sp* conformer is the more stable form, and is the only conformation present in the annealed solid.[30]

Among the corresponding chlorosubstituted enols, the *syn* isomer of *(Z)*-1-chloropropen-2-ol (**b1**) has the lowest energy (E_{rel} = 8.0 kcal/mol), in line with experimental results[31] and calculations on 2-buten-2-ol isomers and other "simple enols."[32] Apart from the general energetic preference of the *syn* forms,[31,32] a further stabilization by an intramolecular hydrogen bond between the enolic OH and a vicinal chloro substituent has been postulated.[33] In contrast, but not unexpectedly, all the other conformers of 3-chloropropen-2-ol are destabilized by 5.0-8.8 kcal/mol.

Compared with chloroacetone, the energy difference between **1,1,1-TrCA** (which adopts a staggered conformation) and its most stable enol (**c1**) is larger (E_{rel} = 13.9 kcal/mol). Moreover, it turns out that **1,1,3-TrCA** is thermodynamically more stable than **1,1,1-TrCA**, at least with respect to their most stable conformers. As for the latter, the structures may be compared with those of **1,1-DiCA** and **1,3-DiCA**, where results of *ab initio* calculations, vibrational spectroscopy and gas phase electron diffraction (**1,3-DiCA**) have been presented.[34,35]

The **1,1-DiCA** molecule exists as two rotameric forms in the vapor and the liquid phases. In the gas phase, the conformer with both chloro substituents in the *anticlinal* position is the most stable. The *sp* conformation becomes more abundant in the liquid and is the only form present in the annealed solid.[34] In the case of **1,3-DiCA**, three potential minima were found; the *ac-ac* conformer is the most stable in the gas phase, albeit the energy difference between the *ac-sp* and *sp-sp* conformations is very small (0.5 and 1.6 kcal/mol, 2.18 and 6.69 kJ/mol).[35]

For **1,1,3-TrCA**, the *sp-ac* conformation -which can be considered as a modification of (*ac-ac*)-**1,3-DiCA** or (*ac*)-**1,1-DiCA**- is calculated to be the most stable, followed by the *sp-sp* conformation (*Table 2*). Remarkably, all the *enols* from **1,1,3-TrCA** have the lowest relative energy in this series of chloroacetones, and the difference between the most stable trichloroenols **d1** and **e1** is very small (ΔE = 0.7 kcal/mol).

Finally, the enols **f1** (*syn*) and **f2** (*anti*) derived from pentachloroacetone do not differ much in energy (ΔE = 0.6 kcal/mol), but are over 12 kcal/mol higher than the ketone conformers. The latter should prefer the *sp-sc* arrangement (*Table 2*).

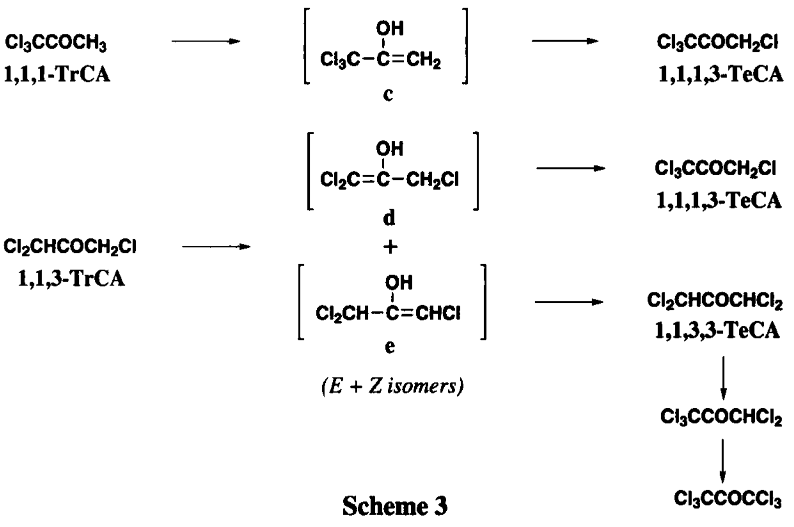
In summary, the calculations suggest that the energy differences between the chloroketones and their enols are of the same order of magnitude as in the case of the parent (unhalogenated) ketones (cf. ΔE_{tot} = 14.38 kcal/mol for acetone,[32] ΔE_{tot} = 13.85 for 2-butanone[32]). If the rate of chlorination was controlled by the activation energy of the enolization step -as is well known for acetone- the fact that higher temperatures are required to chlorinate the tri-and tetrachloroacetones, is difficult to understand. From that fact, one might conclude that polysubstitution of the enolic double bond makes it less nucleophilic and, consequently, leads to increased deactivation toward electrophilic attack by chlorinating species. It is thus understandable that the nature of the latter can influence the regioselectivity of polychlorination.

A simple thermochemical reasoning based on these calculations helps rationalize the fact that chlorination of chloroacetone leads preferencially to **1,1-DiCA** (and then **1,1,1-TrCA**), while chlorination of **1,1,1-TrCA** is retarded. On the other hand, **1,1,3-TrCA** is not expected to exhibit a large regioselectivity on chlorination, although the thermodynamically most stable *enol* **e1** would react to form **1,1,3,3-TeCA**.

3. Experimental Results

In order to investigate the effect of hydrogen chloride in the absence of other catalysts, we prepared a solution of gaseous, dry HCl in acetone. When chlorine gas was passed through this solution at ambient temperature, there was an exothermic reaction which required cooling. After 4 hours, chlorination at 25-30°C resulted in a mixture of di-, tri- and tetrachlorinated acetones, corresponding essentially to Bugrova's results (*see above*).[7] Since our goal was to prepare pentachloroacetone, the chlorination was continued until chlorine gas escaped from the reaction mixture, and the temperature was finally raised to 80°C. However, after 8.5 hours only traces of pentachloroacetone could be detected; the main product was **1,1-DiCA**, and minor amounts of the two trichloroacetones. This finding is in line with Rappe's results for acid-catalyzed deuteration reactions in the deuterioacetic acid/D_2O/DCl system, namely that 'the introduction of one, two or three halogens decreases the proton mobility.'[36] The cause may be that the basicity of the carbonyl oxygen is decreased by an α-chloro substituent.[20,37] The rate of *enol* formation will thus be slower and the substitution of each successive halogen becomes more difficult. Therefore, co-catalysts are required to accelerate the polychlorination.[20]

In order to assess the reactivity of the products formed at an early stage of chlorination, we investigated the chlorination of chloroacetone and **1,1-DiCA**, respectively, under Bugrova's conditions, *i.e.* without a solvent and with pyridine catalyst at 70-80°C with the goal of obtaining pentachloroacetone. Compared with the chlorination of acetone, the reactions of chloroacetone and **1,1-DiCA** with chlorine were less exothermic at the beginning. Starting with chloroacetone, after 7.75 hours reaction time, the main products were pentachloroacetone and hexachloroacetone, as expected. However, a considerable portion of chloroacetone was transformed only into **1,1,1-TrCA**; the ratio was approximately 65:16:19 (pentachloroacetone:hexachloroacetone:**TrCA**). After 4 hrs, essentially the same result was obtained with **1,1-DiCA**, the ratio of pentachloroacetone to **1,1,1-TrCA** being *ca.* 10:1. These findings substantiate the low reactivity of **1,1,1-TrCA** and demonstrate that chlorination of **1,1,3-TrCA** is preferred, and it may be concluded that the rate of formation of *trichloroenol* **c** is retarded and slower than that of *enols* **d** and **e** (*Scheme 3*).



Scheme 3

For the record, chlorination of chloroacetone or of ***1,1-DiCA*** *gives* ***1,1,1-TrCA*** *in a greater or lesser extent and it must be removed by distillation.* Fortunately, the boiling point of **1,1,1-TrCA** is ca. 45°C lower than those of most of the polychloroacetones (*Table 1*). *However, as we repeatedly observed,* ***1,1,3-TrCA, 1,1,3,3-TeCA*** *and pentachloroacetone seem to form a ternary mixture whose boiling point is lower than that of pure tetra- and pentachloroacetones.*

Thus it follows that the most selective process for the preparation of **1,1,3-TrCA** (and ultimately of pentachloroacetone), would start from 1,3-dichloro-2-propanol.[13] However, chromate is used for the oxidation of the dichlorohydrin to **1,3-DiCA**[38] and, to the best of our knowledge, no environmentally friendly procedure exists as of yet.

4. 1,1,1,3-Tetrachloroacetone (1,1,1,3-TeCA)

As far back as 1932, Arndt[39] observed that **1,1,1-TrCA** is suprisingly resistant toward further chlorination; **1,1,1,3-TeCA** is generated after prolonged heating with one equivalent of *sulfuryl chloride* at 180°C.[40,41] If environmental problems and waste disposal are taken into consideration, the synthesis of **1,1,1,3-TeCA** by photochlorination of **1,1,1-TrCA**, evidently a free-radical process, seems to be the preferable route. No further chemicals are required, but special equipment must be used.[42]

For a related case, the bromination of 1,1,1-trifluoroacetone, McBee and Burton[43] introduced conc. sulfuric acid as solvent and pointed out that H_2SO_4 promotes formation of the corresponding enol which is attacked rapidly by the halogen. In line with that result, a patent[44] claims that the reaction of **1,1,1-TrCA** with dichlorine in the presence of conc. sulfuric acid at 50°C gave **1,1,1,3-TeCA** in 46.5% conversion, in addition to pentachloroacetone (2.6%); 51% of **1,1,1-TrCA** was recovered.[44] In our hands, chlorination, according to the patent protocol, of **1,1,1-TrCA**, -which is a non-irritating liquid with no unpleasant smell[39] in contrast to **1,1,3-**

TrCA which has 'a sharp odor and a lacrimatory effect'[7]- led, after 6 hours, to a 35% conversion of the trichloroketone (**1,1,1-TrCA**), to produce a mixture of **1,1,1,3-TeCA** and pentachloroacetone in the ratio of 88.6:11.4. A further experiment, using more dichlorine (saturation of the reaction mixture, 8 hours at 50°C), resulted in a mixture of 48% **1,1,1,3-TeCA**, 47% pentachloroacetone and (unreacted) **1,1,1-TrCA** (5%), *i.e.* a 95% conversion of **1,1,1-TrCA**. These two experiments are once more consistent with the view of a low basicity of the carbonyl group of **1,1,1-TrCA**[37] that must be compensated by a strong proton donor, and show that the rates of the first steps in formation of **1,1,1,3-TeCA** and its chlorination product pentachloroacetone are of comparable order. Hence, a selective synthesis of **1,1,1,3-TeCA** can be achieved only if the chlorination of **1,1,1-TrCA** is run at low conversions (≤ 50%). For laboratory work, this procedure does not seem to be useful.[45] However, exhaustive chlorination of **1,1,1-TrCA** could be used for a synthesis of hexachloroacetone (*see below*).

5. 1,1,3,3-Tetrachloroacetone (TeCA)

The symmetrical **1,1,3,3-TeCA** is anticipated to be formed by chlorination of *(Z)*- and/or *(E)*-1-dichloromethyl-2-chloroethenols (**e1-e4**) (*Scheme 2, p. 555*). However, reaction of **1,1,3-TrCA** with *dichlorine* in presence of pyridine requires higher temperatures (70-80°C, *see below*) and leads to pentachloroacetone and finally to hexachloroacetone (*vide infra*). Evidently, the reaction rate of **1,1,3,3-TeCA** is comparable to that of **1,1,3-TrCA** and of pentachloroacetone. In line with the behavior of **1,1-DiCA**,[40] the reaction of **1,1,3-TrCA** with *sulfuryl chloride* is also slow. When a mixture of these components was heated at reflux (70-80°C), essentially no conversion was observed after 7 hours.[41]

Mioskowski *et al.*[46] introduced tetraethylammonium *trichloride*, generated from tetraethylammonium chloride and dichlorine, as a versatile reagent for chlorinations (and oxidations). Higher quaternary ammonium polychlorides have been used as reagents for chlorination of other unsaturated compounds.[47] Being unaware of these communications at the time, we also found that the reaction of **1,1,3-TrCA** with *sulfuryl chloride* is accelerated by adding *benzyltriethylammonium chloride* (TEBA), albeit only moderately.[48] Carrying out the reaction at 55°C with a 90% conversion (7 days) led to **1,1,3,3-TeCA** as the main product (86%) in addition to pentachloroacetone (4%). However, as mentioned earlier, rectification of the chlorination product was not straightforward and distillation had to be repeated to afford >98% pure **1,1,3,3-TeCA** in 72% yield.

One may speculate that the 'salt effect' of TEBA would no doubt enhance the concentration of chloride ions and the 'polarity' of the reaction medium.[49] An investigation of the monochlorination of acetaldehyde by Gorshkov *et al.* showed that in CCl_4, chosen as a non-polar solvent, HCl/carbonyl complexes are first intermediates. The α-C-H bonds are activated by interaction with the lone pairs of the chlorine atom of a second HCl molecule.[17] On the basis of these authors' findings, the chlorination of chloroacetones (at later stages) would be expected to proceed *via* a complex **A** that then rearranges to the corresponding *enol* intermediate. One might speculate that, in the presence of a quaternary ammonium chloride (or the hydrochlorides of pyridine, quinoline, amines), one HCl molecule might be replaced by an ammonium and a chloride ion (**B**). The latter, presumably, acts as a base, stronger than Cl-H, thus abstracting an α-proton. Time constraints did not permit us to optimize the reaction by variation of the concentration of TEBA and of the reaction temperature.

A **B**

Fig. 1

It occurred to us that exhaustive chlorination of commercially available acetone-dicarboxylic acid (also easily prepared by decarbonylation of citric acid[50]) followed by decarboxylation, would result in a more selective preparation of **1,1,3,3-TeCA**. However, this diacid is a solid and hence must be made to react in solution. It is not readily soluble in dichloromethane, and chlorination of this mixture with *sulfuryl chloride* proved to be very slow and non-selective. Even at a mild temperatures (5-35°C), the product contained 50% pentachloroacetone. With diethyl ether as a co-solvent, the reaction can be performed at a lower temperature (–5 to 0°C). Nevertheless, the resulting **1,1,3,3-TeCA** was contaminated by small amounts of **1,1,3-TrCA** and pentachloroacetone (ca. 10%). It could be purified by crystallization of its tetrahydrate which formed in 70-80% yield. We later observed that the outcome of this chlorination depends on the quality of the acetonedicarboxylic acid. Best results were obtained when it was prepared immediately before use.[50] With the commercial product, a longer reaction time or a higher temperature had to be applied resulting in increasing amounts of pentachloroacetone that were difficult to remove. We suspect that an unknown impurity (possibly traces of sulfuric acid) present in the diacid prepared by us had a catalytic effect. Since this study could not pursued further, the chlorination of acetonedicarboxylic acid in the presence of promoters such as TEBA should be reinvestigated thoroughly.

As expected, the reaction of *dichlorine* with acetonedicarboxylic acid in dichloromethane/dimethylformamide[19] was more rapid. However, a large amount of pentachloroacetone (55%) was formed again (45% **1,1,3,3-TeCA**) at 5-10°C. Finally the reader should be aware of an alternate, selective preparation, albeit an expensive and lengthy one, of **1,1,3,3-TeCA** starting with phloroglucinol.[51]

$$HO_2CCH_2COCH_2CO_2H \longrightarrow HO_2CCCl_2COCCl_2CO_2H \xrightarrow{-2CO_2} \underset{\textbf{1,1,3,3-TeCA}}{Cl_2CHCOCHCl_2}$$

Scheme 4

6. *Pentachloroacetone*

Bugrova *et al.* stated[7] that 'tetrachloro- and pentachloroacetones are obtained by chlorination (of acetone) at higher temperatures (90-110°C) in presence of pyridine. Exhaustive chlorination of acetone in presence of catalytic amounts of pyridine and substituted amines proceeds with gradual increase of temperature to 120-125°C, giving a quantitative yield of hexachloroacetone of 96-98% purity'; we were able to confirm these findings. In order to save time, the first steps of the chlorination of acetone were omitted and commercial **1,1,3-TrCA** was treated with dichlorine and pyridine promoter. After the reaction had started at 50°C, and the temperature allowed to rise to 100°C, the product was pentachloroacetone and hexachloroacetone in approximately equal amounts after 3 hours. The chlorination was more selective at 70-80°C and led to pentachloroacetone, in addition to 8-9% of hexachloroacetone. As mentioned earlier, rectification of the chlorination products is difficult as long as tetrachloroacetones are present in the mixture. *It is thus preferable to allow hexachloroacetone to be generated to a larger extent* than to stop the chlorination as soon as **1,1,3-TrCA** is no longer present. Ideally, the chlorination should be conducted to the point that tetrachloroacetones (**TeCA**) are no longer present. While the mixture of tetrachloroacetones is difficult to separate from pentachloroacetone, contamination of pentachloroacetone with hexachloroacetone does not affect its use in [4+3] cycloadditions.[3]

Moreover, a further problem became apparent: in our hands, the pentachloroacetone prepared by the Bugrova procedure[7] often became turbid on storing, and finally an oil or a white precipitate formed. Pyridine hydrochloride is volatile under the conditions of the distillation. It has been known for a long time that its hydrochloride has a considerable vapor pressure[52] and thus can be distilled[53] or sublimed[54] and occasionally, the salt clogged the head of the distillation column. In order to circumvent that problem, *quinoline,* and *quinoline hydrochlorides* were investigated as less volatile promoters. Indeed, we were able to obtain clear distillates; and it was further discovered that the hydrochlorides of pyridine or of quinoline can be replaced by TEBA (*see above*). TEBA is superior to these hydrochlorides as a promoter because it is quite soluble in the higher chlorinated acetones and, hence, is effective from the beginning of the chlorination reaction at a steady concentration. In contrast, with increasing reaction time the hydrochlorides of pyridine or of quinoline separate as oils and thus their effectiveness as promoters is partly lost.

7. *Waste Disposal - Hexachloroacetone*

As mentioned above, chlorination of acetone results in more or less parts of **1,1,1-TrCA** that must be removed by distillation. **1,1,1-TrCA** and the higher chlorinated acetones may be disposed by treatment with aqueous sodium or potassium hydroxide solution, which effects a facile haloform cleavage.[55,56] Instead of producing chloroform in this way, we preferred to subject the mixture of **1,1,1-TrCA** to exhaustive chlorination at elevated temperatures (120-125°C), using the Bugrova protocol with pyridine as promoter[7] (other promoters were not investigated in this case) to give hexachloroacetone. According to early patents, antimony trisulfide with iodine[57] or activated charcoal[58] are also suitable as promoters for large scale perchlorination. *Reference 56* should be consulted for the perchlorination in acetic acid. Hexachloroacetone has been used as a reagent for several purposes.[59]

CONCLUSIONS

We have presented here improved methods for the preparation of 1,1,3,3-tetrachloroacetone and pentachloroacetone. These compounds are valuable and, in some cases, irreplacable components for [4 + 3] cycloaddition reactions. The discussion of the polychlorination of acetone shows that both calculations and mechanistic investigations in aprotic media, focussing on heats of formation, relative reaction rates and activation energies of these comparatively simple but fundamental reactions should be investigated.

EXPERIMENTAL SECTION

The chemicals used were commercially available, except **1,1-DiCA** that was a gift from Wacker-Chemie GmbH, Munich. Monochloroacetone and quinoline were distilled before use. Pyridine was dried and stored over KOH pellets. Acetonedicarboxylic acid was prepared from citric acid with oleum.[50] Dichloromethane was dried by refluxing with powdered calcium hydride followed by distillation. Diethyl ether was pre-dried over calcium chloride and distilled over sodium. The chlorinations were performed in a well-ventilated hood. Chlorine gas was dried by bubbling through conc. H_2SO_4. In the initial experiments, the stream of gas was controlled by means of a flowmeter (*Rotameter*™). However, having found that consumption of chlorine is not stoichiometric and that some chlorine gas was escaping the condenser, the progress of the reaction was monitored by GLC and by monitoring the reaction temperature (see the following descriptions).

Although a condenser cooled with Dry Ice would be most effective, we used an efficient reflux condenser with water cooled coil and mantle, accepting losses of acetone and chlorine, and, consequent moderate yields since acetone is cheaper than the Dry Ice needed over several hours. **CAUTION:** ***Care must be taken to allow for an exothermic reaction which often follows a brief induction period!***

For distillation of the chlorination mixtures, 25 cm Vigreux colums with evacuated and silvered mantle were used. The final fractional distillations (rectifications) were carried out by means of Spaltrohr columns, effective length 50 or 80 cm with distillation head and a temperature controlled heating bath (Fischer, D-53340 Meckenheim/Rhein, Germany). The 80 cm column had a heating mantle, the temperature of which and the reflux ratio was controlled by a Minitron 5™ unit.

Progress of reactions and fractionations was monitored by gas chromatography (GLC). For GLC, a Hewlett Packard 5710 instrument with flame ionization detector (FID) 18710A and/or a Carlo-Erba-Fractovap 4200 instrument with FID and integrator was used; analyses were made with programmed oven temperature (80→220°C, heating rate 8 K/min) on a 2.3 m or a 2.0 m glass column, respectively, coated with 5% OV 101 on Volaspher A2, 100-120 mesh. Nitrogen (30 mL/min) was used as carrier gas. The percent values represent the relative peak areas obtained by integration of the FID signals.

The purity and composition of the chloroacetones can be checked by recording ^1H

NMR spectra of the distillation fractions, as described by Geller *et al.*[60] Chemical shifts are compiled in *Table 3.*

Table 3. NMR Chemical Shifts (δ values) of Chlorinated Acetones.

Compound	H-1[a]	H-3[a]	Solvent, Reference	C-1	C-2	C-3	Solvent Reference
Chloroacetone	4.05	2.3	CCl_4, b	48.0	198.4	26.3	CCl_4, c
	4.00	2.30	CCl_4, c	48.9	199.1	27.0	CCl_4, d
1,1-Dichloroacetone	5.90	2.41	CCl_4, e	70.2	193.6	22.1	CCl_4, d
	6.2	2.4	CCl_4, b	70.6	194.3	23.1	C_6D_6, f
	5.75	2.44	$CDCl_3$, g	----	----	----	----
	5.93	2.53	$CDCl_3$, h	----	----	----	----
1,3-Dichloroacetone	4.35	4.35	CCl_4, b	47.0	194.9	47.0	$CDCl_3$, i, j
	4.33	4.33	$CDCl_3$, g	----	----	----	----
1,1,1-Trichloroacetone	----	2.60,	CCl_4, e	96.5	186.3	21.1	C_2Cl_4, k
	----	2.62	$CHCl_3$, e	----	----	----	----
1,1,3-Trichloroacetone	6.21	4.61	CCl_4, e	68.3	189.5	44.5	C_6D_6, f
	6.14	4.58	$CHCl_3$, e	----	----	----	----
1,1,1,3-Tetrachloroacetone	----	4.90	CCl_4, e	93.95	183.35	42.0	$CDCl_3$, h
	----	4.85	$CDCl_3$, h	----	----	----	----
1,1,3,3-Tetrachloroacetone	6.52	6.52	CCl_4, e	65.1	183.3	65.1	CCl_4, k
	6.50	6.50	$CDCl_3$, l	----	----	----	----
Pentachloroacetone	----	6.80	CCl_4, e	92.6	179.7	62.1	C_6D_6, f
	----	6.75	$CDCl_3$, l	92.4	178.8	61.6	CCl_4, k
Hexachloroacetone	----	----	----	88.7	173.6	88.7	CCl_4, k

a) Singlet. b) E. Vilsmaier, *Ann.,* **735**, 23 (1970). c) R. Rittner, J. A. Vanin and B. Wladislaw, *Magn. Reson. Chem.* **26**, 51 (1988). d) M. Yalpani, B. Modarai and E. Khoshdel, *Org. Magn. Reson.* **12**, 254 (1979). e) B. A. Geller, I. G. Khaskin, L. K. Skrunts, I. V. Migaichuk, G. K. Rudnev, I. S. Shumilov-Karabutov, *Zh. Prikl. Khim.* **54**, 2476 (1981); *J. Applied Chem. USSR,* (Engl. Transl.) **1982**, 2184. f) H. Bauer, J. Buddrus, W. Auf der Heyde and W. Kimpenhaus, *Angew. Chem.* **97**, 860 (1985). g) C. J. Pouchert, *The Aldrich Library of ^{1}H NMR Spectra,* Edition II, Vol 1., Aldrich Chemical Co., Milwaukee, 1983, p. 380 (figure). h) This work. i) I. Suryanarayana and J. Gasteiger, *Indian J. Chem. Sect. A,* **27A**, 932 (1988). j) J. Barluenga, L. Llavona, J. M. Concellón and M. Yus, *J. Chem. Soc. Perkin 1,* 417 (**1990**). k) W. Kimpenhaus and W. Auf der Heyde, *Ann.,* **1983**, 378. l) C. J. Pouchert, *The Aldrich Library of ^{1}H NMR Spectra,* Edition II, Vol 1., Aldrich Chemical Co., Milwaukee, 1983, p. 381 (figure).

1,1,3,3-Tetrachloroacetone (1,1,3,3-TeCA) by Reaction of 1,1,3-Trichloroacetone (1,1,3-TrCA) with Sulfuryl Chloride.- Benzyltriethylammonium chloride (TEBA) (1.64 g, 7.2 mmol, 1.5 mol-%) was dissolved in **1,1,3-TrCA** (50 mL, 474.0 mmol) and mixed with sulfuryl chloride (39 mL, 480.0 mmol); the flask was protected from moisture by means of a calcium chloride drying tube. The mixture was heated with magnetic stirring at 55°C (oil bath temperature) in a darkened hood for 3 days. The progress of the reaction was monitored by GLC. Since the reaction was incomplete after this time, additional SO_2Cl_2 (20 mL, 246.0 mmol) was added and heating was continued for 2 days (GLC); a further 10 mL of SO_2Cl_2 (123.0 mmol) was added once more, and the mixture heated again for 2 days. At that point, the reaction mixture consisted of unreacted **1,1,3-TrCA** (11%), **1,1,3,3-TeCA** (83%) and pentachloroacetone (6%) according to GLC.The liquid was rectified using a 50 cm Spaltrohr column at reduced pressure (12 Torr, water aspirator). The temperature of the heating bath was 85°C. The first two fractions boiling below 76.5°C (7.5g) consisted of mixtures of ca. 50% of **1,1,3-TrCA**, besides **1,1,3,3-TeCA** and pentachloroacetone. The last fractions (*Nos 6 and 7*, 51.1g), with bp. 78.0-78.5°C were free from ***TrCA*** and contained ***1,1,3,3-TeCA*** (97-98%), besides small amounts of pentachloroacetone (3-2%). The middle fractions (*Nos 3-5*, 31.6g, bp. 76.4-78°C) were rectified once more. The total yield of ***1,1,3,3-TeCA*** was 66.9 g (72%) with a purity > 98%.

1,1,3,3-Tetrachloroacetone (1,1,3,3-TeCA) from the Reaction of Acetonedicarboxylic Acid with Sulfuryl Chloride.- A 1 L three-necked flask containing a magnetic stir bar, and fitted with a low-temperature thermometer, and an efficient condenser with a gas outlet-tube connected with a bubbler, was charged with sulfuryl chloride (160 mL, 1.98 mol), dry dichloromethane (250 mL) and dry diethyl ether (250 mL). A solids addition funnel with PTFE screw conveyor (Feststoff-Dosiertrichter nach Dr. Humbert, Normag™, D-65719 Hofheim am Taunus, Germany, Catalogue (1995) No. SAA 08080) was attached to the flask. The mixture was cooled to -10°C, and freshly prepared acetonedicarboxylic acid (73 g, 0.50 mol)[50] was added with stirring in small portions by means of the screw conveyor at such a rate that the temperature did not exceed -5°C; this addition required 2.5 hours, and the solution became nearly clear. Towards the end, a vigorous gas evolution (CO_2) sets in. Stirring was continued for an additional hour at 0°C and then overnight while the cooling bath came up to room temperature. Finally the mixture was refluxed until gas evolution ceased. The solvent was removed in a rotary evaporator. Water (200 mL) was ***slowly*** and ***cautiously*** added to the remaining liquid, whereupon more gas evolved vigorously. The solution was cooled in a refrigerator whereupon the tetrahydrate of ***1,1,3,3-TeCA*** crystallized as colorless needles (98.4 g, 73%), mp. 45-46°C, *lit.*[51] 48-49°C.

In order to remove the water of hydration, a small amount of diethyl ether was added; the crystals dissolved and two layers formed. The aqueous layer was separated and extracted with ether. The combined ethereal solutions were dried over calcium chloride. The ether was evaporated and the remaining liquid distilled *in vacuo* over P_4O_{10}. A GLC showed that the distillate, bp. 65°C/12 Torr, was better than 99% pure. An alternative method for the dehydration is azeotropic drying with benzene.[35] Note that for [4+3] cycloaddition reactions, the hydrate has been used instead of the ketone (**1,1,3,3-TeCA**).[2a]

Pentachloroacetone from Acetone.

Procedure (a) with TEBA.- A 500 mL three-necked flask containing a magnetic stir bar and fitted with an efficient condenser, a gas inlet tube and a thermometer dipping into the liquid was charged with acetone (200 mL, 2.72 mol, *technical grade*) and TEBA (1.0 g, 4.4 mmol, 0.16 mol-%). Then chlorine gas was bubbled slowly into the solution.

CAUTION: A cooling bath should be made ready. Care must be taken to allow for an exothermic reaction which often follows a brief induction period! However, at the beginning, cooling should not be too strong because accumulated chlorine may react with extreme violence!

The rate of chlorine addition was regulated so that the temperature did not exceed 40°C. After 2 hours, the temperature was allowed to rise slowly to 70°C and chlorination was continued for 6-7 hours; some chlorine gas escaped through the condenser. Finally, the temperature began to drop and steady escape of chlorine was observed. Then additional TEBA (3.0 g, 13.17 mmol, 0.48-%) was added and the mixture heated in an oil bath at 70°C; chlorine was passed continuously for 15 hours. The progress of the reaction was monitored by GLC. The final composition of the mixture was **1,1,1-TrCA** (3%), **TeCA** (1%), pentachloroacetone (69%) and hexachloroacetone (29%).

Volatile products were separated from TEBA by distillation using a 25 cm Vigreux column. The distillate was rectified using a 80 cm Spaltrohr column at reduced pressure (water aspirator, 12 Torr) to yield 271.5 g (43%) of pentachloroacetone, bp. 71°C in better than 99% purity and an additional 52.0 g (8%) of 97% purity, contaminated with 3% **TeCA**.

Procedure (b) with Quinoline.- A solution of quinoline (14.2 g, 0.11 mol, 4.0 mol-%) in 200 mL (2.72 mol) of acetone was treated with chlorine gas as described in *Procedure (a)*. In order to avoid a strong exothermic reaction after the usual induction period, the chlorine gas was diluted with nitrogen (1:1 v/v). After the reaction had started (ca. 10 min.), the nitrogen stream was turned off and the rate of chlorine addition regulated such that the temperature of the mixture remained between 35 and 40°C. After 3 hours, the temperature of the chlorination mixture was allowed to rise to 50-60°C, and the chlorination continued. When the temperature dropped (after 18 hours) and some chlorine gas was escaping the condenser, the mixture was heated in an oil bath at 65-70°C; chlorine was passed more slowly for 13 hours. The mixture was allowed to cool to room temperature, and the thin oily layer which formed on the surface and consisting mainly of quinoline hydrochloride, was removed using a separatory funnel. Distillation of the lower phase chlorination product using a 20 cm Vigreux column at reduced pressure (water aspirator) gave a forerun (**1,1,1-TrCA**), bp. 30-35°C/20 Torr (41.5 g, **1,1,1-TrCA** with 94% purity), followed by the main fraction (bp. 65-70°C/12 Torr, 280 g) consisting of a mixture with 85% pentachloroacetone, 6% hexachloroacetone and 4% tetrachloroacetone. The mixture was rectified by means of a 80 cm Spaltrohr column (reflux ratio 5:1, heating mantle 55-60°C) at reduced pressure (water aspirator, 12 Torr). The first fractions contained **TeCA**, and hence were redistilled. A total of 140.6 g of pentachloroacetone (22%) in > 99% purity was obtained.

Procedure (c) with Quinoline Hydrochloride.- A solution of quinoline hydrochloride (8.3 g, 50.0 mmol, 4.7 mol-%) in acetone (62 mL, 0.845 mol) was treated with chlorine as described in the preceeding experiment. Distillation using Vigreux column gave 11.7 g of **1,1,1-TrCA** (94% purity) and a 71:29 mixture of pentachloroacetone and hexachloroacetone (107 g). Rectification of the latter mixture using a Spaltrohr column gave 49 g (25%) of > 99% pure pentachloroacetone.

Procedure (d) with Pyridine.- A solution of pyridine (3.3 mL, 41.0 mmol, 3.0 mol-%) in acetone (100 mL, 1.36 mol) was treated with chlorine gas as described under *Procedure (b).* In order to avoid a strong exothermic reaction following the usual induction period, the chlorine gas was mixed with nitrogen (ca. 1:1 v/v). When the reaction had started (5-10 min), the nitrogen stream was turned off and the rate of chlorine addition regulated such that the temperature of the mixture remained between 35 and 50°C; occasionally ice water was used for cooling. Toward the end of the vigorous reaction, the temperature of the chlorination mixture was allowed to rise to 60°C, and the chlorination continued. When the temperature had dropped and some chlorine gas was escaping the condenser, the mixture was heated in an oil bath at 60-80°C; chlorine was passed slowly. The progress of the chlorination reaction was monitored by GLC. When the peak of tetrachloroacetone had reached a minimum, chlorination was stopped and nitrogen was bubbled into the mixture. After the mixture had reached room temperature the thin oily layer which formed on the surface and consisting mainly of pyridine hydrochloride, was removed. The lower phase chlorination product was distilled using a 20 cm Vigreux column at reduced pressure (water aspirator). The fractions between 59 and 64°C were collected (145.3 g) and rectified using a 80 cm Spaltrohr column at reduced pressure giving 113.8 g (0.49 mol, 36%) of pentachloroacetone in > 95% purity.

Pentachloroacetone by Chlorination of 1,1,3-Trichloroacetone.- A 250 mL three-necked flask equipped with magnetic stir bar and fitted with an efficient condenser, a gas inlet tube and a thermometer dipping into the liquid, was charged with 1,1,3-trichloroacetone (53 mL, 0.50 mol) and dry pyridine (1.0 mL, 12.5 mmol, 2.48 mol-%). It was heated in an oil bath to 70-80°C. Then, chlorine gas was passed into the solution. The progress of the chlorination reaction was monitored by GLC. After 2.5 hours, **1,1,3-TrCA** had disappeared and pentachloroacetone was the main product, in addition to **1,1,3,3-TeCA** (2%) and hexachloroacetone (3%). Chlorination was continued for 30 min, whereupon chlorine gas escaped in increasing amount. The GLC showed peaks for pentachloroacetone and hexachloroacetone in the ratio of ca. 91:9; the peak for **1,1,3,3-TeCA** had almost vanished. At this point, the chlorination was interrupted. Nitrogen was allowed to bubble through the reaction mixture, and the oil bath removed. When the mixture had reached room temperature, the precipitated crystals (pyridine hydrochloride) were filtered off. The liquid (113 g) was distilled *in vacuo* (water aspirator) using a Vigreux column to give 106 g of a mixture consisting of pentachloroacetone (92%) and hexachloroacetone (8%). This product may be used for [4 + 3] cycloadditions[3] without further purification which can be performed by rectification using a Spaltrohr column.

Acknowledgements.- Financial support by the Fonds der Chemischen Industrie is gratefully acknowledged. Dirk Zierer, Dirk Bongert, Michael Baumhauer, Oliver Schwarz, Frank Schaller, and Jochen Theloke made experimental contributions to this work. We would like to thank Dr. Guntram Rauhut, University of Stuttgart, for the calculations and Prof. J.-P. Anselme, University of Massachusetts Boston, for his help in improving the text.

REFERENCES

1. a) B. Föhlisch, D. Krimmer, E. Gehrlach and D. Käshammer, *Chem. Ber.*, **121**, 1585 (1988). b) K. Lee and J. K. Cha, *J. Am. Chem. Soc.*, **123**, 5590 (2001). c) L. C. Usher, M. Estrella-Jimenez, I. Ghiviriga and D. L. Wright, *Angew. Chem.* **114**, 4742 (2002); *Angew. Chem. Int. Ed.* **41**, 4560 (2002).

2. a) B. Föhlisch, W. Gottstein, R. Herter and I. Wanner, *J. Chem. Research (S)*, 246 (**1981**). b) R. Herter and B. Föhlisch, *Synthesis*, 976 (**1982**). c) M. E. Schwenter and P. Vogel, *Chem. Eur. J.*, **6**, 4091 (2000). d) H. Zinser, S. Henkel and B. Föhlisch, *Eur. J. Org. Chem.* 1344 (**2004**).

3. a) B. Föhlisch, E. Gehrlach and B. Geywitz, *Chem. Ber.*, **120**, 1815 (1987). b) S. Sendelbach, R. Schwetzler-Raschke, A. Radl, R. Kaiser, G. H. Henle, H. Korfant, S. Reiner and B. Föhlisch, *J. Org. Chem.*, **64**, 3398 (1999). c) B. Föhlisch, H. Korfant, H. Meining and W. Frey, *Eur. J. Org. Chem.*, 1335 (**2000**).

4. For an overview see: a) B. J. Weimann, U. Hengartner, A. de Saizieu and C. Wehrli, *'Folic acid'* in *Ullmann's Encyclopedia of Industrial Chemistry*, 6th edition, Vol. 38, p. 247, Wiley-VCH, Weinheim, 2003. b) O. Isler and G. Brubacher, in *Vitamine II*, O. Isler, G. Brubacher, S. Gishla and B. Kräutler (eds.), p. 264, Thieme, Stuttgart-New York, 1988.

5. W. Deinhammer and H. Petersen (to Wacker-Chemie GmbH), *Deutsche Offenlegungsschrift* (*Ger. Offen.*) DE 3.605.484 (Cl. C 07 C 49/ 16), Aug. 27, 1987; *Chem. Abstr.*, **107**, 200926w (1987).

6. Investigated between April, 1988 and September, 1998.

7. L. V. Bugrova, G. K. Rudnev, A. I. Khristich, V. I. Radchenko and L. F. Mishchenko, *Zh. Prikl. Khim.* (Leningrad), **46**, 1529-1533 (1973); *J. Appl. Chem. USSR* **2**, 1627 (1973); *Chem. Abstr.*, **79**, 91499q (1973).

8. Reaction with 1 equivalent of chlorine at 20-25°C is reported to furnish a mixture of **1,1-DiCA**, **1,3-DiCA**, **1,1,1-TrCA** and 'tetrachloroacetone' (unspecified) in a 58.6:6.8: 9.8:16.9 ratio.[7] However, addition of these numbers amount to 117.3%!

9. For an overview see: a) R. Verhé and N. DeKimpe, *'Synthesis and Reactivity of a-Halogenated Ketones'*, in *The Chemistry of Functional Groups, Supplement D, The Chemistry of Halides, Pseudohalides and Azides,* Chapter 19, p 813-931, eds. S. Patai and Z. Rappoport, Wiley, Chichester, 1983. b) N. DeKimpe, and R. Verhé, *The Chemistry of a-Haloketones, a-Haloaldehydes and a-Haloimines*, eds. S. Patai, and Z. Rappoport (Updates from the Chemistry of Functional Groups) Wiley, Chichester, 1988. c) For the early literature, see: R. Stroh, *'Herstellung von Chlorverbindungen durch Umsetzungen mit elementarem Chlor'*, in *Methoden der Organischen Chemie (Houben-Weyl)*, Vol. 5/3, *Halogenverbindungen*, p 615-618, eds. E. Müller, O. Bayer, H. Meerwein and K. Ziegler, Thieme, Stuttgart, 1962.

10. D. P. Wyman and P. R. Kaufman, *J. Org. Chem.*, **29**, 1956 (1964).

11. E. E. Gilbert and C. Woolf (to Allied Chemical & Dye Corp.), US Patent 2 635 118, Apr. 14, 1953; *Chem. Abstr.* **48,** 7051g (1954).

12. T. Nakamichi, H. Nonaka and Y. Goto (to Central Glass Co., Ltd., Japan), Jap. Patent 11246465 A2, Sept. 14, 1999; quoted from *Chem. Abstr.*, **131,** 199416 (2000).

13. This reaction has been performed: G. K. Rudnev, A. I. Khristich, V. I. Radchenko and M. M. Filimonova, *Zh. Prikl. Khim. (Leningrad),* **45,** 923 (1972); *J. Appl. Chem. USSR,* **1,** 951 (1972); *Chem. Abstr.*, **77,** 47868u (1972).

14. Z. Bankowska, *Roczniki Chem.*, **33,** 1319 (1959); *Chem. Abstr.*, **54,** 10841e (1960). This author investigated chlorination in protic acidic media, and found ratios of 5.26-7.14 for **1,1-DiCA/1,3-DiCA**.

15. Z. Bankowska, *Roczniki Chem.*, **32,** 739 (1958); *Chem. Abstr.*, **53,** 4117a (1959).

16. W. Polaczkowa and Z. Bankowska, *Roczniki Chem.*, **30,** 119 (1956); *Chem. Abstr.*, **51,** 205c (1957).

17. For the mechanism of *acetaldehyde* chlorination in a non-polar solvent, see: a) S. V. Gorshkov, Yu. A. Kolbanovskii, T. L. Lebedeva and A. Ya. Rozovskii, *Kinet. Katal.*, **38,** 817 (1997); *Kinet. Catal. (English Transl.),* **38,** 747 (1997); *Chem. Abstr.*, **128,** 127643 (1999). b) S. V. Gorshkov, Yu. A. Kolbanovskii, T. L. Lebedeva and A. Ya. Rozovskii, *Kinet. Katal.*, **39,** 12 (1998); *Kinet. Catal. (Engl. Transl.),* **39,** 8 (1998); *Chem. Abstr.*, **128,** 243644 (1999).

18. A. F. Hegarty, J. P. Dowling, S. J. Eustace and M. McGarraghy, *J. Am. Chem. Soc.*, **120,** 2290 (1998).

19. L. De Buyck, G. Detienne and M. Boelens, *Bull. Soc. Chim. Belges,* **103,** 21 (1994).

20. For the chlorination of *aldehydes* see a) F. Bellesia, L. De Buyck and F. Ghelfi, *Synlett.,* 146 (**2000**). b) F. Bellesia, L. De Buyck, F. Ghelfi, E. Libertini, U. M. Pagnoni and F. Roncagli, Tetrahedron, **56,** 7507 (2000). Following this reasoning, acetone is more basic than an aldehyde and, hence in the latter case, two α-chloro substituents can be introduced easily.

21. Upon bubbling chlorine gas into solutions of pyridine, quinoline, triethylamine, or dimethylformamide in acetone, a white smoke formed instantly. No smoke was observed in the absence of these promoters.

22. L. F. Audrieth, A. Long and R. E. Edwards, *J. Am. Chem. Soc.,* **58,** 428 (1936).

23. F. Kaufler and E. Kunz, *Ber. dtsch. Chem. Ges.*, **42,** 385 (1909), there p. 390.

24. a) M. J. Frazer and W. Gerrard, *J. Chem. Soc.*, 3624 (**1955**). b) J. J. Beereboom, C. D. Djerassi, D. Ginsburg and L. F. Fieser, *J. Am. Chem. Soc.*, **75,** 3500 (1953).

25. R. Stroh in *ref.9c*, p. 943.

26. a) A. S. Dneprovskii, I. V. Krainyuchenko, and T. I. Temnikova, *Zh. Org. Khim.* **14**, 1514 (1978). *J. Org. Chem. USSR*, **14**, 1414 (1978). b) For an overview see: A. Varvoglis, *'The Organic Chemistry of Polycoordinated Iodine'*, VCH, Weinheim, 1992. A. Varvoglis, *'Hypervalent Iodine in Organic Synthesis'*, Academic Press, San Diego, 1997.

27. G. Rauhut, Institut für Theoretische Chemie der Universität Stuttgart, Pfaffenwaldring 55, D-70569 Stuttgart, Germany; http://www.theochem.uni-stuttgart.de/rauhut. Details can be obtained from the author of these calculations: *e-mail*: rauhut@theochem.uni-stuttgart.de.

28. M. J. Aroney, R. J. W. LeFèvre and A. N. Singh, *J. Chem. Soc.*, **1965**, 564.

29. Z. Pawelka, *J. Mol. Struct.*, **172**, 15 (1988).

30. J. R. Durig, J. A. Hardin, H. V. Phan and T. S. Little, *Spectrochim. Acta Series A*, **45**, 1239 (1989).

31. F. Tureček, L. Brabec and J. Korvola, *J. Am. Chem. Soc.*, **110**, 7984 (1988) and the references cited therein.

32. F. Tureček and C. J. Cramer, *J. Am. Chem. Soc.*, **117**, 12243 (1995).

33. L. Zhu, C.-J. Chen and J. W. Bozzelli, *J. Phys. Chem. A*, **104**, 9197 (2000).

34. J. R. Durig, J. A. Hardin and C. I. Tolley, *J. Mol. Struct.*, **224**, 323 (1990).

35. N. Kuze, K. Kobayashi, Y. Masuda, T. Hamada, T. Sakaizumi, O. Ohashi, T. Tsuji, T. Egawa and S. Konaka, *J. Mol. Struct.*, **612**, 171 (2002).

36. C. Rappe, *Acta Chem. Scand.*, **19**, 276 (1965).

37. W. Freiberg, R. Steege, E. Litschko, S. Siegert and C. F. Kröger, *Z. Chem.*, **29**, 144 (1989); *Chem. Abstr.*, **111**, 173513 (1989).

38. a) J. B. Conant and O. R. Quale, *Org. Synth.*, **2**, 13 (1922); *Org. Synth. Coll. Vol.* **1**, 211 (1932). b) S. Torii, T. Inokuchi, S. Matsumoto, T. Saeki and T. Oki, *Bull. Chem. Soc. Jpn*, **63**, 852 (1990).

39. F. Arndt, J. Amende and W. Ender, *Monatsh. Chem.*, **59**, 202 (1932), On p. 215, no experimental details were given but, since the bp. of the components (**1,1,1-TrCA**, bp. 134°C, sulfuryl chloride, bp. 69°C) are lower, an autoclave or a sealed tube must have been used. A printing error (80°C instead of 180°C) is also possible.

40. Attempting to chlorinate **1,1-DiCA** with sulfuryl chloride under radical conditions (AIBN) we also observed a very slow reaction: After 20 hours reflux (70-80°C), the conversion was only 50%; a mixture of **1,1,1-TrCA** and **1,1,3-TrCA** was observed.

41. 3,3-Dichloro-2-butanone follows a similar course; in our hands, two attempts to chlorinate this compound by refluxing it with sulfuryl chloride in dichloromethane led to no reaction

(B. Föhlisch, R. Herter, G. Bühler, unpublished). This ketone is similar to **1,1,1-TrCA** in stereochemistry.

42. M. Kokorudz (to Wyandotte Chemicals Corporation), US Patent 3,361,657, Jan. 2, 1968; *Chem. Abstr.*, **68**, 77755m (1968).

43. E. T. McBee and T. M. Burton, *J. Am. Chem. Soc.*, **74**, 3902 (1953).

44. a) W. W. Levis, Jr. (to Wyandotte Chemicals corporation), US Patent 3,325,545, June 13, 1967; *Chem. Abstr.*, **67**, 73152u (1967). b) French Patent 1,153,416, July 19, 1968; *Chem. Abstr.*, **71**, 60719s (1969).

45. For a preparation from trichloroacetylchloride and diazomethane see: Ch. Gränacher, E. Usteri and M. Geiger, *Helv. Chim. Acta,* **32**, 703 (1949).

46. T. Schlama, K. Gabriel, V. Gouverneur and C. Mioskowski, *Angew. Chem.*, **109**, 2440 (1997). *Angew. Chem. Int. Ed. Engl.*, **36**, 2342 (1997).

47. a) V. M. Zelikman and V. V. Smirnov, *Kinet. Catal.*, (Engl. Transl. of *Kinet. Katal.),* **38**, 595 (1997); *Chem. Abstr.*, **128**, 12995 (1999). b) V. M. Zelikman, V. S. Tyurin, V. V. Smirnov and N. V. Zyk, *Russ. Chem. Bull.*, (English Transl.), **47**, 1541 (1998); *Chem. Abstr.*, **129**, 289736 (1999).

48. H. Zinser, *Dissertation*, Univ. Stuttgart, 1999.

49. For an overview on salt effects, see *e.g.* A. Loupy and B. Tchoubar, *'Salt Effects in Organic and Organometallic Chemistry'*, p.1-6, 43, VCH Weinheim, New York, 1991.

50. R. Adams, H. M. Chiles and C. F. Rassweiler, *Org. Synth. Coll. Vol.* **1**, 10 (1932).

51. T. Zincke and O. Kegel, *Ber. Dtsch. Chem. Ges.*, **22**, 1467 (1889).

52. S. S. Moosath, *Proc. Indian Acad. Sci. Series A*, **48**, 324 (1958); quoted from *Beilsteins Handbuch der Organischen Chemie*, 3. Ergänzungswerk, Vol. 20, p. 2230. For the structure in the gas phase, see S. A. Cooke, G. K. Corlett, D. G. Lister and A. C. Legon, *J. Chem. Soc., Faraday Trans.*, **94**, 837 (1998).

53. L. F. Audrieth, A. Long and R. E. Edwards, *J. Am. Chem. Soc.*, **58**, 428 (1936).

54. D. Klamann, *Monatsh. Chem.*, **83**, 1398 (1952).

55. Ch. Cloëz, *Ann. Chim. (Paris)* [6], **9**, 180 (1886); quoted from *Beilsteins Handbuch der Organischen Chemie*, 4th edition (Hauptwerk), Vol. 2, p. 657.

56. E. G. Edwards, D. P. Evans and H. B. Watson, *J. Chem. Soc.*, 1942 (**1937**); see also W. Gerrard and B. K. Howe, *J. Chem. Soc.*, 505 (**1955**).

57. IG Farbenindustrie AG, French Patent 837 741, Feb. 20, 1939; *Chem. Abstr.*, **33**, 5865^6 (1939); see also ref. 9c.

58. C. Woolf and E. E. Gilbert (to Allied Chemical & Dye Corp.) US Patent 2,635,117, Apr. 14, 1953; *Chem. Abstr.*, **48**, 7051i (1954).

59. For a use in [4+3] cycloaddition reactions see: B. Föhlisch and S. Reiner, *Molecules* **9**, 1 (2004).

60. B. A. Geller, I. G. Khaskin, L. K. Skrunts, I. V. Migaichuk, G. K. Rudnev and I. S. Shumilov-Karabutov, *Zh. Prikl. Khim. (Leningrad)*, **54**, 2476 (1981); *J. Applied Chem. USSR* (Engl. Transl.), **11**, 2184 (1982).

(Received August 13, 2004; in final form October 20, 2004)