REVIEW

The Forgotten Carbonyl Reaction: Chloroacetylation and Bromoacetylation of Carbonyl Compounds

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Halomethyl acetates (**3**) could be prepared from aliphatic, α,β-unsaturated and aromatic aldehydes, as well as from alicyclic ketones with high yields in simple one-pot reactions. Very often, the products didn't have to be purified and could directly be used for synthetic purposes after evaporation of the solvent. Obviously, the 'bad reputation' of the reaction in the literature stemed from the fact that the reactions didn't take place under the best conditions.

Carbonyl compounds (**1**) and acyl halides (**2**) form equilibria which are completely on the side of the halomethyl acetates (**3**) at room temperature (starting with aliphatic and most aromatic aldehydes) and which can be strongly influenced by the reaction parameters. It is crucial to work at low temperature in apolar solvents and to remove (or deactivate) the catalyst before workup.

Reactions may be realized with or without solvents. Side reactions were observed with formaldehyde and acetaldehyde but, with exception of formaldehyde, could be reduced close to zero (see *Fig. 5*). By-products were essentially avoided if the reaction took place in apolar solvents and with a local excess of acetyl chloride. In many cases clean products were available which could directly be used for synthetic purposes.

Halomethyl acetates (**3**) are *bifunctional carbonyl derivatives with two different leaving groups*, whose preparative advantages have been useful for the synthesis of various pentafulvenes, but were especially important for preparing unstable parent fulvenes and fulvalenes.

1. Introduction. – Carbonyl reactions played always an important role in organic chemistry. Therefore, it is quite surprising that a carbonyl reaction which has been discovered around 1900 has been forgotten for many decades. After first experiments by *Henry* [1], *Descudé* reported in 1901 that formaldehyde and acetaldehyde reacted with acetyl chloride (in the presence of *Lewis* acids) to give chloromethyl acetates [2][3]. The reaction remained unnoticed until 1938 when *Kirrmann* applied it to acrolein [4] and then until 1960 when *Euranto* started the first investigation of the scope of the reaction. In several articles, he reported on the synthesis of a series of new chloromethyl acetates [5–7] and was investigating the influence of aldehyde structures and catalysts on the yields as well as the hydrolysis of the products, qualitatively [8].

There are several reasons, why the reaction between carbonyl compounds **1** and acyl halides **2** has rarely been applied so far. The isolation of pure products was difficult [2–4], and the published yields of chloromethyl acetates **3** were surprisingly low [5–7], as the products **3** sometimes were rearranging [4]. Today, we know that in most cases,

[1]) Deceased on May 7, 2015.

the low yields were the result of a destillative fractionation of the products in the presence of the catalyst[2]), so that the reaction has to be revised.

In the course of our synthetic attempts towards pentafulvene [9], heptafulvene [10], and nonafulvene [11], we were interested to obtain bifunctional carbonyl derivatives with two different leaving groups which should react with nucleophiles at low temperature without the possibility of aldol-type side reactions. The simple 'one-pot reaction' of aldehydes with acyl halides in fact gave halomethyl acetates with two different leaving groups (which possibly could even be varied within a certain range) and looked very promising provided that yields and purification could be considerably improved.

In the late 1960's, we successfully improved the procedures and showed that in many cases halomethyl acetates **3** could be prepared at low temperature in nearly quantitative yields. After elucidating the structure of by-products and looking for ways to minimize them, we were studying the influence of reaction parameters on the equilibrium **1** + **2** → **3** and were finally investigating the reaction mechanism which showed similar behavior as the well-known *Friedel–Crafts* acylation.

2. Scope of the Reaction. – 2.1. *Haloalkyl Acetates* (**3a**–**3l**) *from Aliphatic Aldehydes.* Catalyzed by traces of $ZnCl_2$, aliphatic aldehydes easily reacted with acetyl chloride at $-5 \pm 5°$ (see the *general procedure*)[3]). For obtaining pure products and high yields it was important to work at low temperatures and to separate (or destroy) the catalyst before rectification. Under carefully controlled conditions by-products could be avoided and yields were nearly quantitative so that the products **3a**–**3l** didn't even have to be distilled. The only exception was the reaction of paraformaldehyde, where considerable amounts of by-products were observed (*Table 1*). In all the other cases, the reaction sequence was very simple[3]).

By replacing acetyl chloride by acetyl bromide, the equilibrium **1** + **2** → **3** was even more shifted to the right (see later) so that bromomethyl acetates were available with very good yields, too (*Table 1*). Once more, paraformaldehyde was the only exception because by-products were formed which were not easily separated by distillation.

Euranto varied the acyl group in several cases [6][7], but this was not needed for our synthetic applications, as Cl and Br were the better leaving groups anyway. In

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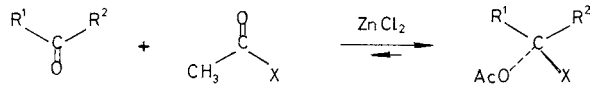
[2]) In most cases, the products have been purified by distillation. If this is done in the presence of the catalyst at a too high temperature, then the equilibrium **1** + **2** → **3** is shifted to the side of the more volatile starting materials!

[3]) *General procedure* [13]: In a dry 3-necked 100 ml-flask equipped with dropping funnel, thermometer, magnetic stirrer, and cooling jacket (topped with a N_2-bubbler) *ca.* 60 mg of anhydrous $ZnCl_2$ were added to 0.33 mol of acetyl chloride **2** (X–Cl). After cooling to $-5°$ and under intensive stirring, 0.3 mol of aldehyde **1** were dropwise added within 20 min. The reaction was exothermic. The mixture was stirred for 45 min at 0°. The catalyst was removed by filtering at 0° through *ca.* 20 g of Al_2O_3 (bas. I, in a small column), followed by rinsing with CH_2Cl_2 (30 ml). After removing the solvent in a rotatory evaporator, another 20 ml of CH_2Cl_2 or Et_2O were added and the solution was concentrated again. The product **3** was checked by NMR, if it could be purified by low-temperature distillation, which was not needed most of the cases. Yields of **3** were usually around 95%.

Table 1. *Haloalkyl Acetates* (**3a**–**3v**) *from Aldehydes and Ketones*



1 **2** X = Cl, Br **3**

Compound	R^1	R^2	X	Yield [%]	Lit.[a])
3a	H	H	Cl	74[b])	[12]
3b	H	H	Br	75[b])	[13]
3c	Me	H	Cl	92	[14]
3d	Et	H	Cl	91	[14]
3e	Pr	H	Cl	95	[14]
3f	^{i}Pr	H	Cl	96	[13]
3g	^{i}Pr	H	Br	95	[15]
3h	Bu	H	Cl	92	[14]
3i	^{i}Bu	H	Cl	97	[13]
3j	^{i}Bu	H	Br	99	[15]
3k	^{t}Bu	H	Cl	95	[13]
3l	^{t}Bu	H	Br	98	[15]
3m	CH=CH_2	H	Cl	68[c])	[15]
3n	AcO–CH=CH	H	Cl	80	[13]
3o	Cl–CH=CH	H	Cl	80	[13]
3p	H–C≡C	H	Cl	94	[14]
3q	2-Furyl	H	Cl	75	[13]
3r	Me	Me	Cl	85[d])	[15]
3s	$(CH_2)_5$	Cl	77[d])	[15]	
3t	$(CH_2)_5$	Br	77.5[d])	[15]	
3u	$(CH_2)_4$	Cl	82[d])	[15]	
3v	$(CH_2)_3$	Cl	93[d])	[14]	

[a]) Literature which contained the experimental procedure. [b]) The distillate contained *ca.* 10% of 1,1′-dichloro- or 1,1′-dibromodimethyl ether, respectively, which were deduced before determining the yield. [c]) Total yield. The distillate contained 90–80 mol-% of **3m** and 10–20 mol-% of (*Z*/*E*)-**4m** (see *Scheme 1*). [d]) Optimal yield: The equilibrium is strongly dependent on the ring size of alicyclic ketones (see *Fig. 3*).

principle however, there would be the option to change the leaving tendency of the AcO group of **3**[4]).

2.2. *Haloalkenyl Acetates* (**3m**–**3q**) *from α,β-Unsaturated Aldehydes. Kirrmann* [4] was the first to investigate the reaction of acrolein with acetyl chloride in the presence of *Lewis* acids and got quite a complex mixture of products[5]). He observed the same (but slower) reaction even without *Lewis* acids (which was then probably catalyzed by traces of acid).

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[4]) It would be easy to *increase* the leaving quality by replacing CH_3COO in **3** by CCl_3COO.

[5]) By accident, both *Descudé* [2][3] and *Kirrmann* [4] were investigating the two reactions with the highest amounts of by-products. This could have been a major reason why the reaction was not applied by chemists!

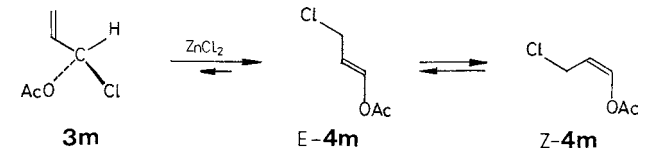
In fact, acrolein reacted with acetyl chloride to give, under kinetic control, 1-chloroprop-2-en-1-yl acetate (**3m**) with a high regioselectivity of *ca.* 95%, which later-on slowly equilibrated by allylic rearrangement to (*E*)-**4m** and (*Z*)-**4m** (*Scheme 1*). $ZnCl_2$ was catalyzing all the processes, so that finally a complex product mixture was obtained (*Fig. 1*), consisting of 10% of **3m**, 40% of (*Z*)-**4m**, and 50% of (*E*)-**4m**.

Much better results were obtained starting with furfural (**1q**), prop-2-ynal (**1p**), 3-acetoxyacrolein (=(1*E*)-3-oxoprop-1-en-1-yl acetate; **1n**) and 3-chloroacrolein (=(2*E*)-3-chloroprop-2-enal; **1o**) where the undesired allylic rearrangement was not observed and products **3n**–**3q** were isolated free of by-products of type **4**. The sensitivity of α,β-unsaturated aldehydes towards polymerization (in the presence of acids and *Lewis* acids) could be seen in a small reduction of the yields (*Table 1*).

2.3. *Haloalkyl Acetates* (**3r**–**3v**) *from Ketones.* Aliphatic, as well as alicyclic ketones, could be reacted with acetyl chloride under appropriate conditions, although at room temperature both starting materials and products could be identified in the equilibrium[6]).

The equilibrium **1** + **2** → **3** was already on the side of the starting materials at room temperature and without solvent for open-chain aliphatic ketones. The product-content was influenced by the length of the aliphatic side chains and was decreasing from 38% (acetone) to 20% (diethyl ketone).

Scheme 1



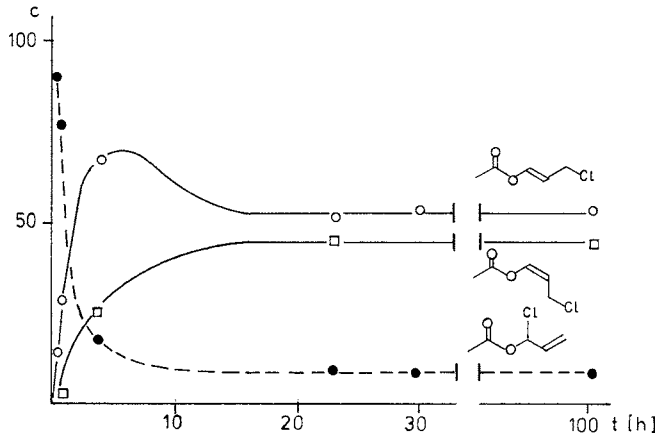


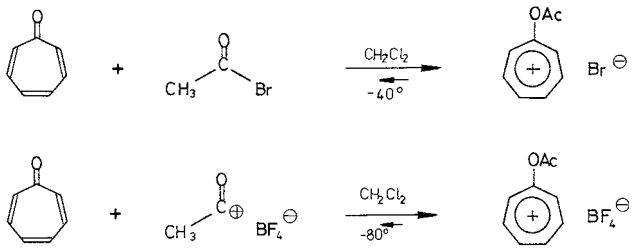
Fig. 1. *Rearrangement of 1-chloroprop-2-en-1-yl acetate* (**3m**; 42°, $ZnCl_2$, without solvent)

6) For more quantitative results concerning parameters influencing the equilibrium, see *Chapter 3.*

For alicyclic ketones, the equilibrium is strongly dependent on the ring size. While for cyclobutanone and cyclohexanone the equilibrium was already on the side of the products **3**, it was on the side of the starting materials for cyclopentanone and cycloheptanone. Despite of that, surprisingly good product yields could be obtained under appropriate conditions (see *Table 1*). In these cases it was important to equilibrate mixtures of **1** + **2** without solvent at low temperature (and to remove the catalyst before workup!).

Preliminary experiments with aromatic ketones (like acetophenone) showed that the equilibrium constant had to be very small. For our synthetic work, *tropone* was a very important ketone. Although there was no visible reaction with acetyl chloride even at low temperature, adding acetyl bromide to a solution of tropone in acetonitrile at $-40°$ gave a yellow precipitate [10] which turned out to be 1-(acetyloxy)tropylium bromide according to X-ray-analysis (*Scheme 2*, top) [16]. As the equilibrium was already on the side of the starting materials at room temperature, tropone preferably reacted with the more electrophilic acetyl fluoroborate at $-80°$ to give 1-(acetyloxy)-tropylium tetrafluoroborate with yields around 70% (*Scheme 2*, bottom). This proved to be the key-compound for the successful synthesis of heptafulvenes and sesquifulvalenes [10].

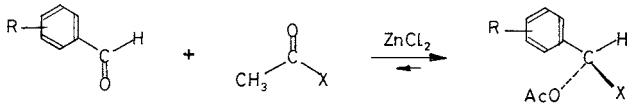
Scheme 2 [10][16]



2.4. *Halo(aryl)methyl Acetates* (**5a**–**5k**) *from Aromatic Aldehydes. Table 2* shows that halo(aryl)methyl acetates **5** were easily available from a variety of aromatic aldehydes. Normally, the equilibrium was strongly on the side of the products **5**, but, in contrast to aliphatic aldehydes, it could already be measured (see *Chapter 3*). Compared with R = H, $-M/-I$-substituents at the benzene ring shifted the equilibrium in direction of the product **5**, while $+M/+I$-substituents shifted it in direction of the starting materials. That's why, starting with *p*-methoxy- or *p*-dimethylaminobenzaldehyde, product yields were decreasing, and by-products were increasing. From a preparative point of view, it was better to start with an excess of acetyl chloride which could easily be removed by distillation. According to *Table 2*, bromo(aryl)methyl acetates **5** were easily available from aromatic aldehydes as well; products like **5h** and **5k** would react more easily with nucleophiles than chloro(aryl)methyl acetates **5g** and **5j**, respectively.

3. Position of the Equilibrium [18]**.** – 3.1. *Influence of the Structure of the Carbonyl Compound*. For aliphatic aldehydes, the equilibrium was strongly on the side of the

Table 2. *Halo(aryl)methyl Acetates* (**5a**–**5k**) *from Aromatic Aldehydes*



1 **2** X = Cl, Br **5**

Compound	R	X	Yield [%][a])	Lit.[b])
5a	4-O_2N	Cl	99	[15]
5b	3-O_2N	Cl	99	[15]
5c	4-CN	Cl	99	[15]
5d	3-Cl	Cl	96	[15]
5e	4-Cl	Cl	96	[15]
5f	4-Br	Cl	97	[15]
5g	H	Cl	97	[13][15]
5h	H	Br	99	[15]
5i	4-F	Cl	96	[15]
5j	4-Me	Cl	99	[15]
5k	4-Me	Br	99	[15]

[a]) Yield after removing the catalyst and the solvent. [b]) Literature with the experimental procedure.

product and could not be measured by ^{1}H-NMR-spectroscopy[7]). On the other hand, equilibrium constants of aromatic aldehydes were quite easily available, although the equilibrium was on the side of the products, too. One started with ca. 10% solutions of pure halo(aryl)methyl acetate **5**, added a trace of $ZnCl_2$ and equilibrated in the NMR instrument. The results are shown in *Fig. 2* and in *Table 3*.

Compared with benzaldehyde ($K_c = 11.2$), the equilibrium constant K_c of the reaction $\mathbf{1} + \mathbf{2} \rightarrow \mathbf{5}$ was increased by $-M/-I$-substituents at the benzene ring. For chlorine in *para*-position the superposition of $-I$- and $+M$-effects can nicely be seen compared with chlorine in the *meta*-position. According to *Fig. 2*, there is a linear relationship between log $K_c/K_{c(0)}$ and *Hammett* substituent constants σ^+ [19][20].

Table 3. *Equilibrium Constants* K_c *of the Reaction* $\mathbf{1} + \mathbf{2} \rightarrow \mathbf{5}$ *of Aromatic Aldehydes*

R of the Aromatic Aldehyde	K_c	Log $K_c/K_{c(0)}$
4-O_2N	50.4	0.644
4-CN	39.3	0.535
3-O_2N	33.8	0.470
3-Cl	18.0	0.196
4-Cl	11.9	0.023
H	11.2	0.000
4-Br	10.3	– 0.046
4-F	6.3	– 0.256
4-Me	4.4	– 0.412
4-MeO	1.4	– 0.910

7) Measurement *ca.* 1974; ^{1}H-NMR-instrument: *Varian A-60A* [17].

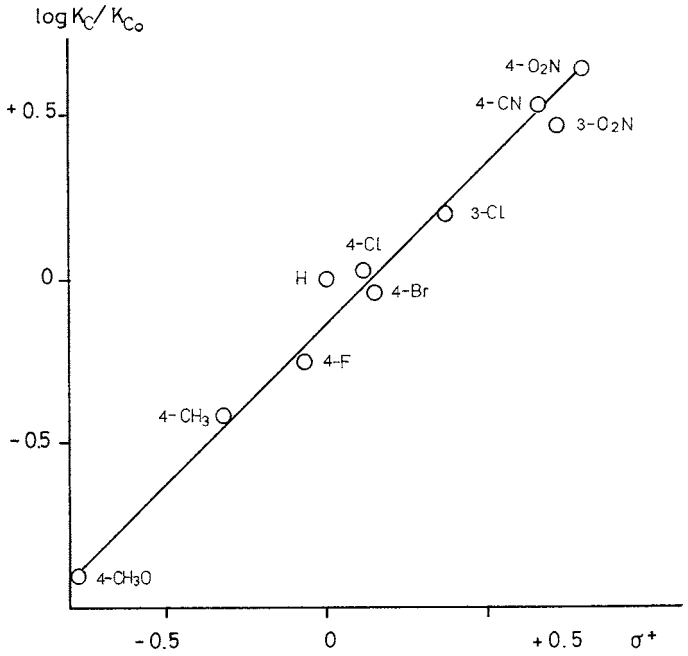


Fig. 2. Hammett *plot of* $\log K_c/K_{c(o)}$ *and* σ^+ *of the reaction* **1** + **2** → **5** *of aromatic aldehydes*

Because of this relationship, we believe that the equilibrium was mainly influenced by the thermodynamic stability of the aromatic aldehyde.

In equilibria of open-chain aliphatic ketones, product content, as well as equilibrium constants, decreased with increasing numbers of C-atoms in the side chains (see *Fig. 3*, bottom). Both steric as well as inductive effects of the alkyl substituents may be responsible. At 20°, equilibrium constants K_c of all the tested ketones were small (K_c between 0.15 and 0.05, some were too small to be measured).

For alicyclic ketones, product contents, as well as equilibrium constants, were strongly dependent on the ring size (*Fig. 3*). While for cyclobutanone and cyclohexanone (without solvent) the product **3** was dominating, the equilibrium for cyclopentanone was already on the side of the starting materials **1** + **2**, and it further decreased from cycloheptanone to cyclooctanone. Without any doubt, steric effects played an important role in these equilibria[8]).

The equilibrium constants of the reactions of aromatic ketones were supposed to be very small. Attempts to react acetophenone with acetyl chloride and to determine the K_c-value were not successful.

3.2. *Influence of the Structure of the Acetyl Halide.* The influence of the halogen atom of the acetyl halide has been investigated by NMR in the system benzaldehyde/acetyl halide [18]. It turned out that equilibrium constants were strongly increas-

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[8]) The 'cyanohydrin-reaction' of alicyclic ketones with HCN [21] showed a very similar dependence of the equilibria on the ring size. For a discussion of the importance of steric effects, see [18].

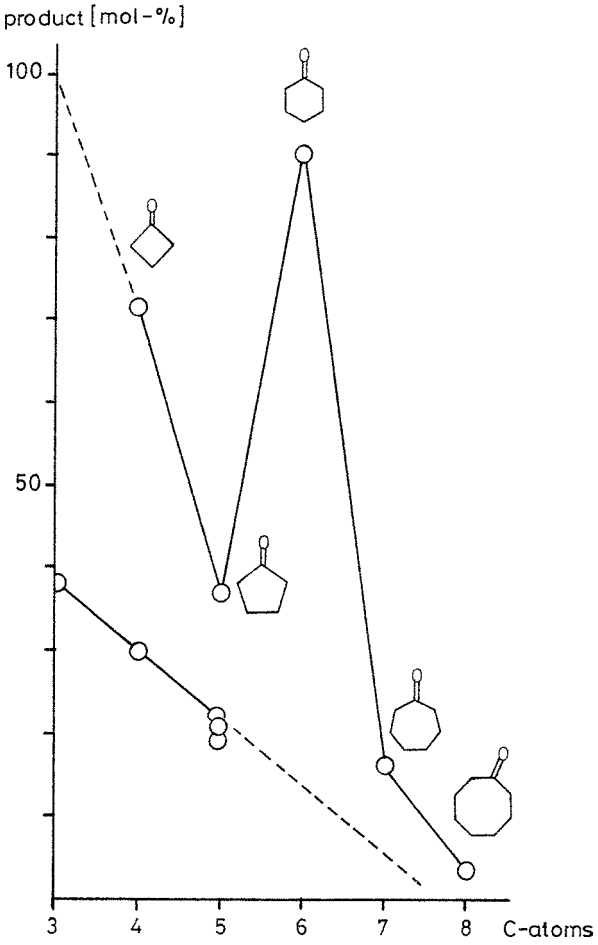


Fig. 3. *Influence of the ring-size* (top) *and the chain length* (bottom) *on the equilibrium* **1**+**2**→**3** *of ketones*

ing from F to Cl, Br, and I[9]), since ΔG^0 gets more and more negative in the same sequence.

3.3. *Influence of Solvent Polarity.* The equilibrium was strongly influenced by the solvent polarity.

In the system benzaldehyde/acetyl chloride, the equilibrium constant K_c was strongly decreasing with increasing solvent polarity. There is a linear correlation between log K_c and the E_T-value according to *Dimroth* and *Reichardt* [22][23]. Our interpretation was that polar solvents were stabilizing the starting materials **1** and **2** [18].

3.4. *Influence of Temperature.* In the course of the reaction between a carbonyl compound and an acetyl halide, one σ- as well as one π-bond were broken, while two

[9]) For more Tables with K_c and discussions of results, see [18].

new σ-bonds were formed. In total, during the reactions **1** + **2** → **3** (*Table 1*) and **1** + **2** → **5** (*Table 2*), a π-bond was transformed into a more stable σ-bond. A qualitative estimate of the bond energies suggested that the reaction enthalpy ΔH^0 should have been negative. On the other hand, the equilibrium should be strongly influenced by the temperature, because two molecules form one product molecule, and the reaction entropy ΔS^0 was supposed to be strongly negative. This was confirmed by the experiments giving $\Delta H^0 = -9.0$ kcal/mol, as well as $\Delta S^0 = -25.2$ cal/K·mol [18] for the formation of **5g**.

3.5. *Summary.* At room temperature, the equilibria **1** + **2** → **3** (*Table 1*), as well as **1** + **2** → **5** (*Table 2*), were favoring the products, starting with aliphatic, α,β-unsaturated and aromatic aldehydes. For open-chain and alicyclic ketones, starting materials, as well as products, were present in the reaction mixture; in the case of aromatic ketones, the starting materials **1** + **2** were strongly favored.

By choosing optimal conditions, high product yields could be obtained even in cases where the equilibrium is relatively unfavorable. Optimal conditions were low reaction temperatures, unpolar solvents, and high concentrations of starting materials, as well as replacing Cl by Br in the acetyl halide. Furthermore, unpolar solvents effectively reduced the amounts of eventual by-products (see *Chapter 4*).

It has to be pointed out again that ideal reaction conditions were useless unless the catalyst was deactivated or separated (*e.g.* by low-temperature filtration) before workup!

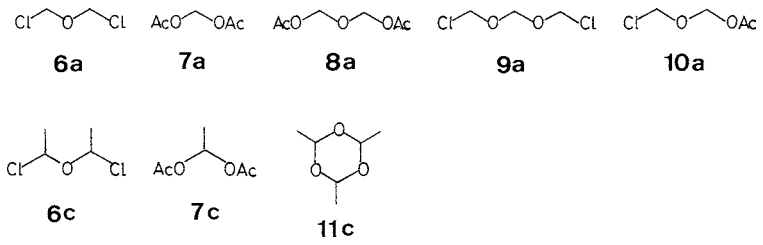
4. By-Products [24]**.** – The first reports concerning the 'chloroacetylation' of carbonyl compounds gave the impression that this new reaction would result in considerable amounts of by-products. *Descudé* [2][3] reported in 1901 that the reaction of paraformaldehyde with acetyl chloride produced acetic anhydride, bis(chloromethyl) ether (**6a**) and methanediyl diacetate (**7a**) besides the main product chloromethyl acetate (**3a**). In 1938, *Kirrmann* [4] reacted acrolein with acetyl chloride and found – besides of the envisaged 1-chloroprop-2-en-1-yl acetate (**3m**) – the products of an allylic rearrangement (*Scheme 1*) which even dominated after equilibration was complete. And later on, *Euranto* [6][7] was pointing at several by-products as well.

Our results showed that – with exception of formaldehyde and acrolein – by-products can be avoided by choosing optimal reaction conditions [24]!

4.1. *Influence of the Structure of the Aliphatic Aldehyde on the Amount of By-Products.* In reactions of aliphatic aldehydes, the most dominant by-products were the bis(chloroalkyl) ethers **6**, as well as the methanediyl diacetates **7** (while normally the concentration of **6** was somewhat higher than that of **7**). Formaldehyde produced by far the highest amount of by-products (then came acetaldehyde) and showed a tendency to form small amounts of oligomeric products as well (*Table 4*). Starting with acetaldehyde the trimer **11c** was formed in the presence of *Lewis* acids and disappeared towards the end of the reaction.

According to *Fig. 4*, the amount of by-products decreased with increasing length of the aliphatic side chain, and it is interesting to note that the amount of bis(chloroalkyl) ethers **6** is always higher than the content of methanediyl diacetates **7**. Highest amounts of by-products were observed for formaldehyde and acetaldehyde. If one connected the results of aldehydes with unbranched side chains (*Fig. 4*), then one observed lower

Table 4. *Isolated or Spectroscopically Identified By-Products in Reactions of Paraformaldehyde and Acetaldehyde with Acetyl Chloride*



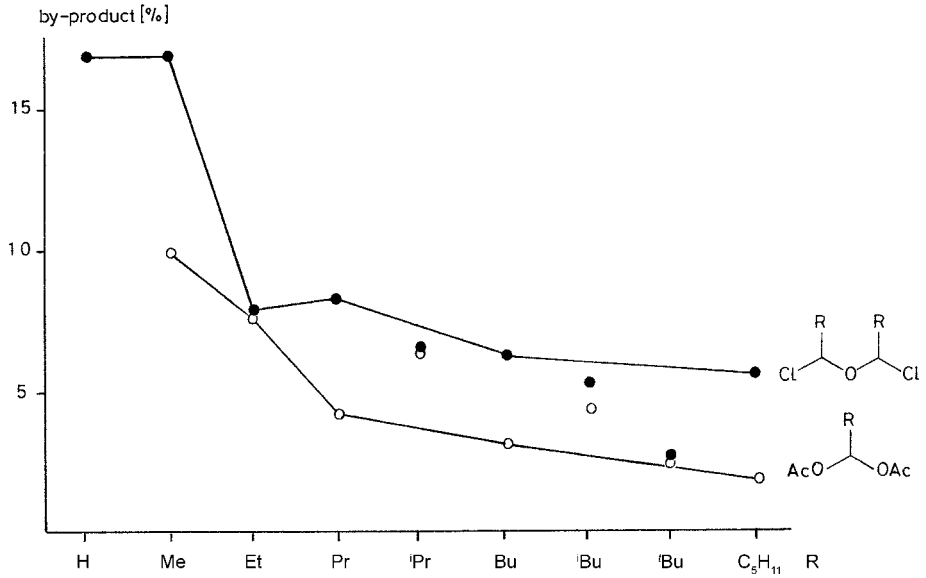


Fig. 4. *Amounts of by-products formed from aliphatic aldehydes* (conditions for a *high content* of **6** and **7**)[10])

contents of **6** for aldehydes branched in α- or β-position than for aldehydes with unbranched aliphatic skeletons. On the other hand, in such cases the content of methanediyl diacetates **7** increased and even approached the content of **6**!

Finally, it is essential to note that the results of *Fig. 4* have been obtained under conditions for a high content of by-products. Under ideal conditions, the amount of by-products dropped dramatically to the range of 1–2% even for acetaldehyde, due to the strong influence of the reaction parameters on the product distribution.

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10) Formaldehyde was reacted as paraformaldehyde, which reduced the amount of by-products. On the other hand, all the other aldehydes were reacted in monomeric form. This increased the amount of by-products [24] and explained the 'inconsistency' of *Fig. 4:* Starting with monomeric formaldehyde, the amount of **6a** would be much higher!

4.2. *Influence of Reaction Parameters* [24]. The influence of the reaction parameters on the content of by-products has been investigated for the example acetaldehyde/acetyl chloride which give the highest amounts of by-products besides of formaldehyde, and where main product **3c**, as well as by-products **6c** and **7c**, were easily recognized in the ^{1}H-NMR spectra.

A minimum content of by-products **6c** and **7c** was observed under the following conditions [24]: in diluted solutions; in unpolar solvents; using an extreme ratio of **1c** and **2** (and especially small concentrations of acetaldehyde (**1c**)[11]); at relatively high concentrations of the catalyst; and at low reaction temperatures.

Fig. 5 impressively shows that in the system acetaldehyde/acetyl chloride the content of the by-products was strongly influenced by the reaction parameters and that it was worthwhile to use optimal reaction conditions. In the example of *Fig. 5*, the product **3c** could directly be used for synthetic purposes without distillation, just after removing the solvent!

4.3. *Explaining the Formation of By-Products.* In order to explain the formation of by-products one had to take the results of kinetic investigations (see later [25]) into account, which supported a mechanism proceeding over ionic or at least polar intermediates and which supported the reaction of an 'O-complexed acetyl chloride' with the carbonyl oxygen (see *Scheme 3*, top row) as rate-determining step. The hereby formed ionic intermediate **12** could either be stabilized by intramolecular transfer of chloride (to give the main product **3**), or by reaction with a second molecule of aldehyde (**12** → **14**, which was facilitated at a high concentration of the aldehyde). If the

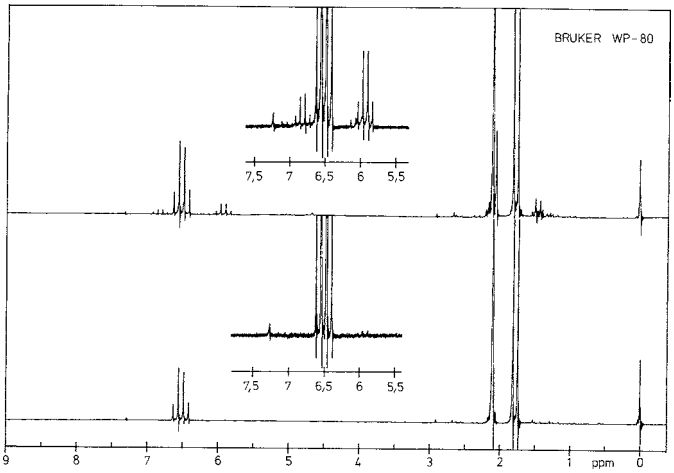
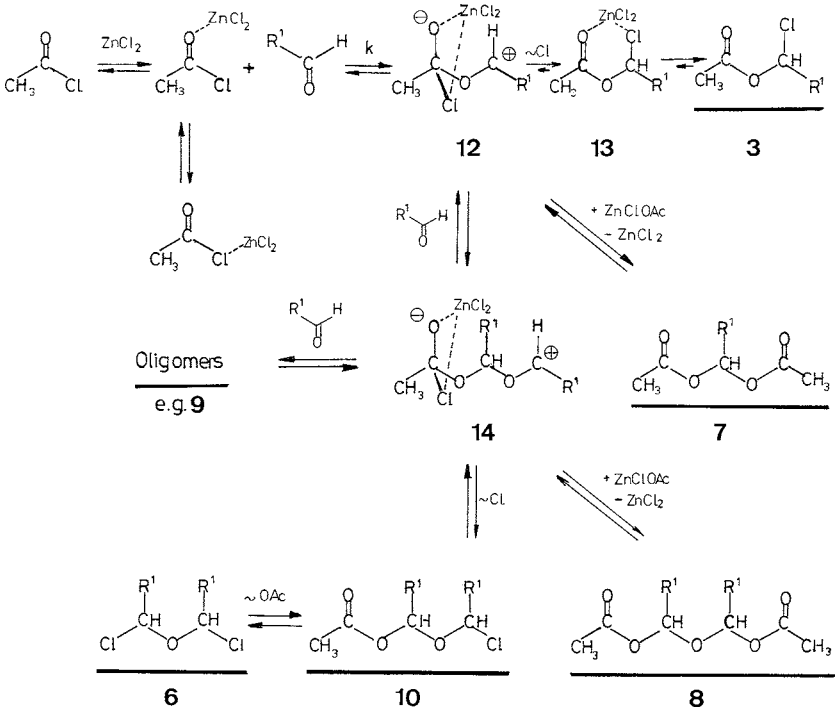


Fig. 5. *^{1}H-NMR spectra of the reaction product* **3c** *without purification.* Top: reaction of acetaldehyde with acetyl chloride (conditions for a high content of by-products); bottom: same reaction (conditions for a small content of by-products).

[11]) Either by slowly and dropwise adding of the aldehyde to a slight excess of the acetyl chloride, or by using trimeric (**11c**) or polymeric aldehyde (*e.g.* paraformaldehyde which depolymerized in contact with $ZnCl_2$).

Scheme 3. *Formation of By-Products: Reasonable Explanation*[12])



chloride shifted, then **10** was the product, otherwise oligomerization continued. It seemed that the catalyst $ZnCl_2$ could exchange acetate against chloride in **10**, hereby producing the main by-product bis(chloroalkyl) ether **6** besides AcOZnCl, which had the possibility to transfer acetate to all the carbonium ions present in solution. So, acetate transfer to the most important carbonium ion **12** gave methanediyl diacetate **7**, and transfer to the oligomeric carbonium ion **14** gave minor amounts of **8**.

5. Remarks Concerning the Reaction Mechanism[12]) [25]**.** – At first sight, there seems to be a close similarity between the 'chloroacetylation of carbonyl compounds' and the quite well-known '*Friedel–Crafts* acylation of benzenoid compounds', which has been investigated in considerable detail [26][27]. In both cases, a *π-system* is attacked by an electrophile which is formed by contact of a *Lewis* acid and an acyl halide. While according to *Friedel–Crafts* the hereby formed '*σ*-complex' was stabilized by deprotonation and aromatization, the sequence ended in our case with a halogen-shift (*Scheme 4*). For *Friedel–Crafts* acylations, two electrophilic species have been discussed [26][27], namely the O-complexed acyl halide as well as the acyl cation, which was formed from the Cl-complexed acyl halide.

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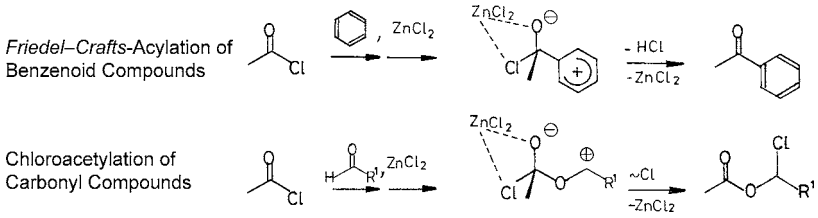
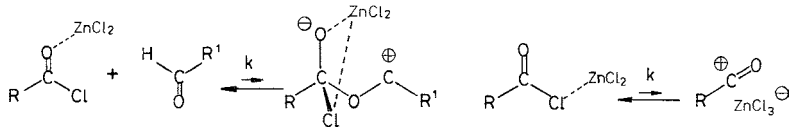
[12]) For more detailed kinetic results and an extensive discussion of the reaction mechanism, see [25].

Scheme 4. *Reasonable Reaction Mechanisms*



Reaction of Aliphatic and Aromatic Aldehydes with Acetyl Chloride: The conversion of acetyl chloride with pivaldehyde is an overall second-order reaction proceeding first-order with respect to both the acetyl chloride and the aldehyde [18][25]. Similar results were obtained for acetaldehyde, isobutanal, and benzaldehyde[13]) in various solvents, while polar solvents were increasing the reaction rate. Furthermore, the reaction was strongly accelerated by electron-donating substituents of the aromatic aldehyde. We assume that acylation of the aldehyde by the 'O-complexed acetyl chloride' was the rate-determining step (see *Scheme 5*, left side, and *Scheme 3*, top row).

Scheme 5



Reaction of Aldehydes with Benzoyl Chlorides: In reactions with aldehydes, benzoyl chlorides showed a kinetically different behavior from aliphatic acyl chlorides: The reaction was first-order with respect to the benzoyl chloride, but zero-order with respect to the aliphatic or aromatic aldehyde. Polar solvents were accelerating. Furthermore, changing from the system 4-chlorobenzoyl chloride/pivaldehyde (=2,2-dimethylpropanal) to the system 4-methoxybenzoyl chloride/pivaldehyde, the reaction rate was dramatically increasing by a factor 3500! These results suggested that the rate-determining step was the formation of the benzoyl cation (*Scheme 5*, right side), while the subsequent reactions (acylation and chloride shift) were comparably fast.

Our investigations showed that the formal **analogy** between '***Friedel–Crafts* acylation**' [26][27] and '**chloroacetylation of carbonyl compounds**' [15] can be substantiated by kinetic investigations [25].

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[13]) A different behavior is observed for aromatic aldehydes with strong $+I/+M$-substituents in *para*-position, it can be explained with a partial deactivation of the catalyst [25].

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