

Studies on the Reaction between Chloral and Alcohols

V. A Study of the Formation of Chloral(*R*)-Menthol Hemiacetal

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The formation of chloral(*R*)-menthol hemiacetal has been studied by kinetic methods. The overall process has been found to consist of at least two parallel reactions, one catalyzed by acetic acid and another which is not catalyzed by acetic acid. A third reaction, catalyzed by impurities in the chloral, has also been found to take place but can be largely reduced by careful purification of the chloral.

The overall reaction order with respect to chloral, menthol, and acetic acid in the acid catalyzed reaction is shown to be approximately 1, 0, and 0.5, respectively. This means that the rate-determining step is a reaction between chloral and acetic acid, and that the rate of hemiacetal formation is independent of the menthol concentration. The reaction order with respect to acetic acid is explained by the fact that acetic acid exists primarily as a dimeric species in inert solvents.

In the uncatalyzed hemiacetal formation, the reaction order is approximately 1 with respect to both chloral and menthol. This means that the rate-determining step is a direct reaction between chloral and menthol. In both the catalyzed and the uncatalyzed process epimerization between the two diastereomeric hemiacetals occurs. An explanation of these experimental facts is suggested.

As part of our continuing studies of the reaction between chloral and alcohols¹⁻⁴ we have investigated the kinetics of both the acid catalyzed and the uncatalyzed reversible formation of different chloral hemiacetals in inert solvents.

The idea of using kinetic methods in combination with equilibrium determinations to study the formation of (chloral) hemiacetals is not a new one. Polarimetric and UV methods have been used. Herz and Kuntze,⁵ using the polarimetric methods studied the kinetics of the exchange reaction between optically active chloral hemiacetals, $\text{CCl}_3\text{CH}(\text{OH})\text{OR}^*$, and optically inactive alcohols, ROH (1).



The reaction was found to follow a reversible second order reaction scheme. Willcox and Brunell,^{6,7} also using a polarimetric method, studied the influence of different aliphatic alcohols on the equilibrium in reaction (1). The position of the equilibrium was shown to depend on the degree and position of branching present in the alcohols. Herold *et al.*⁸⁻¹¹ investigated the influence of the solvent on the position of the equilibrium and the rate of formation of a number of hemiacetals by UV spectroscopy. It was observed that half-lives of the hemiacetals were very dependent on the dipolar character of the solvent. Furthermore, the existence of a hemiacetal-alcohol complex was discussed. It was suggested that the formation of such a complex may explain the observation that the equilibrium constant of reaction (2) depends on the initial



concentrations of both chloral and the alcohol. The concentrations of alcohol and hemiacetal were both calculated from the measured concentration of chloral. Cantacuzene,¹² utilizing UV spectroscopy, expanded the investigations of Herold *et al.*, specifically with respect to the acid catalyzed hemiacetal formation. The relation between the rate constants for this reaction and the polarity of the atoms neighbouring the hydroxyl and the aldehyde group was discussed. For the purpose of explaining the solvolytic and catalytic influences on the hemiacetal formation, several reaction models were suggested.

The aims of our investigations are twofold. First, by comparing the initial rates of both the catalyzed and uncatalyzed hemiacetal formation and by determining the reaction order with respect to those components entering into the rate-determining step, to obtain a better understanding of the reaction mechanism. The earlier kinetic studies were all carried out with equimolar initial concentrations of both chloral and alcohol, a procedure which is known to give an oversimplified picture of the reaction. For acid catalyzed hemiacetal formation with several types of alcohols and using a more varied kinetic treatment, we found that the rate-determining step was the reaction between chloral and the catalyst and that varying the concentration of the alcohol did not influence the initial rate. Second, to obtain further information by examining the influence of different groups in the alcohol molecule on the initial rate of the uncatalyzed hemiacetal formation. The reason to omit a catalyst, is that, because of the above-mentioned fact that the alcohol often does not take part in the rate-determining step, no information about the influence of the reacting alcohol can be obtained from the catalyzed reactions by initial rate-determinations.

The catalyzed hemiacetal formation is shown to consist of three parallel reactions: a) a reaction catalyzed by added acetic acid, b) an uncatalyzed reaction and c) a reaction catalyzed by impurities in the chloral. The content of the catalyzing impurities in the chloral can vary considerably from one preparation to another, and it is difficult to obtain two identical chloral samples even by careful purification. It is therefore necessary when comparing results to take care that these come from experiments in which the same sample of chloral has been used. The measured initial rate of the catalyzed hemiacetal formation $v_{1(0,K)}$ (the figure 1 means that the reaction is forward) can be expressed as a sum of three contributions, (3).

$$\begin{aligned}
 v_{1(0,K)} &= v_{1(0,k)} + v_{1(0,uk)} + v_{1(0,k')} & (3) \\
 v_{1(0,k)} &\text{ refers to reaction a) } \\
 v_{1(0,uk)} &\text{ » » » b) } \\
 v_{1(0,k')} &\text{ » » » c) }
 \end{aligned}$$

Without added catalyst the measured initial rate of hemiacetal formation $v_{1(0,UK)}$ can be expressed as the sum of two contributions, (4)

$$v_{1(0,UK)} = v_{1(0,uk)} + v_{1(0,k')} \quad (4)$$

$v_{1(0,k)}$ is obtained by subtracting $v_{1(0,UK)}$ from $v_{1(0,K)}$. But even this corrected initial rate will not be exactly the same for different samples of chloral, but the discrepancy can be minimized, but not eliminated by choosing concentrations of chloral and alcohol such that $v_{1(0,uk)}$ and $v_{1(0,k')}$ are as small as possible. Even though the rate constants may not be precise, they can still be useful when comparing results obtained under the same experimental conditions and thus lead to an understanding of some of the factors determining the formation of chloral hemiacetals.

This paper is primarily concerned with investigations of the formation of the chloral hemiacetal of menthol, and it will serve as a presentation of the kinetic treatments to be used in the future.

TREATMENT OF DATA

The reactions were all carried out at 25°C in heptane with acetic acid as the catalyst. The concentration of chloral was determined by UV spectroscopy. The other concentrations were deduced from the stoichiometry of eqn. (2).

The experiments treated in this paper are shown in Fig. 1a and b, and 2a, b, and c. In Fig. 1a and b the course of the uncatalyzed hemiacetal formation

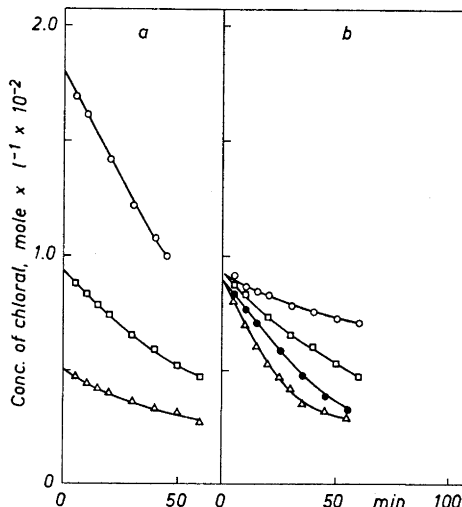


Fig. 1a and b. The course of the uncatalyzed hemiacetal formation of chloral (*R*)-menthol hemiacetal is illustrated by a plot of the chloral concentration versus time for various initial concentrations of chloral and (*R*)-menthol. In Fig. 1a the initial concentrations of chloral are: \circ 2×10^{-2} M, \square 1×10^{-2} M, and \triangle 0.5×10^{-2} M. The initial concentration of (*R*)-menthol is 10×10^{-2} M. In Fig. 1b the various initial concentrations of (*R*)-menthol are: \circ 5×10^{-2} M, \square 10×10^{-2} M, \triangle 20×10^{-2} M, and $+$ 40×10^{-2} M. The starting concentration of chloral is 1×10^{-2} M.

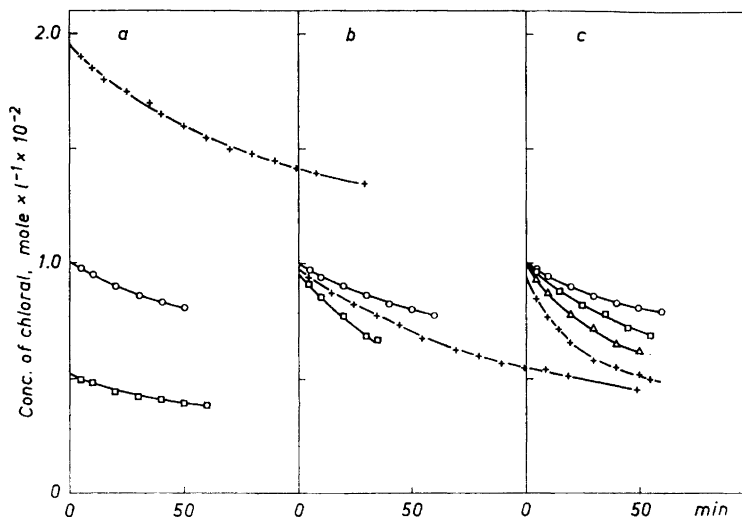


Fig. 2a, b, and c. The course of the catalyzed formation of chloral (*R*)-menthol hemiacetal is illustrated by a plot of the chloral concentration *versus* time at various initial concentrations of chloral, (*R*)-menthol, and acetic acid. In Fig. 2a the initial concentrations of chloral are: + 2×10^{-2} M, \square 1×10^{-2} M, and \circ 0.5×10^{-2} M. The initial concentrations of (*R*)-menthol and acetic acid are 1×10^{-2} M and 1×10^{-4} M. In Fig. 2b the initial concentrations of (*R*)-menthol are: \circ 1×10^{-2} M, + 2×10^{-2} M, and \square 5×10^{-2} M. The initial concentrations of chloral and acetic acid are 1×10^{-2} M and 1×10^{-4} M. In Fig. 2c the initial concentrations of acetic acid are \circ 1×10^{-4} M, \square 2×10^{-4} M, \triangle 5×10^{-4} M, and + 10×10^{-4} M. The initial concentrations of chloral and (*R*)-menthol are both 1×10^{-2} M.

is illustrated by a plot of the chloral concentration *versus* time, and in Fig. 2a, b, and c the course of the catalyzed hemiacetal formation is shown in the same way.

Uncatalyzed hemiacetal formation. If $v_{1(0,k')}$ is small compared with $v_{1(0,uk)}$ eqn. (4) can be converted into eqn. (5).

$$v_{1(0,UK)} = -\left(\frac{d[\text{Chl}]}{dt}\right)_{0,UK} = v_{1(0,uk)} = k_{1(uk)}[\text{Chl}]_0^a[\text{ROH}]_0^b \quad (5)$$

The term $-\left(\frac{d[\text{Chl}]}{dt}\right)_{0,UK}$ is the measured initial rate of change in chloral concentration and $\left(\frac{d[\text{Chl}]}{dt}\right)_{0,UK}$ is the initial rate of change in hemiacetal concentration for the uncatalyzed reaction. $[\text{Chl}]_0$ and $[\text{ROH}]_0$ are the starting concentrations of chloral and alcohol, respectively. a and b are the reaction orders with respect to chloral and the alcohol, respectively. $k_{1(uk)}$ is the rate constant for hemiacetal formation.

The reaction order with respect to chloral, a , is determined by plotting the logarithm of $-\left(\frac{d[\text{Chl}]}{dt}\right)_{0,UK}$ *versus* the logarithm of the different initial concentrations of chloral, while keeping the initial concentration of alcohol constant (see Table 1). The reaction order with respect to menthol, b , is determined, in the same way, by plotting the logarithm of $-\left(\frac{d[\text{Chl}]}{dt}\right)_{0,UK}$ *versus* the logarithm of different initial concentrations of menthol, while keeping the starting concentration of chloral constant (see Table 1). The slopes of lines

Table 1. The initial rate and the corresponding rate constant for the formation of chloral (*R*)-mentol hemiacetal in the uncatalyzed process.

Starting concentrations mole $\times 1^{-1} \times 10^2$		Initial rate of the uncatalyzed hemiacetal formation, $v_{1(0,uk)}$ mole $\times 1^{-1} \times \text{min}^{-1} \times 10^6$	Rate-constant $v_{1(0,uk)} / ([\text{Chl}]_0 \times [\text{ROH}]_0)^a$ mole $^{-1} \times 1 \times \text{sec}^{-1} \times 10^8$
Chloral	(<i>R</i>)-menthol		
0.50	10.0	5.0	1.7
1.00	10.0	9.6	1.6
2.00	10.0	19.0	1.6
1.00	5.00	4.5	1.5
1.00	20.0	14.8	1.1
1.00	40.0	20.6	0.8

^a $[\text{Cl}]_0$ and $[\text{ROH}]_0$ refer to the starting concentrations of chloral and (*R*)-menthol.

Chl and ROH in Fig. 3 represent the reaction order with respect to chloral and menthol, respectively. Fig. 3 shows that both a and b , in the concentration range of 1×10^{-2} – 1×10^{-1} M, tend toward a value of 1. Accordingly, the forward reaction can be described by a second order rate equation (6).

$$-d[\text{Chl}]/dt = k_{1(uk)}[\text{Chl}][\text{ROH}] \quad (6)$$

If $[\text{ROH}]_0 \gg [\text{Chl}]_0$ eqn. (6) can be treated as a first-order reaction and is converted into eqn. (7) by integration.

$$-\log[\text{Chl}] = k'_{1(uk)} \times t + C \quad (7)$$

$$k'_{1(uk)} = k_{1(uk)}[\text{ROH}]_0$$

During the initial stages of the reaction, a plot of $\log [\text{Chl}]$ versus time should thus give a straight line. Such straight lines have in fact been found using various initial concentrations of chloral and menthol (Fig. 4a and b).

At concentrations of menthol greater than 10^{-1} M, the reaction order with respect to this component seems to decrease. This phenomenon has been explained as a consequence of increasing association of menthol at higher concentrations.¹³ IR-Spectroscopic investigations of 10^{-2} , 10^{-1} , and 1 M heptane solutions of menthol confirm this hypothesis. At a menthol concentration of 10^{-2} M in heptane, IR-spectroscopy indicates that the monomeric form is the predominant species (Fig. 5a). At higher concentrations the mole-percentage of the monomeric form has been calculated from the extinction coefficients of the absorption due to the non-hydrogen bonded hydroxyl group (Table 2, Fig. 5a, b, and c).

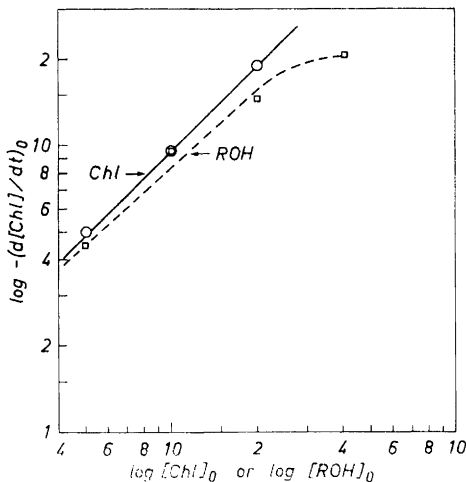


Fig. 3. A plot of the logarithm of the initial rate of the uncatalyzed hemiacetal formation, $v_{i(0,UK)}$ versus the logarithm of various initial concentrations of chloral (O, line Chl) and of (*R*)-menthol (□, line ROH). The chloral plot (—) includes the following initial concentrations of chloral 0.5×10^{-2} M, 1×10^{-2} M, and 2×10^{-2} M. The initial concentration of (*R*)-menthol is 10×10^{-2} M. The (*R*)-menthol plot (---) includes the following initial concentrations of (*R*)-menthol 5×10^{-2} M, 10×10^{-2} M, 20×10^{-2} M and 40×10^{-2} M. The initial concentration of chloral is 1×10^{-2} M. The slope of line (Chl) and line (ROH) are 1.0 and 0.90.

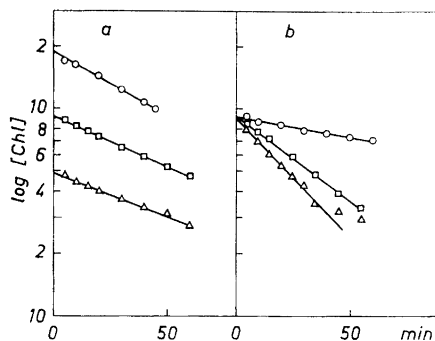


Fig. 4a and b. The uncatalyzed hemiacetal formation treated as a first-order reaction by plotting the logarithm of the chloral concentration versus time. In Fig. 4a the initial concentrations of chloral are: O 2×10^{-2} M, □ 1×10^{-2} M and Δ 0.5×10^{-2} M. The initial concentration of (*R*)-menthol is 10×10^{-2} M. In Fig. 4b the initial concentrations of (*R*)-menthol are: O 5×10^{-2} M, □ 20×10^{-2} M, and Δ 40×10^{-2} M. The initial concentration of chloral is 1×10^{-2} M.

Table 2. The mole % of monomeric menthol at different stoichiometric concentrations, in heptane, determined by IR-spectroscopy.

Path-length l (m/m)	Concentration C (moles/l)	T (transmittance)		D (optical density) $D = 2 - \log T$	Extinction coefficient ϵ	mole % of monomer ^a
		base %	peak %			
1.0	10^{-2}	98.8	91.1	0.0353	35.3	100
0.1	10^{-1}	98.6	91.6	0.0320	32.00	90.6 ^b
1.0	10^{-1}	91.0	43.0	0.03207	32.07	91.0
0.1	1	86.5	67.0	0.1109	11.09	31.4 ^b

^a $\epsilon = D/Ce$ (C being the molar concentration of monomeric menthol). mole % = $\epsilon/35.3$.

^b Using an abscissa scale $\times 10$.

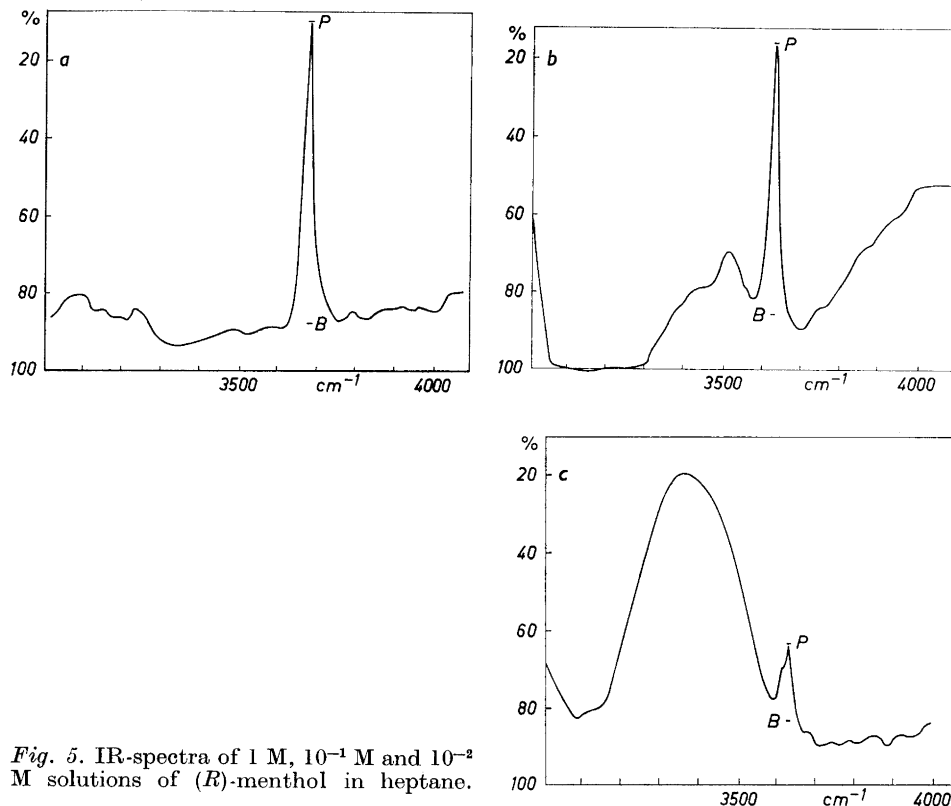


Fig. 5. IR-spectra of 1 M, 10^{-1} M and 10^{-2} M solutions of (*R*)-menthol in heptane.

Catalyzed hemiacetal formation. If the experimental conditions mentioned in the introduction are fulfilled, eqn. (3) can be converted to eqn. (8).

$$v_{1(0,K)} - v_{1(0,UK)} = -\left(\frac{d[\text{Chl}]}{dt}\right)_{0,K} \left(\frac{d[\text{Chl}]}{dt}\right)_{0,UK} = v_{1(0,k)} = -k_{1(k)}[\text{Chl}]_0^a [\text{ROH}]_0^b [\text{HA}]_{s,0}^c \quad (8)$$

$-\left(\frac{d[\text{Chl}]}{dt}\right)_{0(K)}$ is the initial rate of change in chloral concentration for the catalyzed reaction. $[\text{HA}]_{s,0}$ refers to the stoichiometric initial concentration of the acid. c is the reaction order with respect to the acid and $k_{1(k)}$ is the rate constant for the catalyzed hemiacetal formation.

Table 2 shows the values of $v_{1(0,k)}$ at various initial concentrations of chloral, menthol, and acetic acid. The reaction orders a , b , and c for the catalyzed hemiacetal formation, determined in the same way as for the uncatalyzed reaction, tend toward values of 1, 0, and 0.5, respectively (Fig. 6). If the concentration of acetic acid can be considered to be constant during the reaction and equal to $[\text{HA}]_{s,0}$, the differential form of the rate equation will be:

$$-d[\text{Chl}]/dt = k'_{1(k)}[\text{Chl}] + k_{1(uk)}[\text{Chl}][\text{ROH}] \quad (9)$$

$$k'_{1(k)} = k_{1(k)}[\text{HA}]_{s,0}^{\frac{1}{2}} \text{ where } k'_{1(k)} \text{ is proportional to } [\text{HA}]_{s,0}^{\frac{1}{2}}$$

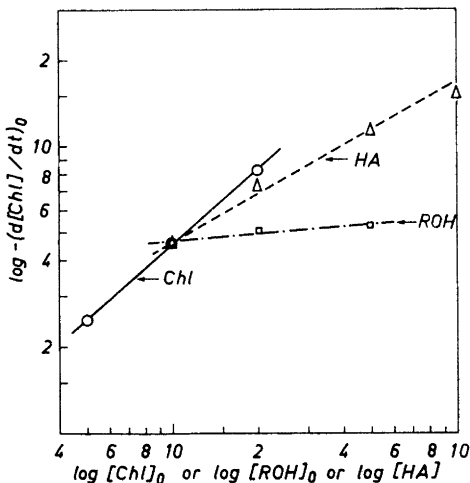


Fig. 6. A plot of the logarithm of the initial rate of the catalyzed hemiacetal formation, $v_{1(0,k)}$ versus the logarithm of different initial concentrations of chloral (O, line Chl), (*R*)-menthol (\square , line ROH), and acetic acid (\triangle , line HA). The chloral plot (—) includes the following initial concentrations of chloral 0.5×10^{-2} M, 1×10^{-2} M and 2×10^{-2} M. The initial concentrations of (*R*)-menthol and acetic acid are 1×10^{-2} M and 1×10^{-4} M. The ROH plot (---) includes the following initial concentrations of (*R*)-menthol 1×10^{-2} M, 2×10^{-2} M, and 5×10^{-2} M. The initial concentrations of chloral and acetic acid are 1×10^{-2} M and 1×10^{-4} M. The HA plot (— · —) includes the following initial concentrations of acetic acid: 1×10^{-4} M, 2×10^{-4} M, 5×10^{-4} M, and 10×10^{-4} M. The initial concentrations of chloral and (*R*)-menthol are both 1×10^{-2} M. The slopes of line (Chl), line (ROH), and line (HA) are 0.88, 0.06, and 0.55.

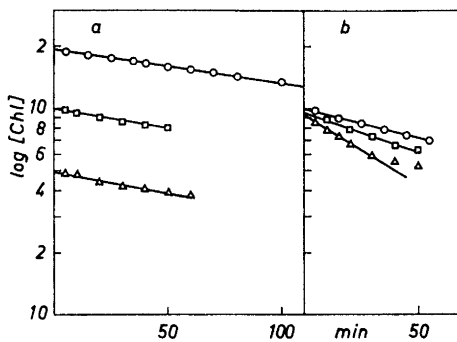


Fig. 7a and b. The catalyzed hemiacetal formation, neglecting the uncatalyzed contribution, treated as a first-order reaction by plotting the logarithm of the chloral concentration versus time. In Fig. 7a the initial concentrations of chloral are: O 2×10^{-2} M, \square 1×10^{-2} M, and \triangle 0.5×10^{-2} M. The initial concentrations of (*R*)-menthol and acetic acid are 1×10^{-2} M and 1×10^{-4} M. In Fig. 7b the initial concentrations of acetic acid are: O 2×10^{-4} M, \triangle 5×10^{-4} M, and \square 10×10^{-4} M. The initial concentrations of chloral and (*R*)-menthol are both 1×10^{-2} M.

Eqn. (9) can be integrated, but if $[\text{ROH}]_0$ is not much larger than $[\text{Chl}]_0$, the last term in (9) can be neglected and eqn. (9) can be simplified to eqn. (10).

$$-d[\text{Chl}]/dt = k'_{1(k)}[\text{Chl}] \quad (10)$$

By integration this equation gives:

$$\ln[\text{Chl}] = -k'_{1(k)} \times t + C = k_{1(k)} \times [\text{HA}]_{s,0}^{\frac{1}{2}} \times t + C \quad (11)$$

By plotting the logarithm of chloral concentration versus time for various initial concentrations of chloral and acetic acid, straight lines are obtained

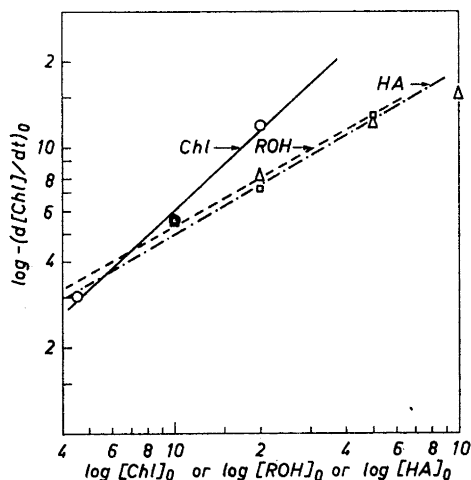
Table 3. The initial rate and the corresponding rate-constant for the catalyzed formation of chloral (*R*)-menthol hemiacetal.

Starting concentrations mole $\times 1^{-1} \times 10^2$			Initial rate of the catalyzed hemiacetal formation (mole $\times 1^{-1} \times \text{min}^{-1} \times 10^5$)			Rate-constant $v_{1(0,k)} / ([\text{Chl}]_0 \times [\text{HA}]_0^{1/2})$ mole $^{-1/2} \times 1^{1/2} \times \text{sec}^{-1} \times 10^3$
Chloral	(<i>R</i>) menthol	acetic acid	$v_{1(0,K)}$	$v_{1(0,UK)}$	$v_{1(0,k)}$	
0.50	1.00	1.00×10^{-2}	3.0	0.5	2.5	8.4
1.00	1.00	1.00×10^{-2}	5.6	1.0	4.6	7.7
2.00	1.00	1.00×10^{-2}	10.2	2.0	8.2	7.0
1.00	2.00	1.00×10^{-2}	7.2	2.0	5.2	8.5
1.00	5.00	1.00×10^{-2}	10.3	5.0	5.3	8.8
1.00	1.00	2.00×10^{-2}	8.0	1.0	7.0	8.3
1.00	1.00	5.00×10^{-2}	12.2	1.0	11.2	8.3
1.00	1.00	10.0×10^{-2}	15.4	1.0	14.4	7.6

for the early stages of the reaction (Fig. 7a and b). This supports the assumptions leading to eqn. (10).

Determination of reaction order from double logarithmic plots has been carried out, without correction for the uncatalyzed reaction (Table 3, Fig. 8).

Fig. 8. A plot of the logarithm of the initial rate of the catalyzed hemiacetal formation, $+v_{1(0,k)}$, neglecting the uncatalyzed contribution, versus the logarithm of various initial concentrations of chloral (\circ , line Chl), of (*R*)-menthol (\square , line ROH), and of acetic acid (\triangle , line HA). The Chl plot (—) includes the following initial concentrations of chloral: 0.5×10^{-2} M, 1×10^{-2} M, and 2×10^{-2} M. The initial concentrations of (*R*)-menthol and acetic acid are 1×10^{-2} M and 1×10^{-4} M. The ROH plot (---) includes the following initial concentrations of (*R*)-menthol: 1×10^{-3} M, 2×10^{-3} M, and 5×10^{-3} M. The initial concentrations of chloral and acetic acid are 1×10^{-2} M and 1×10^{-4} M. The HA plot (---) includes the following initial concentrations of acetic acid: 1×10^{-4} M, 2×10^{-4} M, 5×10^{-4} M, and 10×10^{-4} M. The initial concentrations of chloral and (*R*)-menthol are both 1×10^{-2} M. The slopes of line (Chl), line (ROH), and line (HA) are 0.93, 0.55, and 0.56.



This leads to reaction orders of 1, 0.5, and 0.5 with respect to chloral, menthol, and acetic acid, respectively, in the catalyzed reaction, suggesting that menthol exists primarily as a dimer. However, the spectroscopic evidence mentioned above shows that this is not the case, and therefore we conclude that the uncatalyzed reaction can not be neglected.

DISCUSSION

Catalyzed hemiacetal formation. It is well known that acetic acid exists partly as a dimer in inert solvents¹⁴



and that the forward and reverse reactions are both very fast. From eqn. (12), the concentration of monomeric acid, $[\text{HA}]$, will be proportional to the square-root of the concentration of dimeric acid, $[\text{HA}\cdots\text{HA}]$

$$[\text{HA}] = K_{\text{HA}}^{-\frac{1}{2}} [\text{HA}\cdots\text{HA}]^{\frac{1}{2}} \quad (13)$$

K_{HA} is the equilibrium constant

Because of extensive dimerization, the concentration of dimeric acid will be nearly equal to one-half the stoichiometric concentration of the acid, $[\text{HA}]_{s,0}$ and eqn. (13) can be converted to (14).

$$[\text{HA}] \simeq (1/2)^{\frac{1}{2}} K_{\text{HA}}^{-\frac{1}{2}} \times [\text{HA}]_{s,0}^{\frac{1}{2}} \quad (14)$$

The initial rate of the catalyzed hemiacetal formation can then be expressed by eqn. (15), which explains why the reaction order with respect to acetic acid is 0.5.

$$v_{1(0,k)} = k_{1(k)} (1/2)^{\frac{1}{2}} K_{\text{HA}}^{-\frac{1}{2}} \times [\text{HA}]_{s,0}^{\frac{1}{2}} \times [\text{Chl}] \quad (15)$$

The observation that the reaction orders with respect to chloral and menthol are 1 and 0, respectively, indicates that hemiacetal formation consists of at least three consecutive reactions. To determine the actual sequence of events in the reaction of chloral with menthol catalyzed by acetic acid different reaction possibilities are analyzed in scheme 1. From an inspection of scheme 1, the most reasonable interpretation of rate-equation (15) is given by case 1a, where the hemiacetal formation consists of a slow, rate-determining reaction between chloral and acetic acid forming a chloral acetic acid intermediate, $\text{Chl}\cdots\text{HA}$. This intermediate reacts with menthol to form a chloral, acetic acid, menthol intermediate, $\text{Chl}\cdots\text{HA}\cdots\text{ROH}$. This second intermediate must be introduced in the reaction scheme to account for the observed mutarotation of chloral hemiacetals prepared from optically active alcohols.¹⁻⁴ This mutarotation is a result of epimerization between the two possible hemiacetals, $\text{H}(R)$ and $\text{H}(S)$ (16).



As discussed in an earlier paper³ we suggest, because of the observed epimerization, that this intermediate is cyclic (Fig. 9). Finally, $\text{Chl}\cdots\text{HA}\cdots\text{ROH}$ decomposes to hemiacetal and acetic acid.

Scheme 1. Reaction possibilities for the catalyzed hemiacetal formation and their corresponding rate-equations.

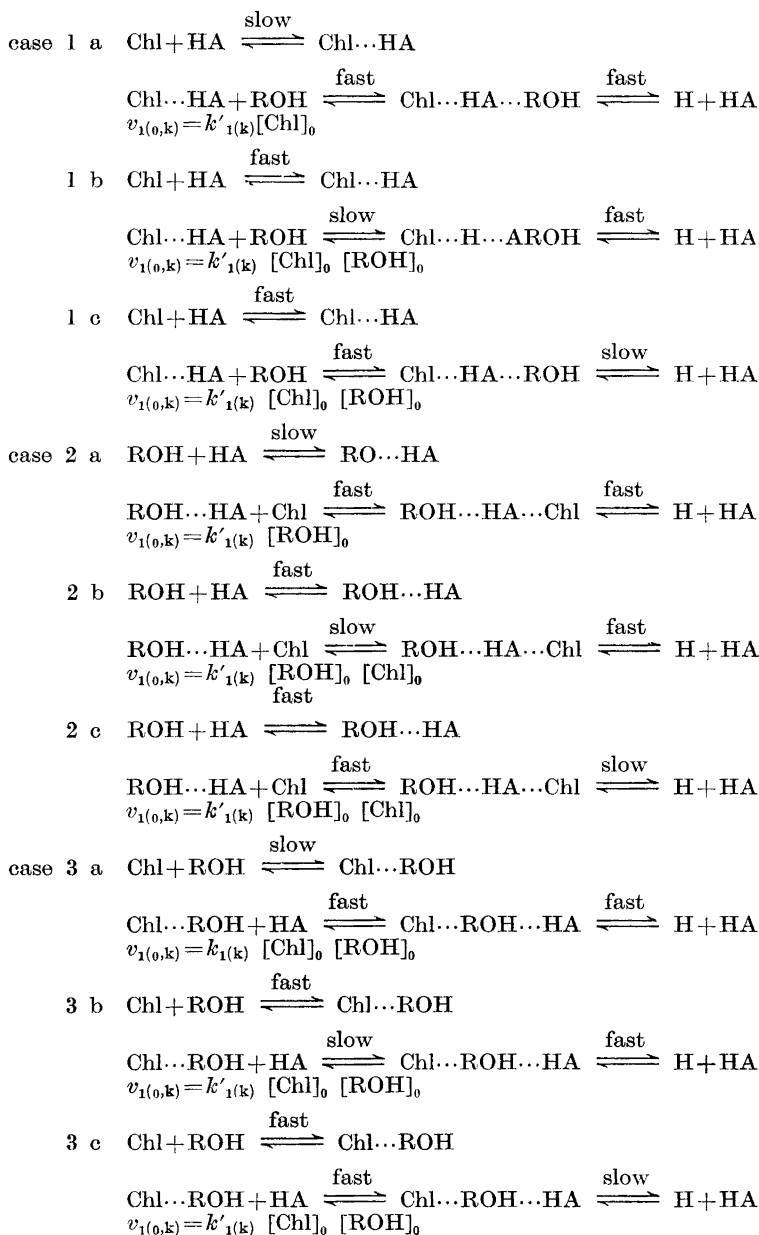


Table 4. The equilibrium constant of $\text{Chl} + \text{ROH} \rightleftharpoons \text{H}$, determined at different starting concentrations of chloral, menthol and acetic acid.

$[\text{Chl}]_0^a$	$[\text{ROH}]_0^a$	$[\text{HA}]_0^a$	$[\text{Chl}]_e^b$	$[\text{ROH}]_e^b$	$[\text{H}]_e^b$	K^c
1×10^{-2}	1×10^{-2}	1×10^{-4}	0.43×10^{-2}	0.43×10^{-2}	0.57×10^{-2}	310
2×10^{-2}	1×10^{-2}	1×10^{-4}	1.15×10^{-2}	0.15×10^{-2}	0.85×10^{-2}	490
1×10^{-2}	2×10^{-2}	1×10^{-4}	0.29×10^{-2}	1.29×10^{-2}	0.71×10^{-2}	190
2×10^{-2}	2×10^{-2}	2×10^{-4}	0.68×10^{-2}	0.68×10^{-2}	1.33×10^{-2}	290
1×10^{-2}	0.5×10^{-2}	10×10^{-4}	0.62×10^{-2}	0.12×10^{-2}	0.38×10^{-2}	510
0.5×10^{-2}	1×10^{-2}	10×10^{-4}	0.17×10^{-2}	0.67×10^{-2}	0.33×10^{-2}	290
0.5×10^{-2}	0.5×10^{-2}	10×10^{-4}	0.24×10^{-2}	0.24×10^{-2}	0.26×10^{-2}	450
1×10^{-2}	10×10^{-2}	1×10^{-4}	0.14×10^{-2}	9.14×10^{-2}	0.86×10^{-2}	67
10×10^{-2}	10×10^{-2}	1×10^{-2}	0.22×10^{-1}	0.22×10^{-1}	0.78×10^{-1}	160

^a $[\text{Chl}]_0$, $[\text{ROH}]_0$, and $[\text{HA}]_0$ refer to the starting concentrations.

^b $[\text{Chl}]_e$, $[\text{ROH}]_e$, and $[\text{H}]_e$ refer to the equilibrium concentrations of these components.

$[\text{H}]_e$ is equal to $[\text{Chl}]_0 - [\text{Chl}]_e$ and $[\text{ROH}]_e$ equal to $[\text{ROH}]_0 - [\text{H}]_e$.

^c $K = [\text{H}]_e / [\text{Chl}]_e [\text{ROH}]_e$.

If hemiacetal formation follows exclusively case Ia (scheme 1), it should be possible to calculate the concentration of chloral at any time, when $[\text{Chl}]_0$, $[\text{ROH}]_0$, $[\text{HA}]_0$, and K are known, by using the following rate-equation (17) which includes the forward and the reverse reaction:

$$-d[\text{Chl}]/dt = k'_{1(k)} [\text{Chl}] - K/k_{1(k)} [\text{H}] \quad (17)$$

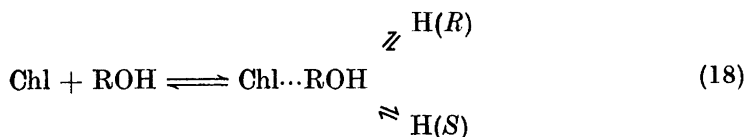
$[\text{H}]$ is the hemiacetal concentration

and equals $[\text{Chl}]_0 - [\text{Chl}]$

K is the equilibrium constant for reaction (1)

But, as mentioned in the introduction, this calculation cannot be performed because of the lack of a real equilibrium constant for reaction (1) (see Table 4). By considering the possible existence of an addition compound between hemiacetal and alcohol we hope to arrive at a rate equation more general than (17).

Uncatalyzed hemiacetal formation. The fact that the reaction orders with respect to chloral and menthol are both 1 indicates that the uncatalyzed hemiacetal formation occurs by direct reaction between chloral and menthol (18).



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