

Studies of the Reaction between Chloral and Alcohols

VII. A Study of the Formation of Chloral Hemiacetals of Aliphatic Primary and Aliphatic and Alicyclic Secondary Alcohols

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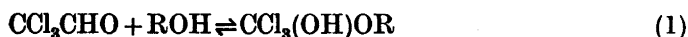
The kinetics of the uncatalyzed and the catalyzed (by acetic acid) formation of chloral hemiacetals of a large number of primary and secondary aliphatic and alicyclic alcohols have been studied by UV spectroscopy.

The catalyzed chloral hemiacetal formation is shown to consist of two parallel reactions, one of which is catalyzed by acetic acid.

Investigations of the catalyzed formation of chloral hemiacetals of 1- and 2-propanol indicate that primary and secondary alcohols follow the same reaction mechanism. The catalyzed chloral hemiacetal formation consists of at least three steps. The first step is the formation of a chloral acetic acid reaction complex, $\text{Chl}\cdots\text{HA}$. This complex reacts in the second step with alcohol forming a second reaction complex, $\text{Chl}\cdots\text{HA}\cdots\text{ROH}$. In a third step $\text{Chl}\cdots\text{HA}\cdots\text{ROH}$ decomposes to hemiacetal and acetic acid. The reaction orders of straight chain alcohols are found to be between 0.2 and 0.8. When β -disubstituted alcohols are used the reaction orders of the alcohols are found to be 1.0. This means that the reaction between $\text{Chl}\cdots\text{HA}$ and alcohol, or the decomposition of $\text{Chl}\cdots\text{HA}\cdots\text{ROH}$, becomes the rate determining step in the chloral hemiacetal formation. A rate expression is derived from a steady state treatment of the catalyzed reaction. This expression leads to a steric constant, f , which gives information about the bulkiness of the alcohols in this reaction. The initial rate and f are discussed from a conformational point of view. Model studies lead to the assumption that only the equatorial hydroxyl group in the menthols can react with $\text{Chl}\cdots\text{HA}$. The differences in the initial rate of the menthols will therefore be a measure of the concentration of the e -hydroxyl group conformer, rather than a measure of the steric bulk of the alcohol.

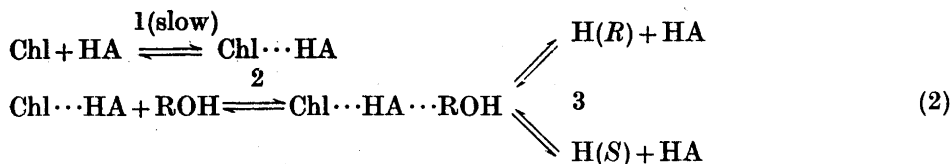
In the uncatalyzed reaction of secondary and sterically hindered alcohols the formation of a chloral alcohol complex is the slow step. Straight chain primary alcohols react by a complicated mechanism involving several molecules of both chloral and alcohol.

As a part of our studies of the reactions between chloral and various alcohols,¹⁻⁶ we reported, and discussed, some kinetic investigations of the uncatalyzed and the acetic acid catalyzed formation of chloral (*R*)-menthol hemiacetal (1)⁵



ROH: alcohol

The reaction orders with respect to chloral, (*R*)-menthol, and acetic acid were determined. This was done by measuring the initial rate at different concentrations of the component. A plot of the logarithm of the initial rate versus the logarithm of the concentrations yielded a straight line. The reaction order was obtained from the slope of this line. The observed catalyzed reaction was found to consist of two parallel reactions, *i.e.* a catalyzed and an uncatalyzed reaction. The contribution from the latter to the overall reaction is so important that it cannot be neglected. The reaction orders in the real catalyzed reaction of chloral, (*R*)-menthol and acetic acid were found to be about 1.0, 0.0, and 0.5, respectively. This indicated that the rate determining step is a reaction between chloral and acetic acid, and accordingly we proposed the following reaction mechanism for the formation of the two diastereomeric hemiacetals, H(*R*) and H(*S*) (2)



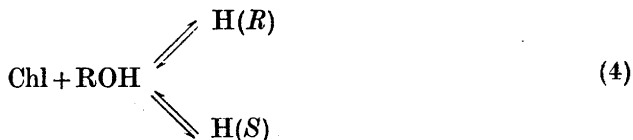
Chl: chloral HA: acetic acid



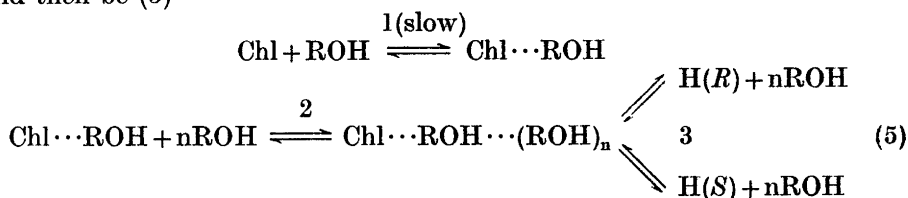
Observation of epimerization^{1-4,6} between H(*R*) and H(*S*) made us believe that a ring closure of Chl \cdots HA \cdots ROH was necessary in order to establish a steric correspondance (asymmetric induction) between the centre that becomes asymmetric in the chloral part of the hemiacetal and the asymmetric centre of the alcohol part, see Fig. 1. The compound B, in Fig. 1, was assumed to be less stable than A because the medium group, M, (with respect to steric bulk) was closer to the very bulky trichloromethyl group in B than in A. Therefore the initial rate of the hemiacetal formation from A was higher than from B. The reaction order, 0.5, of acetic acid, was explained by the fact that carboxylic acids are almost completely dimerized in inert solvents (3)⁷



In the uncatalyzed reaction the reaction orders of chloral and (*R*)-menthol were both found to be approximately 1. This indicated that the rate determining step was a reaction between one molecule of chloral and one molecule of (*R*)-menthol (4)



In this case, too, epimerization (but at a slower rate) was observed. The ring closure mentioned above made necessary the introduction of a reaction complex having the ability to cyclize. We suggested $\text{Chl}\cdots(\text{ROH})_2$ and $\text{Chl}\cdots(\text{ROH})_3$, Fig. 2a and b. Similar structures have been proposed by Bell⁸ in another connection. A reasonable addition to the reaction mechanism in (4) would then be (5)



In this case alcohol may be regarded as catalyzing the hemiacetal formation.

The investigations reported in this paper consist of determinations of the initial rates of both the uncatalyzed and the catalyzed formation of chloral

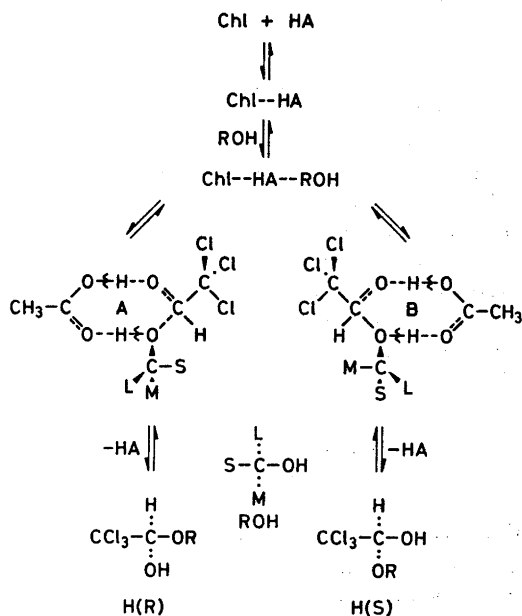


Fig. 1. Possible reaction paths in the catalyzed chloral hemiacetal formation.

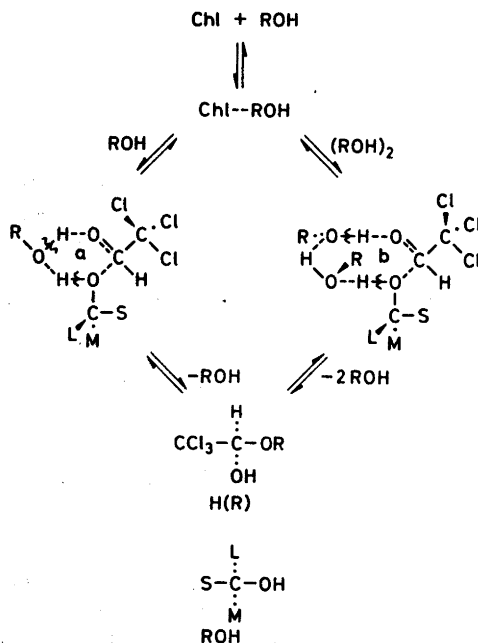


Fig. 2. Possible reaction paths in the uncatalyzed chloral hemiacetal formation.

hemiacetals of a number of primary and secondary aliphatic and alicyclic secondary alcohols. From these determinations the reaction orders for chloral, alcohol, and acetic acid are calculated. The rate constant $\vec{k}_{1,k}$ and $f = \vec{k}_{1,k}/\vec{k}_{2,k}$ in the catalyzed reaction (2) are estimated. The influence of branching in the alcohols on the initial rate is examined, in an attempt to assess the general validity of the proposed reaction mechanism (2).

As mentioned previously⁵ the idea of using kinetics in the study of chloral hemiacetal formation is not a new one. Herz and Kuntze⁹ and Willcox and Brunel^{10,11} have used polarimetry and Herold *et al.*¹²⁻¹⁵ and Cantacuzene¹⁶ have used UV spectroscopy. These authors, however, all proposed simpler mechanisms for the hemiacetal formation.

RESULTS AND DISCUSSION

The reactions were all carried out at 25.0°. The chloral concentration was determined by UV spectroscopy. The concentrations of alcohol and hemiacetal were deduced from the stoichiometry of eqn. (1). The initial rate, $\vec{v}_{0,k}$ of the real catalyzed reaction was calculated as shown in eqn. (6)

$$\vec{v}_{0,k} = \vec{v}_{0,K} - \vec{v}_{0,UK} \quad (6)$$

$\vec{v}_{0,k}$:	Foreward initial rate of the catalyzed reaction
$\vec{v}_{0,K}$:	» » » » » observed catalyzed reaction
$\vec{v}_{0,UK}$:	» » » » » » uncatalyzed reaction

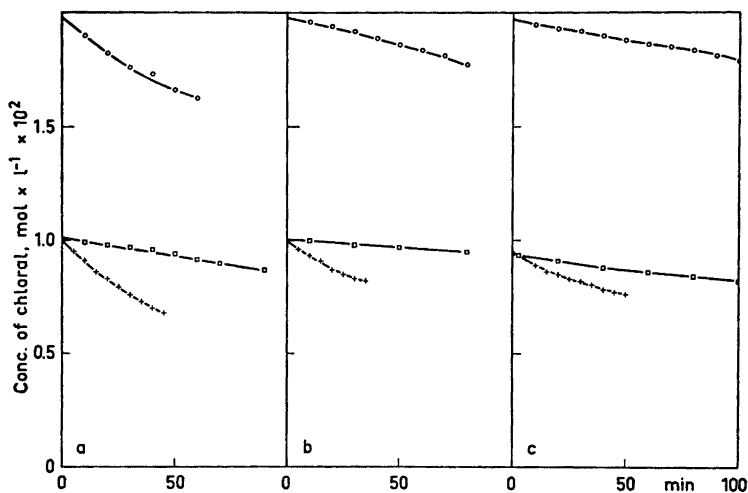
In the rate expressions (7) and (8) the appropriate reaction orders are expressed by the letters, a , b and c in the catalyzed reaction, and by a' and b' in the uncatalyzed reaction.

$$\vec{v}_{0,k} = \vec{k}_k [\text{Chl}]_0^a [\text{ROH}]_0^b [\text{HA}]_0^{s,c} \quad (7)$$

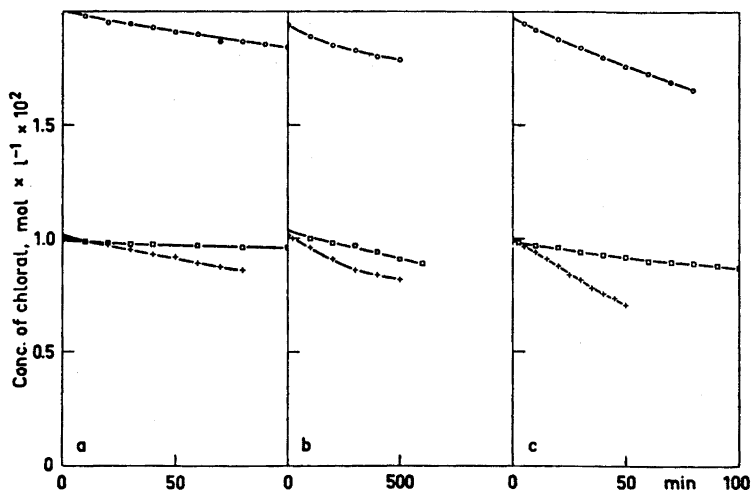
$$\vec{v}_{0,UK} = \vec{k}_{UK} [\text{Chl}]_0^{a'} [\text{ROH}]_0^{b'} \quad (8)$$

The indices s and 0 stand for stoichiometric and initial, respectively. As mentioned in the introduction, the reaction orders were found from the slope of the straight lines obtained by plotting the logarithm of the initial rate against the logarithm of the initial concentration of the considered component.

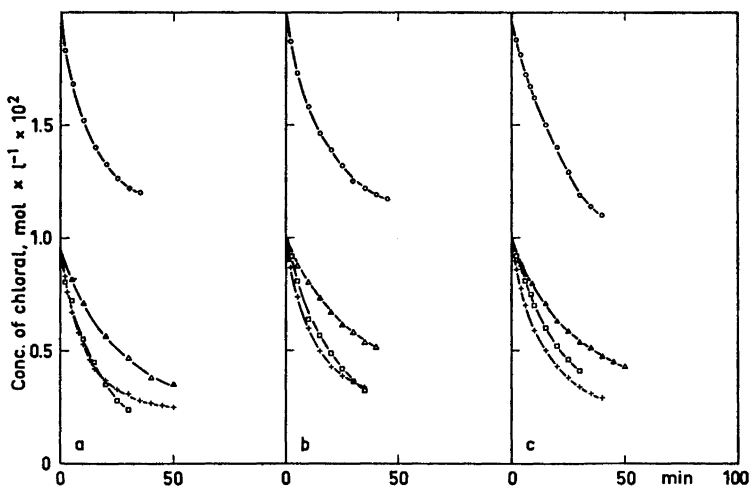
Primary alcohols. The course of the uncatalyzed hemiacetal formation from straight chain alcohols (methanol, ethanol, and propanol) as is shown in Figs. 3a, b, and c. Figs. 4a, b, and c shows the corresponding course for β - and γ -branched alcohols, exemplified by 2-methyl-1-propanol, 2,2-dimethyl-1-butanol and 3,3-dimethyl-1-butanol. The catalyzed reaction course is shown in Figs. 5, 6a, b, and c, and is illustrated by the same examples as above. The initial rates of the measured uncatalyzed and catalyzed reactions, and the



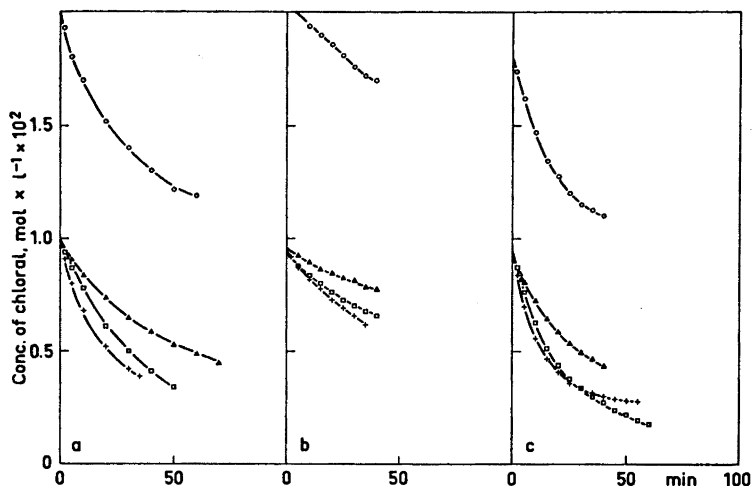
Figs. 3a, b, and c. The course of the uncatalyzed formation of chloral hemiacetals of methanol, ethanol, and 1-propanol, respectively, illustrated by a plot of the chloral concentration versus time at various initial concentrations of chloral and the alcohols: □, Conc. of chloral and alcohol are 10^{-2} M; +, Conc. of chloral and alcohol are 10^{-2} and 2×10^{-2} M; ○, Conc. of chloral and alcohol are 2×10^{-2} and 10^{-2} M.



Figs. 4a, b and c. The course of the uncatalyzed formation of chloral hemiacetals of 2-methyl-1-propanol, 2,2-dimethyl-1-butanol, and 3,3-dimethyl-1-butanol, respectively, illustrated by a plot of the chloral concentrations *versus* time at various initial concentrations of chloral and the alcohols: □, Conc. of chloral and alcohol are 10^{-2} M; +, Conc. of chloral and alcohol are 10^{-2} and 2×10^{-2} M; ○, Conc. of chloral and alcohol are 2×10^{-2} and 10^{-2} M.



Figs. 5a, b and c. The course of the catalyzed formation of chloral hemiacetals of methanol, ethanol, and 1-propanol, respectively, illustrated by a plot of the chloral concentrations *versus* time at various initial concentrations of chloral, the alcohols, and acetic acid: △, Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 10^{-2} , and 10^{-4} M, respectively; ○, Conc. of chloral, alcohol, and acetic acid are 2×10^{-2} , 10^{-2} , and 10^{-4} M, respectively; □, Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 2×10^{-2} , and 10^{-4} M, respectively; +, Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 10^{-2} , and 4×10^{-4} M, respectively.



Figs. 6a, b, and c. The course of the catalyzed formation of chloral hemiacetals of 2-methyl-1-propanol, 2,2-dimethyl-1-butanol, and 3,3-dimethyl-1-butanol, respectively, illustrated by a plot of the chloral concentrations *versus* time at various initial concentrations of chloral, the alcohols and acetic acid: Δ , Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 10^{-2} , and 10^{-4} M, respectively; \circ , Conc. of chloral, alcohol, and acetic acid are 2×10^{-2} , 10^{-2} , and 10^{-4} M, respectively; \square , Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 2×10^{-2} , and 10^{-4} M, respectively; $+$, Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 10^{-2} , and 4×10^{-2} M, respectively.

calculated real catalyzed reaction, together with the reaction orders for chloral, alcohol, and acetic acid are listed in Table 1. The figures and the table show:

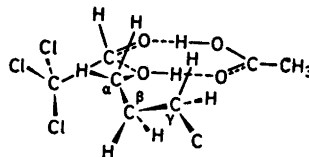
1. The initial rates of the real catalyzed reaction are 10–30 times larger than that of the corresponding uncatalyzed reaction. This can be explained by the fact that acetic acid is a better hydrogen-bonder than the alcohols and therefore a better catalyst. When straight chain alcohols are used the initial rates in the uncatalyzed and the catalyzed reactions seem to be rather unaffected by chain length.

2. Strong branching introduced in the β -position to the hydroxyl group, exemplified by 2,2-dimethyl-1-butanol, is found to decrease the initial rate in both reactions by a factor of 5. Double branching in the γ -position and single branching in the β -position, exemplified by 3,3-dimethyl-1-butanol and 2-methyl-1-propanol, are found to decrease the initial rate much less. This indicates that a marked steric effect is obtained only after introduction of two methyl groups in the β -position. Fig. 7 illustrates how groups in the β -position will give rise to more steric interaction with the ring atoms and trichloromethyl group in the cyclic reaction complex, $\text{Chl} \cdots \text{HA} \cdots \text{ROH}$, than groups placed in the γ -position (see Newman¹⁷). In the uncatalyzed reaction the reaction order changes characteristically when going from straight chain to increasingly branched alcohols. As already mentioned,⁵ different amounts of catalytic impurities in different batches of chloral influence the “un-

Table 1. Initial rates of a) measured uncatalyzed, b) measured catalyzed, and c) calculated catalyzed formation of chloral hemiacetals made from primary alcohols, and the reaction orders for chloral, alcohol, and acetic acid.

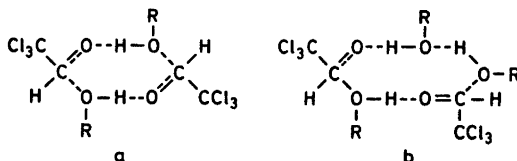
Formula	Initial concentrations $\text{mol} \times \text{l}^{-1} \times 10^2$			Initial rates of the hemiacetal formation $(\text{mol} \times \text{l}^{-1} \times \text{sec}^{-1} \times 10^6)$			Reaction orders for				
	chloral	alcohol	acetic acid	$\vec{v}_{0,k}$	$\vec{v}_{0,uk}$	$\vec{v}_{0,k}$	uncatalyzed reaction		real catalyzed reaction		
							chloral	alcohol	chloral	alcohol	acetic acid
CH_3OH	1.00	1.00	1.00×10^{-2}	3.7	0.23	3.5	2.0	2.5	0.92	0.26	0.51
	2.00	1.00	1.00×10^{-2}	7.5	0.93	6.5					
	1.00	2.00	1.00×10^{-2}	5.5	1.3	4.2					
	1.00	1.00	4.00×10^{-2}	7.3	0.23	7.1					
$\text{CH}_3\text{CH}_2\text{OH}$	1.00	1.00	1.00×10^{-2}	3.4	0.17	3.2	1.8	2.5	1.0	0.39	0.52
	2.00	1.00	1.00×10^{-2}	7.0	0.60	6.4					
	1.00	2.00	1.00×10^{-2}	5.2	0.97	4.2					
	1.00	1.00	4.00×10^{-2}	6.8	0.18	6.6					
$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$	1.00	1.00	1.00×10^{-2}	3.2	0.17	3.0	0.92	2.3	1.0	0.48	0.57
	2.00	1.00	1.00×10^{-2}	6.3	0.32	6.0					
	1.00	2.00	1.00×10^{-2}	5.0	0.82	4.2					
	1.00	1.00	4.00×10^{-2}	6.8	0.17	6.6					
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	1.00	1.00	1.00×10^{-2}	3.3	0.13	3.2	1.8	2.3	0.96	0.46	0.53
	2.00	1.00	1.00×10^{-2}	6.7	0.47	6.2					
	1.00	2.00	1.00×10^{-2}	5.0	0.63	4.4					
	1.00	1.00	4.00×10^{-2}	6.8	0.13	6.7					
$\text{CH}_3\text{CH}(\text{CH}_3)\text{CH}_2\text{OH}$	1.00	1.00	1.00×10^{-2}	2.3	0.067	2.2	1.7	2.2	0.86	0.40	0.50
	2.00	1.00	1.00×10^{-2}	4.2	0.22	4.0					
	1.00	2.00	1.00×10^{-2}	3.2	0.30	2.9					
	1.00	1.00	4.00×10^{-2}	4.5	0.067	4.4					
$\text{CH}_3\text{CH}_2\text{C}(\text{CH}_3)_2\text{CH}_2\text{OH}$	1.00	1.00	1.00×10^{-2}	0.75	0.033	0.72	1.0	1.0	0.96	0.96	0.53
	2.00	1.00	1.00×10^{-2}	1.5	0.067	1.4					
	1.00	2.00	1.00×10^{-2}	1.4	0.067	1.4					
	1.00	1.00	4.00×10^{-2}	1.5	0.033	1.5					
$\text{CH}_3\text{C}(\text{CH}_3)_2\text{CH}_2\text{CH}_2\text{OH}$	1.00	1.00	1.00×10^{-2}	2.7	0.18	2.5	2.1	2.5	1.1	0.40	0.40
	2.00	1.00	1.00×10^{-2}	6.0	0.78	5.2					
	1.00	2.00	1.00×10^{-2}	4.3	1.0	3.3					
	1.00	1.00	4.00×10^{-2}	4.5	0.18	4.3					

Fig. 7. Model showing the steric influence of β - and γ -branching in the alcohol part of the reaction complex, $\text{Chl} \cdots \text{HA} \cdots \text{ROH}$.



catalyzed" reactions to a certain degree. This causes an error in the estimation of the initial rate, rendering difficult the direct comparison of initial reaction rates found by using different batches of chloral.

When straight chain alcohols are used the reaction orders of chloral and alcohol are about 1.8 and 2.3, respectively, showing that more than one molecule of each component reacts before or in the rate-determining step. This may indicate a mixture of reaction complexes having the general composition $(\text{Chl})_m \cdots (\text{ROH})_n$ with $n \geq m$. Such structures might be $\text{Chl} \cdots \text{ROH}$, $\text{Chl} \cdots (\text{ROH})_2$, $(\text{Chl})_2 \cdots (\text{ROH})_2$, $(\text{Chl})_2 \cdots (\text{ROH})_3$. The structures of such reaction complexes may be more or less cyclic (see Figs. 2a and b and Figs. 8a and b). In the case of the β, β -branched 2,2-dimethyl-1-butanol, the reaction



Figs. 8a and b. Possible models of the two cyclic reaction complexes $(\text{Chl})_2 \cdots (\text{ROH})_2$ and $(\text{Chl})_2 \cdots (\text{ROH})_3$.

orders of chloral and alcohols are both found to be 1.0. This means that the rate-determining step now becomes a reaction between one molecule of chloral and one molecule of alcohol.

In the catalyzed reaction the reaction orders of chloral and acetic acid are found to be about 1.0 and 0.5, respectively, but the reaction order of alcohol varies from 0.2 to 1.0 when going from less to more bulky alcohols (see Table 1). This suggests the following reaction mechanism (9)



H: hemiacetal

A reaction order of the alcohol between 0 and 1 means that step 1 is only partly rate-determining. If the reaction order is 1.0, as in the case with bulky

alcohols, it means that either step 2 or step 3 is rate-determining. In this case the forward reaction can be described by the following rate equation (10)

$$\vec{v}_k = \vec{k}_k [\text{HA}]_{0,s}^{\frac{1}{2}} [\text{Chl}] [\text{ROH}] \quad (10)$$

The concentration of monomeric acetic acid is nearly equal to $(\frac{1}{2})^{\frac{1}{2}} K_{\text{HA}}^{-\frac{1}{2}} [\text{HA}]_{0,s}^{\frac{1}{2}}$; the factor $(\frac{1}{2})^{\frac{1}{2}} K_{\text{HA}}^{-\frac{1}{2}}$ being included in \vec{k}_k . K_{HA} refers to eqn. (3).

When $[\text{Chl}]_0 = [\text{ROH}]_0$, and the contribution from the uncatalyzed reaction to the total reaction is neglected, a plot of $1/[\text{Chl}]$ against time gives a straight line in the initial part of the reaction for the case of 2,2-dimethyl-1-butanol

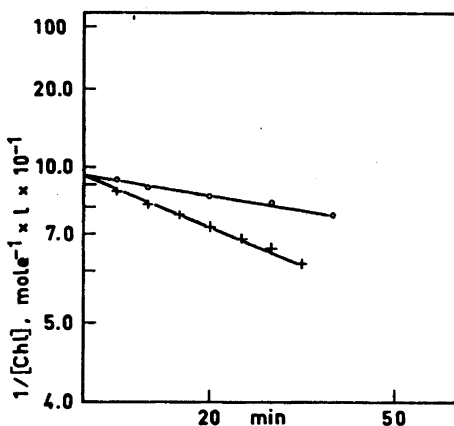


Fig. 9. The catalyzed formation of chloral hemiacetal of 2,2-dimethyl-1-butanol, neglecting the uncatalyzed contribution, treated as second-order reaction by plotting $1/[\text{Chl}]$ versus time; O, Initial conc. of chloral and alcohol are 10^{-2} M and initial conc. of acetic acid 10^{-4} M; +, Initial conc. of chloral and alcohol are 10^{-2} M and initial conc. of acetic acid 4×10^{-4} M.

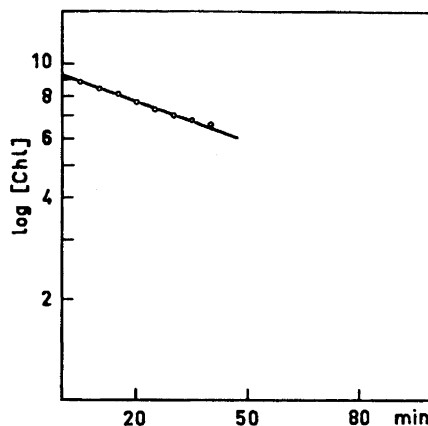


Fig. 10. The catalyzed formation of chloral hemiacetal of 2,2-dimethyl-1-butanol, neglecting the uncatalyzed contribution, treated as first-order reaction by plotting $\log [\text{Chl}]$ versus time. The initial concentrations of chloral, alcohol and acetic acid are 10^{-2} , 2×10^{-2} , and 10^{-4} M, respectively.

(Fig. 9). If $[\text{Chl}]_0 < [\text{ROH}]_0$ (still neglecting the contribution from the uncatalyzed reaction) a plot of $\log [\text{Chl}]$ against time yields a straight line for the first part of the reaction, Fig. 10. The rate constant obtained from treating the experimental data as first order, *viz.* second order reaction, together with that calculated from initial rate of the catalyzed reaction is given in Table 2. The two latter treatments give almost identical rate constants.

In the first case, when the reaction orders of chloral, alcohol, and acetic acid are 1.0, 0.2–0.8, and 0.5, respectively, the forward reaction can be described by the following rate equation (11)

$$\vec{v}_k = \vec{k}_k [\text{HA}]_{0,s}^{\frac{1}{2}} [\text{Chl}] [\text{ROH}]^{0.2-0.8} \quad (11)$$

Table 2. Determination of \vec{k}_k for 2,2-dimethyl-1-butanol by means of second-order treatment, first-order treatment and initial rate treatment.

Formula	Initial concentrations mol $\times 10^{-1} \times 10^{-2}$			Determination of \vec{k}_k mol $^{-1} \times 10^1 \times \text{sec}^{-1}$		
	chloral	alcohol	acetic acid	neglecting $\vec{v}_{0,uk}$		without neglecting $\vec{v}_{0,uk}$
				second-order treatment ^a	first-order treatment ^b	initial rate treatment ^c
CH ₃ CH ₂ C(CH ₃) ₂ CH ₂ OH	1.00	1.00	1.00 $\times 10^{-2}$	1.03		0.71
	1.00	2.00	1.00 $\times 10^{-2}$		0.69	0.68
	1.00	1.00	4.00 $\times 10^{-2}$	1.15		0.73

$$^a \vec{k}_k = (1/[\text{Chl}])/[\text{HA}]_{0,s}^{\frac{1}{2}} \times \text{time.}$$

$$^b \vec{k}_k = \log[\text{Chl}]/([\text{HA}]_{0,s}^{\frac{1}{2}} \times [\text{ROH}]_0 \times \text{time}).$$

$$^c \vec{k}_k = v_{0,k}/([\text{HA}]_{0,s}^{\frac{1}{2}} \times [\text{ROH}]_0).$$

A reasonable interpretation of eqn. (11) is obtained from the reaction mechanism (9) given above using the steady state treatment on $\text{Chl} \cdots \text{HA}$ (12)

$$\frac{d[\text{Chl} \cdots \text{HA}]}{dt} = \vec{k}_{1,k}[\text{HA}]_{0,s}^{\frac{1}{2}}[\text{Chl}] - \vec{k}_{1,k}[\text{Chl} \cdots \text{HA}] - \vec{k}_{2,k}[\text{Chl} \cdots \text{HA}][\text{ROH}] + \vec{k}_{2,k}[\text{HA}]_{0,s}^{\frac{1}{2}}[\text{H}] = 0 \quad (12)$$

Separation of $[\text{Chl} \cdots \text{HA}]$ gives (13)

$$[\text{Chl} \cdots \text{HA}] = \frac{\vec{k}_{1,k}[\text{HA}]_{0,s}^{\frac{1}{2}}[\text{Chl}] + \vec{k}_{2,k}[\text{HA}]_{0,s}^{\frac{1}{2}}[\text{H}]}{\vec{k}_{1,k} + \vec{k}_{2,k}[\text{ROH}]} \quad (13)$$

Inserting $[\text{Chl} \cdots \text{HA}]$ in the rate-equation (14)

$$v_k = -d[\text{Chl}]/dt = \vec{k}_{1,k}[\text{HA}]_{0,s}^{\frac{1}{2}}[\text{Chl}] - \vec{k}_{1,k}[\text{Chl} \cdots \text{HA}] \quad (14)$$

gives eqn. (15)

$$v_k = \vec{k}_{1,k}[\text{HA}]_{0,s}^{\frac{1}{2}}[\text{Chl}] - \frac{\vec{k}_{1,k}(\vec{k}_{1,k}[\text{HA}]_{0,s}^{\frac{1}{2}}[\text{Chl}] + \vec{k}_{2,k}[\text{HA}]_{0,s}^{\frac{1}{2}}[\text{H}])}{\vec{k}_{1,k} + \vec{k}_{2,k}[\text{ROH}]}$$

$$v_k = \frac{[\text{HA}]_{0,s}^{\frac{1}{2}}(\vec{k}_{1,k}\vec{k}_{2,k}[\text{Chl}][\text{ROH}] - \vec{k}_{1,k}\vec{k}_{2,k}[\text{H}])}{\vec{k}_{1,k} + \vec{k}_{2,k}[\text{ROH}]} \quad (15)$$

$$v_k = \frac{[\text{HA}]_{0,s}^{\frac{1}{2}}(\vec{k}_{1,k}[\text{Chl}][\text{ROH}] - f \cdot \vec{k}_{2,k}[\text{H}])}{f + [\text{ROH}]}$$

$$f = \vec{k}_{1,k}/\vec{k}_{2,k}$$

Excluding terms connected with the reverse reaction we obtain the following rate equation describing the forward reaction (16)

$$\vec{v}_k = \frac{\vec{k}_{1,k}[\text{HA}]_{0,s}^{\ddagger}[\text{Chl}][\text{ROH}]}{f + [\text{ROH}]} \quad (16)$$

$$\begin{aligned} \vec{k}_{1,k} &= \vec{k}_1 \cdot K_{\text{HA}}^{-\ddagger} \cdot \left(\frac{1}{2}\right)^{\ddagger} \\ \vec{k}_{2,k} &= \vec{k}_2 \cdot K_{\text{HA}}^{-\ddagger} \cdot \left(\frac{1}{2}\right)^{\ddagger} \end{aligned}$$

The factor f is, due to $\vec{k}_{2,k}$, a measure of the steric influence of the alcohol on the rate of the hemiacetal formation. The β -branched alcohols, such as 2,2-dimethyl-1-butanol, yield large f values. When f is large and also greater than $[\text{ROH}]$ eqn. (16) becomes:

$$\vec{v}_k = (\vec{k}_{1,k}/f)[\text{HA}]_{0,s}^{\ddagger}[\text{Chl}][\text{ROH}] \quad (17)$$

If $[\text{ROH}]_0 > [\text{Chl}]_0$ eqn. (17) can be treated as a pseudo-first-order reaction. As already shown in Fig. 9, a straight line is obtained in the first part of the reaction when $\log [\text{Chl}]$ is plotted against time. If $f \ll [\text{ROH}]$ eqn. (16) becomes:

$$\vec{v}_k = \vec{k}_{1,k}[\text{HA}]_{0,s}^{\ddagger}[\text{Chl}] \quad (18)$$

Eqn. (18) holds reasonably well for straight chain primary alcohols such as methanol, ethanol, 1-propanol, and 1-butanol, provided $[\text{ROH}]_0 \geq 2 \times 10^{-2}$ M (see Table 4). The most common case is when f and $[\text{ROH}]$ are of similar magnitude. It is not then possible to reduce eqn. (16) to a simpler equation and the reaction order of the alcohol varies with the initial concentration. The influence of f and the initial concentration of alcohol on the reaction order of the latter is treated later on in this paper (see Table 8 and Fig. 17). In order to determine $\vec{k}_{1,k}$ and f eqn. (16) is converted to eqn. (19)

$$[\text{ROH}]_0 = \frac{\vec{k}_{1,k}[\text{HA}]_{0,s}^{\ddagger}[\text{Chl}]_0[\text{ROH}]_0}{\vec{v}_{0,k}} - f \quad (19)$$

Table 3. Determination of $\vec{k}_{1,k}$ and f for 1-propanol.

Formula	$\vec{k}_{1,k}^a$	$f = \vec{k}_{1,k}/\vec{k}_{2,k}^a$
	$\text{mol}^{-\ddagger} \times \text{l}^{\ddagger} \times \text{sec}^{-1} \times 10^{\ddagger}$	$\text{mol} \times \text{l}^{-1} \times 10^{\ddagger}$
$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$	4.85	0.40

^a $\vec{k}_{1,k}$ and f refer both to eqn. (19)

$$[\text{ROH}]_0 = \frac{\vec{k}_{1,k}[\text{HA}]_{0,s}^{\ddagger}[\text{Chl}]_0[\text{ROH}]_0}{\vec{v}_{0,k}} - f$$

and are determined from the line in Fig. 11.

By measuring $\vec{v}_{0,k}$ at various $[\text{ROH}]_0$, keeping $[\text{Chl}]_0$ and $[\text{HA}]_{0,s}$ constant, $\vec{k}_{1,k}$ and f are obtained from a plot of $[\text{ROH}]_0$ against $[\text{HA}]_{0,s}^{\frac{1}{2}}[\text{Chl}]_0/[\text{ROH}]_0/\vec{v}_{0,k}$. This has been done for the non branched 1-propanol; the results are given in Table 3 and in Fig. 11, and show a straight line relationship. Table 4 shows the values of $\vec{k}_{1,k}$, obtained from eqn. (18) by the use of the initial rates given

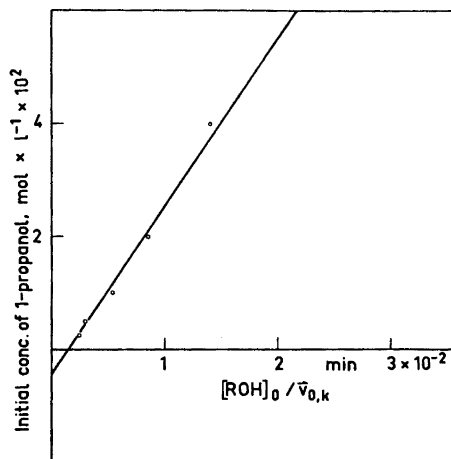
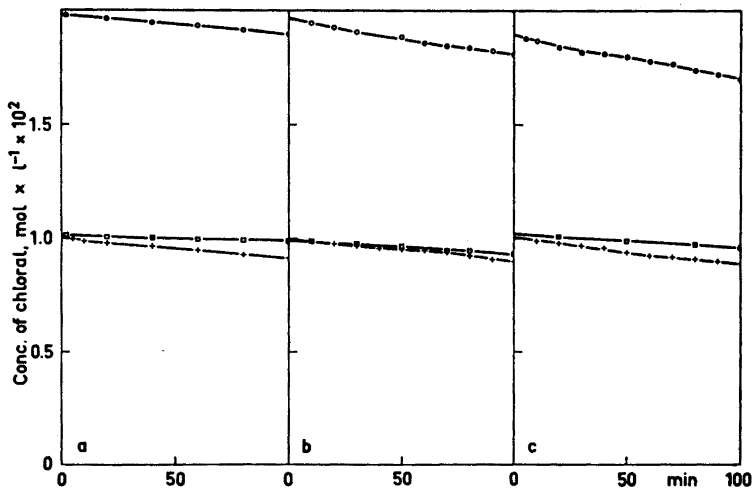


Fig. 11. Determination of $\vec{k}_{1,k}$ and f for 1-propanol chloral hemiacetal from a plot of $[\text{ROH}]_0$ versus $[\text{ROH}]_0/\vec{v}_{0,k}$.



Figs. 12a, b, c, and d. The course of the uncatalyzed formation of chloral hemiacetals of straight chain secondary alcohols as 2-propanol, 2-butanol and 2-pentanol, respectively, illustrated by a plot of the chloral concentrations versus time at various initial concentrations of chloral and the alcohols: \square , Conc. of chloral and alcohol are 10^{-2} M; $+$, Conc. of chloral and alcohol are 10^{-2} and 2×10^{-2} M; \circ , Conc. of chloral and alcohol are 2×10^{-2} and 10^{-2} M, respectively.

Table 4. Determinations of $\vec{k}_{1,k}$ and f for various primary alcohols.

Formula	Initial concentrations $\text{mol} \times \text{l}^{-1} \times 10^{-3}$			$\vec{k}_{1,k}$ $\text{mol}^{-1} \times \text{l}^{\frac{1}{2}} \times \text{sec}^{-1} \times 10^3$	f^c $\text{mol} \times \text{l}^{-1} \times 10^2$
	chloral	alcohol	acetic acid		
CH ₃ OH	1.00	1.00	1.00 × 10 ⁻³	3.5	0.44
	1.00	2.00	1.00 × 10 ⁻³	4.2	
CH ₃ CH ₂ OH	1.00	1.00	1.00 × 10 ⁻³	3.2	0.54
	1.00	2.00	1.00 × 10 ⁻³	4.2	
CH ₃ CH ₂ CH ₂ OH	1.00	1.00	1.00 × 10 ⁻³	3.0	0.62 ^d
	1.00	2.00	1.00 × 10 ⁻³	4.2	
CH ₃ CH ₂ CH ₂ CH ₂ OH	1.00	1.00	1.00 × 10 ⁻³	3.2	0.54
	1.00	2.00	1.00 × 10 ⁻³	4.4	
(CH ₃) ₂ CHCH ₂ OH	1.00	1.00	1.00 × 10 ⁻³	2.2	1.2
	1.00	2.00	1.00 × 10 ⁻³	2.9	
CH ₃ CH ₂ C(CH ₃) ₂ CH ₂ OH	1.00	1.00	1.00 × 10 ⁻³	0.72	5.8 ^d
	1.00	2.00	1.00 × 10 ⁻³	1.4	
CH ₃ C(CH ₃) ₂ CH ₂ CH ₂ OH	1.00	1.00	1.00 × 10 ⁻³	2.5	0.94
	1.00	2.00	1.00 × 10 ⁻³	3.3	

$$a \vec{v}_{0,k} = \frac{\vec{k}_{1,k}[\text{HA}]_0^{\frac{1}{2}}[\text{Ch}]_0[\text{ROH}]_0}{f + [\text{ROH}]_0}; \text{ eqn. (16) used on the initial rate.}$$

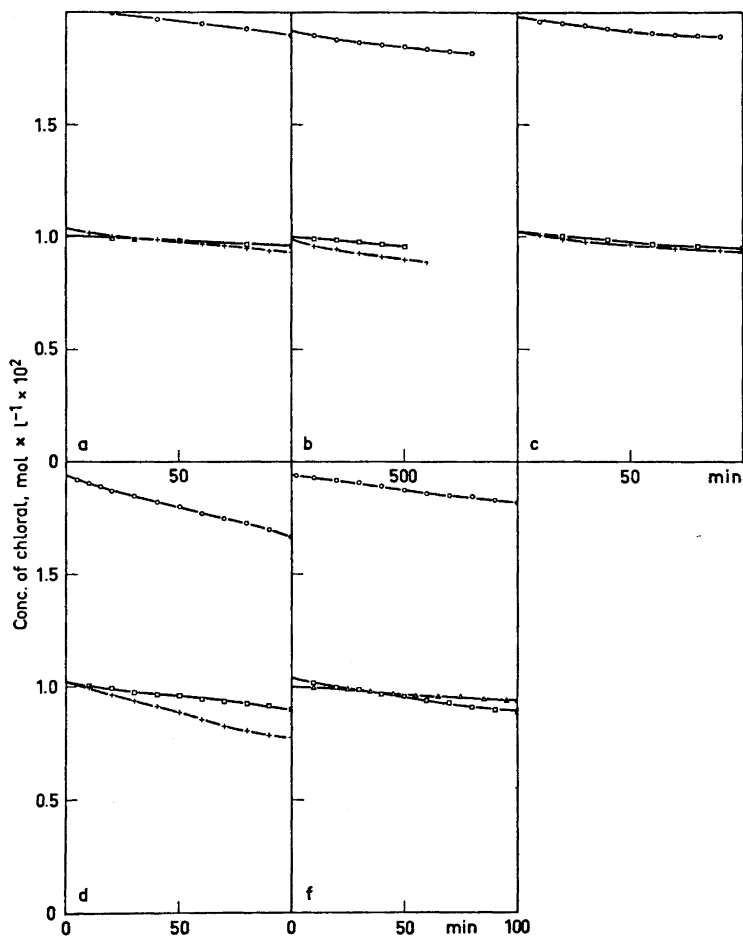
^b As precise value for $\vec{k}_{1,k}$ is used 4.85×10^{-3} which is that given in Table 3.

^c The more precise value for f given in Table 3 is 0.40×10^{-2} . The value of f of 0.62 for 1-propanol is obtained from a single determination of $\vec{v}_{0,k}$.

^d It is also possible to calculate f for CH₃CH₂C(CH₃)₂OH from $\vec{k}_k = \vec{k}_{1,k}f$ using $\vec{k}_{1,k} = 4.87 \times 10^{-3}$; f is then found to be 6.7×10^{-3} .

in Table 1, of various primary alcohols. When the alcohol concentration is 2×10^{-2} M the $\vec{k}_{1,k}$ values for the straight chain alcohols agree reasonably well with that for 1-propanol (Table 3). In addition values of f calculated on basis of eqn. (20), which is derived from eqn. (19), are given in this Table.

$$f = \vec{k}_{1,k}[\text{HA}]_0[\text{Chl}]_0[\text{ROH}]_0 / v_{0,k} - [\text{ROH}]_0 \quad (20)$$



Figs. 13a, b, c, d, and f. The course of the uncatalyzed formation of chloral hemiacetals of branched secondary alcohols as 3-methyl-2-butanol, 3,3-dimethyl-2-butanol, 4-methyl-2-pentanol, 4,4-dimethyl-2-pentanol, and 2,6-dimethyl-4-heptanol, respectively, illustrated by a plot of the chloral concentration *versus* time at various initial concentrations of chloral and the alcohols: □, Conc. of chloral and alcohol are 10^{-3} M; + Conc. of chloral and alcohol are 10^{-2} and 2×10^{-2} M; ○, Conc. of chloral and alcohol are 2×10^{-2} and 10^{-2} M.

The value for $\bar{k}_{1,k}$ from 1-propanol given in Table 3 is used. The f value for 2,2-dimethyl-1-butanol is 12 times larger than that calculated for straight-chain alcohols, while 2-methyl-1-propanol and 3,3-dimethyl-1-butanol only give values twice as large. In contrast to this the initial rate of 2,2-dimethyl-1-butanol is 5 times smaller than that calculated for straight-chain alcohols.

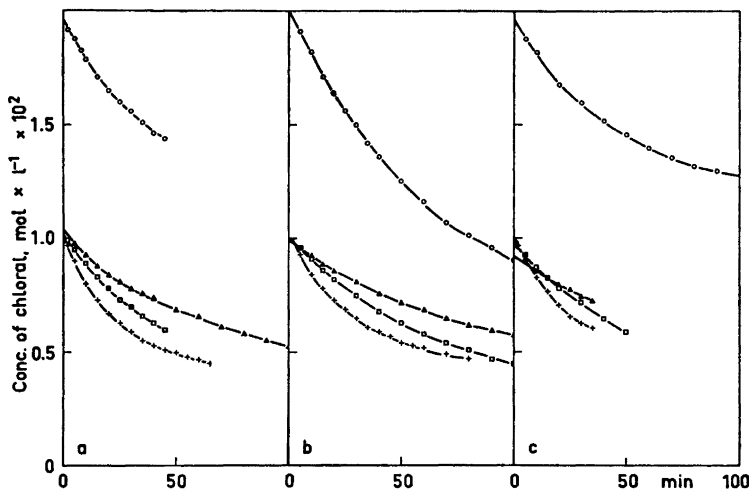
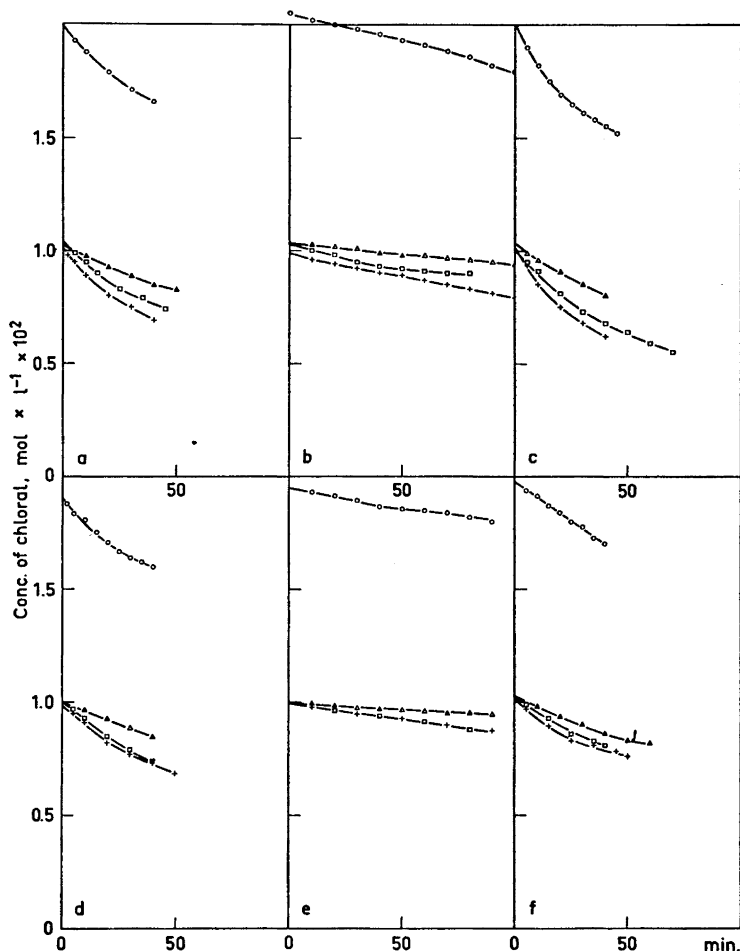


Fig. 14a, b and c. The course of the catalyzed formation of chloral hemiacetal of non branched secondary alcohols as 2-propanol, 2-butanol, and 2-pentanol, respectively, illustrated by a plot of the chloral concentrations *versus* time at various initial concentrations of chloral, alcohols, and acetic acid: Δ , Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 10^{-2} , and 10^{-4} M; \circ , Conc. of chloral, alcohol, and acetic acid are 2×10^{-2} , 10^{-2} , and 10^{-4} M, respectively; \square , Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 2×10^{-2} , and 10^{-4} M, respectively; $+$, Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 10^{-2} , and 4×10^{-4} M, respectively.

Sec. alcohols. Figs. 12a, b, and c show the course of the uncatalyzed formation of chloral hemiacetals of straight chain secondary alcohols: 2-propanol, 2-butanol and 2-pentanol. The same reaction with branched alcohols: 3-methyl-2-butanol, 3,3-dimethyl-2-butanol, 4-methyl-2-pentanol, 4,4-dimethyl-2-pentanol, and 2,6-dimethyl-4-heptanol is shown in Figs. 13a, b, c, d, and f. Figs. 14a, b, and c and Figs. 15a, b, c, d show the course of the corresponding catalyzed reactions. Figs. 15e and f represent the course of the catalyzed reactions of 2,4-dimethyl-3-pentanol and 2,6-dimethyl-4-heptanol. The initial rates of the observed uncatalyzed and catalyzed reactions and that of the calculated catalyzed reactions are listed in Table 5. This table also lists the reaction orders with respect to chloral, alcohol and acetic acid and values for f (eqn. (20)).

A comparison of values from Tables 1 and 5 shows that the initial rates of the uncatalyzed reaction of straight chain primary alcohols are almost twice the initial rates of straight chain secondary alcohols. Increased branching in the β -position leads to a marked decrease in the initial rate, as illustrated by



Figs. 15a, b, c, d, e, and f. The course of the catalyzed formation of chloral hemiacetals of branched secondary alcohols as 3-methyl-2-butanol, 3,3-dimethyl-2-butanol, 4-methyl-2-pentanol, 4,4-dimethyl-2-pentanol, 2,4-dimethyl-3-pentanol, and 2,6-dimethyl-4-heptanol, respectively, illustrated by a plot of the chloral concentrations *versus* time at various initial concentrations of chloral, alcohol, and acetic acid: Δ , Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 10^{-2} , and 10^{-4} M, respectively; \circ , Conc. of chloral, alcohol, and acetic acid are 2×10^{-2} , 10^{-2} , and 10^{-4} M, respectively; \square , Conc. of chloral, alcohol, and acetic acid are 10^{-2} , 2×10^{-2} , and 10^{-4} M, respectively; $+$, Conc. of chloral, alcohol and acetic acid are 10^{-2} , 10^{-2} , and 4×10^{-2} M, respectively.

3,3-dimethyl-2-butanol. The initial rate with 2,4-dimethyl-3-pentanol was too low to be determined.

In contrast to the primary alcohols, branching introduced in the γ -position in secondary alcohols (exemplified by 4,4-dimethyl-2-pentanol and 2,6-dimethyl-4-heptanol) causes a marked decrease in the initial rate. The ratio

Table 5. Initial rates of a) measured uncatalyzed, b) measured catalyzed, and c) calculated catalyzed formation of chloral hemiacetals made from *sec* alcohols, and reaction orders for chloral, alcohol, and acetic acid.

Formula	Initial concentrations $\text{mol} \times \text{l}^{-1} \times 10^2$			Initial rate of hemiacetal formation $\text{mol} \times \text{l}^{-1} \times \text{sec}^{-1} \times 10^6$			Reaction orders				f ($\text{mol} \times \text{l}^{-1} \times 10^4$) of the real catalyzed reaction	
	chlo- ral	alco- hol	acetic acid	$v_{0,k}$	$v_{0,nk}$	$v_{0,k}$	uncatalyzed reaction			real catalyzed reaction		
							chlo- ral	alco- hol	chlo- ral	alco- hol		acetic acid
$\text{CH}_3\text{CHOHCH}_3$	1.00	1.00	1.00×10^{-2}	1.4	0.067	1.3	1.0	1.0	0.88	0.62		2.7
	2.00	1.00	1.00×10^{-2}	2.5	0.13	2.4						
	1.00	2.00	1.00×10^{-2}	2.1	0.13	2.0	1.0	1.0		0.50		
	1.00	1.00	4.00×10^{-2}	2.7	0.067	2.6						
$\text{CH}_3\text{CHOHCH}_2\text{CH}_3$	1.00	1.00	1.00×10^{-2}	1.2	0.12	1.1	1.1	1.1	1.2	0.54	0.56	3.4
	2.00	1.00	1.00×10^{-2}	2.8	0.25	2.5						
	1.00	2.00	1.00×10^{-2}	1.8	0.17	1.6	0.52	0.52				
	1.00	1.00	4.00×10^{-2}	2.5	0.12	2.4						
$\text{CH}_3\text{CHOH}(\text{CH}_2)_2\text{CH}_3$	1.00	1.00	1.00×10^{-2}	1.1	0.083	1.0	0.68	0.68	1.1	0.68	0.63	4.8
	2.00	1.00	1.00×10^{-2}	2.3	0.13	2.2						
	1.00	2.00	1.00×10^{-2}	1.8	0.18	1.6	1.1	1.1				
	1.00	1.00	4.00×10^{-2}	2.5	0.083	2.4						
$\text{CH}_3\text{CH}_2\text{CHOHCH}_2\text{CH}_3$	1.00	1.00	1.00×10^{-2}	0.75	0.042	0.71	1.2	1.0	0.98	0.76	0.70	5.8
	2.00	1.00	1.00×10^{-2}	1.5	0.10	1.4						
	1.00	2.00	1.00×10^{-2}	1.3	0.083	1.2	1.0	1.0				
	1.00	1.00	4.00×10^{-2}	2.0	0.042	1.9						
$\text{CH}_3(\text{CH}_2)_2\text{CHOH}(\text{CH}_2)_2\text{CH}_3$	1.00	1.00	1.00×10^{-2}	0.67	0.067	0.60	1.0	1.0	1.2	0.87	0.70	7.1
	2.00	1.00	1.00×10^{-2}	1.5	0.13	1.4						
	1.00	2.00	1.00×10^{-2}	1.2	0.13	1.1	1.0	1.0				
	1.00	1.00	4.00×10^{-2}	1.7	0.067	1.6						

Table 5. Continued.

CH ₃ CHOHCH(CH ₃) ₂	1.00	1.00	1.00 × 10 ⁻²	0.67	0.083	0.59	1.0	1.0	1.1	0.90	0.70	7.2
	2.00	1.00	1.00 × 10 ⁻²	1.5	0.17	1.3						
	1.00	2.00	1.00 × 10 ⁻²	1.3	0.17	1.1						
	1.00	1.00	4.00 × 10 ⁻²	1.7	0.083	1.6						
CH ₃ CHOHCH ₂ CH(CH ₃) ₂	1.00	1.00	1.00 × 10 ⁻²	1.0	0.083	0.92	0.86	0.86	1.2	0.70	0.60	4.3
	2.00	1.00	1.00 × 10 ⁻²	2.3	0.15	2.1						
	1.00	2.00	1.00 × 10 ⁻²	1.7	0.15	1.5						
	1.00	1.00	4.00 × 10 ⁻²	2.2	0.083	2.1						
CH ₃ CHOHC(CH ₃) ₃	1.00	1.00	1.00 × 10 ⁻²	0.15	0.017	0.14	1.1	1.1	1.0	1.1	0.55	3.3
	2.00	1.00	1.00 × 10 ⁻²	0.33	0.037	0.29						
	1.00	2.00	1.00 × 10 ⁻²	0.33	0.033	0.30						
	1.00	1.00	4.00 × 10 ⁻²	0.32	0.017	0.30						
CH ₃ CHOHCH ₂ C(CH ₃) ₃	1.00	1.00	1.00 × 10 ⁻²	0.67	0.022	0.65	1.0	1.0	1.2	1.0	0.45	6.5
	2.00	1.00	1.00 × 10 ⁻²	1.5	0.043	1.5						
	1.00	2.00	1.00 × 10 ⁻²	1.3	0.047	1.3						
	1.00	1.00	4.00 × 10 ⁻²	1.2	0.022	1.2						
(CH ₃) ₂ CHCHOHCH(CH ₃) ₂ ^a	1.00	1.00	1.00 × 10 ⁻¹	0.15	very small	0.15			1.0	0.92	0.46	9.9
	2.00	1.00	1.00 × 10 ⁻¹	0.30		0.30						
	1.00	2.00	1.00 × 10 ⁻¹	0.28		0.28						
	1.00	1.00	4.00 × 10 ⁻¹	0.28		0.28						
(CH ₃) ₂ CHCH ₂ CHOHCH ₂ CH(CH ₃) ₂	1.00	1.00	1.00 × 10 ⁻²	0.58	0.10	0.48	1.0	1.0	1.2	1.1	0.59	9.1
	2.00	1.00	1.00 × 10 ⁻²	1.3	0.20	1.1						
	1.00	2.00	1.00 × 10 ⁻²	1.2	0.23	1.0						
	1.00	1.00	4.00 × 10 ⁻²	1.2	0.10	1.1						

^a Notice that the concentration of acetic acid is 10⁻³ M. Therefore, if the values of initial rates are compared with other initial rates, they must be divided by a factor of √10.

between the initial rate of the uncatalyzed reaction and the catalyzed reaction is similar to that found with primary alcohols. The reaction orders for chloral and alcohol in the uncatalyzed reaction are, in all cases, both found to be about 1.0, in contrast to those found with respect to primary alcohols. This indicates that the rate-determining step is a reaction between one molecule of chloral and one molecule of alcohol.

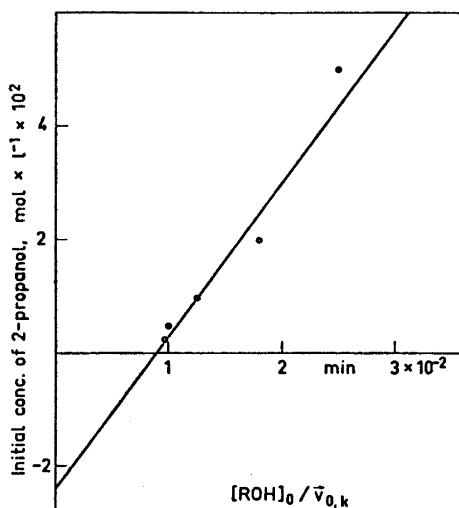
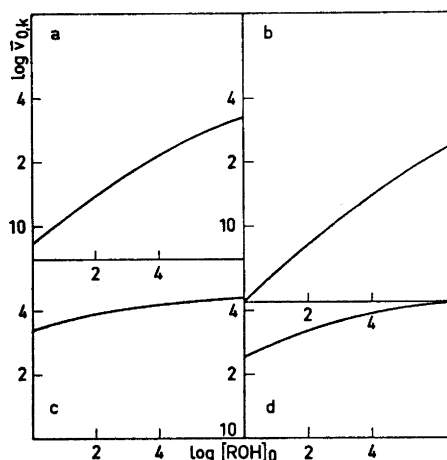


Fig. 16. Determination of $\bar{k}_{1,k}$ and f of 2-propanol chloral hemiacetal from a plot of $[\text{ROH}]_0$ versus $[\text{ROH}]_0/\bar{v}_{0,k}$.



Figs. 17a, b, c, and d. An illustration of the calculated reaction orders with respect to alcohols as a function of the steric constant, f , and the initial concentrations of alcohol. The curves represent a plot of $\log \bar{v}_{0,k}$ versus $\log [\text{ROH}]_0$. In a, b, c, and d the values of f are 0.5×10^{-2} , 1×10^{-2} , 5×10^{-2} , and 10×10^{-2} mol \times l $^{-1}$, respectively. In all cases the initial concentrations of chloral and acetic acid are 10^{-2} and 10^{-4} M. The initial concentrations of alcohol varies between 10^{-2} and 10×10^{-2} M.

Following eqn. (19), we plotted $[\text{2-propanol}]_0$ against $[\text{HA}]_0 \cdot [\text{Chl}]_0 / [\text{2-propanol}]_0 / \bar{v}_{0,k}$. The plot gave a straight line just as was the case with 1-propanol (Fig. 16). The values of $\bar{k}_{1,k}$ and f are listed in Table 7. $\bar{k}_{1,k}$ has nearly the same value as that found for 1-propanol. This indicates that the reaction mechanism proposed in (9) for primary alcohols is also applicable for secondary ones. The value of f is about 6 times larger than that for 1-propanol. The increased value of f is expected since the smaller α -hydrogen atom in ethanol is substituted with the larger methyl group.

In Table 8 the initial rate of the catalyzed hemiacetal formation is calculated from eqn. (16) for different values of f at alcohol concentrations of 10^{-2} and 2×10^{-2} M. The concentrations of chloral and acetic acid are 10^{-2} and 10^{-4} M.

alicyclic secondary alcohols, and the reaction orders for chloral, alcohol, and acetic acid.

Formula	Initial concentrations $\text{mol} \times 10^{-1} \times 10^3$			Initial rate of hemiacetal formation $\text{mole} \times 10^{-1} \times \text{sec}^{-1} \times 10^6$			Reaction orders				$f \text{ mol} \times 10^{-1} \times 10^6$ of the real catalyzed reaction	
	chloral	alcohol	acetic acid	$\bar{v}_{0,k}$	$\bar{v}_{0,uk}$	$\bar{v}_{0,k}$	uncatalyzed reaction			Real catalyzed reaction		
							chloral	alcohol	chloral	alcohol		acetic acid
Cyclohexanol	1.00	1.00	1.00×10^{-3}	1.6	0.12	1.5	1.1	2.4	1.0	0.18	0.61	2.2
	2.00	1.00	1.00×10^{-3}	3.3	0.25	3.0						
	1.00	2.00	1.00×10^{-3}	2.3	0.63	1.7						
	1.00	1.00	4.00×10^{-2}	3.6	0.12	3.5						
Cyclopentanol	1.00	1.00	1.00×10^{-2}	2.2	0.062	2.1	1.8	2.4	1.2	0.25	0.45	1.3
	2.00	1.00	1.00×10^{-2}	5.3	0.22	5.1						
	1.00	2.00	1.00×10^{-2}	2.8	0.32	2.5						
	1.00	1.00	4.00×10^{-2}	4.0	0.062	3.9						
(R)-Menthhol	1.00	1.00	1.00×10^{-2}	0.82	0.080	0.74	0.91	0.81	0.92	0.85		5.6
	2.00	1.00	1.00×10^{-2}	1.6	0.15	1.4						
	1.00	2.00	1.00×10^{-2}	1.4	0.14	1.3						
Isomenthol	1.00	1.00	1.00×10^{-2}	0.13	0.026	0.10	0.89	0.94	1.0	0.85		48
	2.00	1.00	1.00×10^{-2}	0.25	0.048	0.20						
	1.00	2.00	1.00×10^{-2}	0.23	0.050	0.18						
Neomenthol ^a	1.00	1.00	1.00×10^{-1}	0.025	0.0050	0.020	1.0	1.2	1.3	0.93		760
	2.00	1.00	1.00×10^{-1}	0.058	0.010	0.048						
	1.00	2.00	1.00×10^{-1}	0.050	0.012	0.038						
Borneol	1.00	1.00	1.00×10^{-2}	0.020	0.0033	0.017	1.0	1.0	0.91	0.91		290
	2.00	1.00	1.00×10^{-2}	0.039	0.0067	0.032						
	1.00	2.00	1.00×10^{-2}	0.039	0.0067	0.032						
Isoborneol	1.00	1.00	1.00×10^{-2}	0.010	0.0033	0.0067	0.60	0.60	1.2	1.2		725
	2.00	1.00	1.00×10^{-2}	0.020	0.0050	0.015						
	1.00	2.00	1.00×10^{-2}	0.020	0.0050	0.015						

Neoisomenthol — see in the footnote b.

^a Notice that the concentration of acetic acid is 1×10^{-3} . To compare the initial rates of neomenthol with initial rates of the other alcohols, the former should be divided by $\sqrt{10}$.

^b The initial rate for this alcohol was earlier found to be 2.8 larger than the initial rate found for neomenthol.

Table 7. Determination of $\vec{k}_{1,k}$ and f for 2-propanol chloral hemiacetal.

Formula	$\vec{k}_{1,k}^a$	$f = \vec{k}_{1,k}/\vec{k}_{2,k}^a$
	$\text{mol}^{-\frac{1}{2}} \times \text{l}^{\frac{1}{2}} \times \text{sec}^{-1} \times 10^3$	$\text{mol} \times \text{l}^{-1} \times 10^3$
$\text{CH}_3\text{CHOHCH}_3$	4.51	2.40

^a $\vec{k}_{1,k}$ and f refer both to eqn. (19)

$$[\text{ROH}]_0 = (\vec{k}_{1,k}[\text{HA}]^{\frac{1}{2}}_0[\text{Chl}]_0[\text{ROH}]_0)/\vec{v}_{0,k} - f$$

and are determined from Fig. 16.

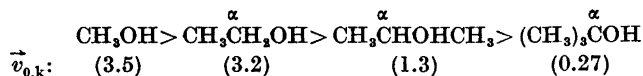
The $\vec{k}_{1,k}$ value of 4.8×10^{-2} , which is the value given in Table 3 for 1-propanol, is used in all these calculations. The reaction order of the alcohol is determined, by means of these calculated values, as described in the introduction.

In Figs. 17a, b, c, and d the influence of both f and the initial concentration of the alcohol on the reaction order of the alcohol is illustrated by a plot of $\log \vec{v}_{0,k}$ ($\vec{v}_{0,k}$ calculated as in Table 8) against $\log [\text{ROH}]_0$ for different chosen values of f . Fig. 17 shows that when $f \gg [\text{ROH}]_0$ the reaction order of the alcohol increases toward 1. The reaction order decreases with f and when $f \ll [\text{ROH}]_0$ a reaction order of 0 will be obtained. The reaction order also decreases when $[\text{ROH}]_0$ is increased and *vice versa*.

As a measure of the steric bulk of the alcohols f is to be preferred to the initial rate. The initial rate is only partly affected by that reaction step where the alcohol enters into the hemiacetal formation, but can still be used as a qualitative measure. It should be emphasized that when f is large, compared with the alcohol concentration, f and $\vec{v}_{0,k}$ are approximately inversely proportional. This is exemplified by 2-propanol ($f = 2.4 \times 10^{-2}$ and $\vec{v}_{0,k} = 1.30 \times 10^{-6}$) and 3,3-dimethyl-2-butanol ($f = 31 \times 10^{-2}$ and $\vec{v}_{0,k} = 0.15 \times 10^{-6}$). However, when f changes from 0.4×10^{-2} (1-propanol) to 2.4×10^{-2} (2-propanol) the initial rate only changes from 3.0×10^{-6} to 1.30×10^{-6} .

By use of the values of the initial rates (or f values) of the real catalyzed reaction with primary and secondary alcohols listed in Tables 1 and 5, the influence of different groups, placed in different positions in the alcohol molecule, can be summarized as follows:

a. The influence of α -branching



The decrease in conformational freedom of the alcohol by the formation of the reaction complex, $\text{Chl} \cdots \text{HA} \cdots \text{ROH}$ is believed to be of importance in determining the reaction rate. This decrease is more important for ethanol than for

Table 3. Catalyzed chloral hemiacetal formation. Calculated initial rates and reaction orders for alcohol using two initial alcohol concentrations and various f values.

$[\text{ROH}]_0$ $10^2 \times \text{mol} \times \text{l}^{-1}$		$f = \vec{k}_{1,k} / \vec{k}_{2,k} \quad \text{mol} \times \text{l}^{-1} \times 10^2$											
		500	100	50	20	10	5	2	1	0.5	0.1	0.05	0.01
1.00	$\vec{v}_{0,k}$ $\text{mol} \times \text{l}^{-1} \times \text{sec}^{-1} \times 10^{7a}$	0.097	0.48	0.95	2.31	4.41	8.1	16.2	24.2	32.4	44.1	46.2	48.0
2.00	$\vec{v}_{0,k}$ $\text{mol} \times \text{l}^{-1} \times \text{sec}^{-1} \times 10^7$	0.194	0.95	1.87	4.41	8.1	13.9	24.2	32.4	38.8	46.2	47.3	48.3
	Reaction-order ^b of the alcohol	~ 1	0.99	0.97	0.93	0.88	0.76	0.58	0.42	0.25	0.07	0.03	0.01

^a $\vec{v}_{0,k} = (\vec{k}_{1,k} [\text{HA}]_0^2 [\text{Ch}]_0 [\text{ROH}]_0) / (f + [\text{ROH}]_0)$. The $\vec{k}_{1,k}$ value from Table 3 is used: $\vec{k}_{1,k} = 4.85 \times 10^{-2}$.

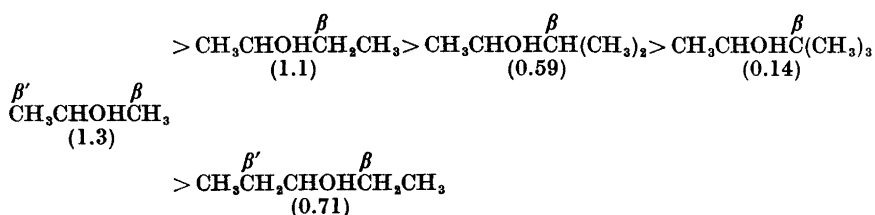
^b The reaction order of alcohol is obtained from a plot of $\log \vec{v}_{0,k}$ versus $\log [\text{ROH}]_0$.

methanol, due to the α -methyl group in ethanol. Since there are two α -methyl groups in 2-propanol and three in 2-methyl-2-propanol these alcohols react much slower than ethanol.

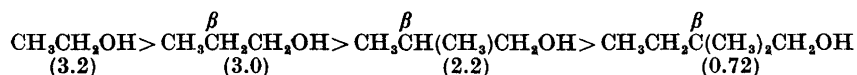
The energetically most stable conformations of the $\text{Chl}\cdots\text{HA}\cdots\text{ROH}$ are those in which the α -substituted methyl groups are placed farthest away from the trichloromethyl group (and the ring atoms).

The decrease in rate is much smaller going from methanol to ethanol than going from ethanol to 2-propanol. This would also be expected from the above conformational point of view.

b. The influence of β -branching

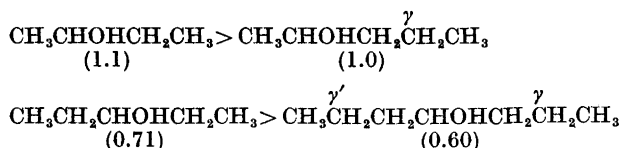


The rate for 2-butanol is smaller than that for 2-propanol due to the fact that, in contrast to the methyl group, the ethyl group has the possibility of interacting with the ring atoms as well as with the trichloromethyl group in $\text{Chl}\cdots\text{HA}\cdots\text{ROH}$. The introduction of another methyl group in the β' -position (3-pentanol) causes a further decrease in conformational freedom on formation of the reaction complex, and therefore a lower rate. This effect is not as large as that observed on further β -substitution, giving 3-methyl-3-butanol and 3,3-dimethyl-2-butanol, where a considerable drop in rate is observed.

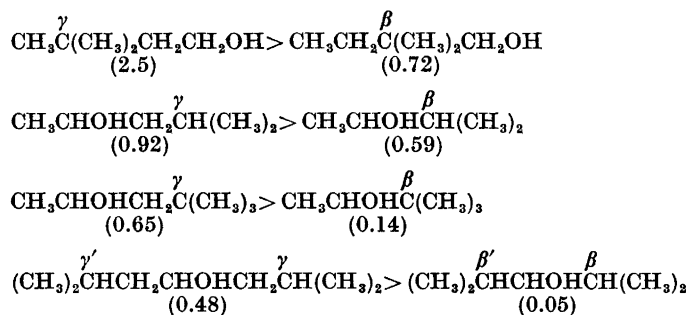


The restrictions in conformational possibilities when introducing methyl groups in the β -position are much smaller for primary alcohols than for secondary ones and therefore a smaller decrease in rate is found. Only when three alkyl groups are introduced in the β -position, as in 2,2-dimethyl-1-butanol, a marked decrease in rate is observed. Comparing the values in *a* with those in *b* it is seen that the influence of α -branching is larger than that of β -branching. This is exemplified by 1-propanol and 2-propanol which may be considered as, respectively, α - and β -substituted derivatives of ethanol.

c. The influence of γ -branching



The rate influence from γ -branching showed by 2-pentanol and 4-heptanol, is not very important. Molecular models show that γ -methyl groups may easily be placed in such a way that there is practically no interaction with the trichloromethyl group or the ring atoms.



This is further demonstrated in the above scheme where corresponding β - and γ -substituted alcohols are compared.

Alicyclic sec. alcohols. Table 6 gives the initial rates and the reaction orders for the following alicyclic sec. alcohols: Cyclopentanol, cyclohexanol, (*R*)-menthol,* (*S*)-isomenthol, (*S*)-neomenthol, ((*R*)-neoisomenthol), (*R*)-borneol, and (*S*)-isoborneol. Fig. 18 shows the stereoformulae of the conformations of the last six alcohols. The Table shows that the initial rates of the catalyzed reactions for cyclopentanol and cyclohexanol are of the same magnitude as that of 2-propanol but larger than that of 3-pentanol. This can be explained by the loss in conformational freedom in the alcohol on the formation of $\text{Chl}\cdots\text{HA}\cdots\text{ROH}$. The loss of freedom is less when the alcohol hydroxyl group is placed on a rigid ring.

In the menthol series only the conformer with the *e*-hydroxyl group reacts (see Eliel¹⁸). The conformer with the *a*-hydroxyl group will interact too strongly with the trichloromethyl group and the ring atoms in $\text{Chl}\cdots\text{HA}\cdots\text{ROH}$. The rates for the menthols then reflect the equilibrium concentration of the reactive conformer. (The percentage of this conformer for (*R*)-menthol is nearly 100). The rates are in the following order

menthol	isomenthol	neoisomenthol	neomenthol
(0.74)	(0.10)	(0.016)	(0.007)

To a lesser extent the rate may also be dependent on whether the methyl and especially the isopropyl group, are equatorial or axial. Models studies show that the position of these groups is of minor importance. Borneol and isoborneol both have only one possible conformation. The reactivity depends only on the crowding in the reaction complex $\text{Chl}\cdots\text{HA}\cdots\text{ROH}$. In the

* The reaction order of (*R*)-menthol given in this paper does not agree with that given in a previous paper.⁶ This can be explained by the fact that the reaction order for alcohols is found to vary with the alcohol concentrations and with catalytic amounts of impurities in different batches of chloral. This, however, does not change the proposed reaction mechanism.

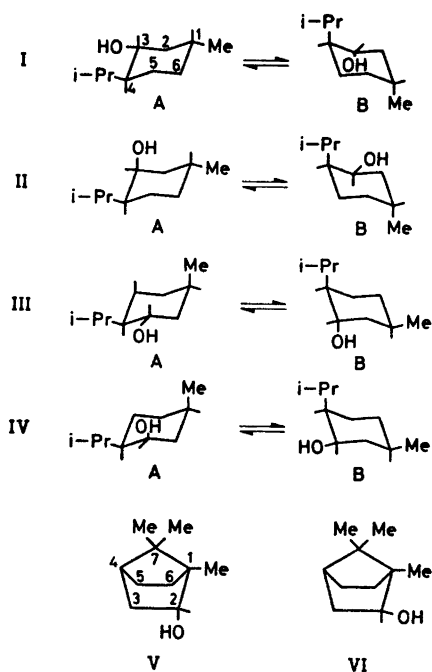


Fig. 18. IA-IB, IIA-IIB, IIIA-IIIIB, and IVA-IVB shows the stereoformulas of the conformations of *(R)*-menthol, *(S)*-neomenthol, *(S)*-isomenthol, and *(R)*-neoisomenthol, respectively, and V and VI the stereoformulas of *(R)*-borneol and *(S)*-isoborneol.

borneol reaction complex the bridging isopropylidene group is turned away from both the ring and the trichloromethyl group. This is not the case with isoborneol which has an equatorial hydroxyl group. On the other hand an interaction with the axial hydrogen atoms is possible for borneol but not for isoborneol, where only the equatorial hydrogen atom can interact. The methyl group in position (1) interacts strongly in both cases but to a greater extent in the isoborneol case. As a result, a relative low reaction rate would be expected in both cases, but with isoborneol reacting more slowly than borneol. This agrees with the observations.

Borneol
(0.017)

Isoborneol
(0.007)

On basis of the experiments reported and discussed in both this and a previous paper we hope in the future to be able to give a more exact picture of the chloral-hemiacetal formation.

EXPERIMENTAL

Some of the UV-measurements were made on a Perkin-Elmer 37 UV-spectrophotometer as reported in previous papers, but in the greater part of this investigation a Pye-Unicam-Philips spectrophotometer model SP 800 was used.

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