Tetrahedron. Vol. 30, pp. 419 to 425. Pergamon Press 1974. Printed in Great Britain

OXIDATION OF ALCOHOLS BY N-CHLOROSUCCINIMIDE—A KINETIC STUDY

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(*Received in the UK* 22 *May* 1973; *Accepted for publication* 21 *September* 1973)

Abstract—The kinetics of oxidation of alcohols by N-chlorosuccinimide (NCS) have been studied. The independence of rate on the concentration and structure of alcohol and the fractional order dependence on concentrations of added H^+ and Cl^- suggest that the reaction proceeds through the formation of Cl_2 generated in a steady concentration in a slow step followed by a rapid uptake of the alcohol. A rate expression for the observed kinetics has been suggested. This behaviour is contrasted with that of an analogous system *viz*, NBS and alcohol and is also compared with the Orton rearrangement.

INTRODUCTION

N-Halogeno compounds are known to be versatile oxidising agents.[1] The kinetics of oxidation of alcohols by NBS have been investigated in detail recently.[2,3] The authors have established that the reaction was composed of two stages, the first a slow reaction between NBS and alcohol followed by a rapid reaction between alcohol and Br_2 formed as a result of the interaction between NBS and Br^-, one of the products. They have further achieved a total supression of the second stage by the addition of mercuric salts. In what follows, we present a detailed study of the differential behaviour of the chlorine analogue of NBS viz., N-chlorosuccinimide (NCS).[4]

RESULTS AND DISCUSSION

Dependence on [*NCS*]. The oxidation of propan-2-ol by NCS was studied at 0·1M $HClO_4$ in the presence of 0·1M $NaClO_4$. The reaction was characterised by an induction period. This was followed by a regular first order reaction with respect to NCS for over 60% of the reaction (Fig 1). It was also observed that the rate of the reaction does not depend upon the concentration of the alcohol (Table 1). The induction period was not observed when the reaction was carried out in the presence of added chloride (Fig 1).

Dependence on [Cl^-]. The dependence of rate on the concentration of Cl^- at constant alcohol concentration was studied with propan-2-ol at three acid concentrations (0·1M, 0·2M and 0·3M $HClO_4$) in aqueous medium (Table 2). The order in Cl^-, however, is not simple as seen from the plot of k_{obs} *vs* [Cl^-] (Fig 2). The data for 0·1M $HClO_4$ when cast as a double reciprocal plot of $1/k_{obs}$ *vs* $1/[Cl^-]$ exhibit a linear relationship with a definite Y-intercept (Fig 3). Thus the rate-law is of the form

$$\frac{1}{k_{obs}} = \frac{1}{k} + \frac{1}{kK[Cl^-]}$$

The values of k and K were found to be 9×10^3 sec^{-1} and 14·0 respectively. The dependence of the rate on [Cl^-] is, however, different at 0·2M and 0·3M $HClO_4$ solutions. Over the concentration range 0·02–0·05M NaCl, there exists a clean first order dependence on [Cl^-]. At higher chloride concentration again the dependence is not simple (Table 2).

Dependence of alcohol in the presence of added chloride. It was observed that the rate of the reaction is independent of the concentration and structure of the alcohol in the presence of added chloride (Table 3).

Lack of kinetic isotope effect. The absence of a primary kinetic isotopic effect as evidenced by the identical reactivities of the protio and deutero compounds (Table 3) shows that the reaction does not involve the cleavage of the C—H bond on the secondary carbon atom in the slow step of the reaction—a feature which is quite different from what was observed in the oxidation of these substrates by Br_2 or NBS.

Table 1. Dependence of rate on alcohol concentration

Solvent: 100% H_2O Temp. 55°

Propan-2-ol (M)	$HClO_4$ (M)	μ	$k_1 \times 10^5$ sec^{-1}
0·02418	0·1	0·2	1·31
0·03082	0·1	0·2	1·38
0·04836	0·1	0·2	1·33
0·01236	0·001	0·1	4·26
0·06144	0·001	0·1	4·20

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[a] Forms part of the Ph.D. thesis of the author, University of Madras, India (1970)

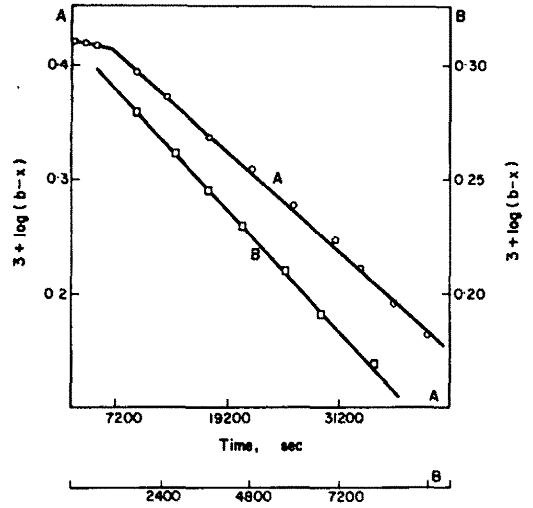


Fig 1. A— First order plot for reaction between NCS and propan-2-ol in the absence of added chloride: B—First order plot for the NCS-propan-2-ol reaction in the presence of added chloride $(b - x) = [NCS]_{total}$.

Table 2. Dependence of rate on Cl^- concentration $[\text{Propan-2-ol}] = 0{\cdot}02332M$ Solvent: 100% H_2O Temp. 55° $[NCS] = 0{\cdot}0015M$

$HClO_4$ (M)	Cl^- (M)	$k_{obs} \times 10^5$ sec^{-1}
0·1	0·01	1·57
	0·02	2·38
	0·03	3·20
	0·04	4·05
	0·05	4·42
	0·06	4·52
	0·08	5·64
	0·1	6·40
	0·2	9·86
0·2	0·02	2·20
	0·03	3·39
	0·05	5·80
	0·10	6·06
	0·20	8·64
0·3	0·02	2·56
	0·03	3·86
	0·05	6·66
	0·10	7·67
	0·20	12·6

Dependence on $[H^+]$. At constant alcohol and chloride concentrations, the dependence of rate on acidity was studied over the range 0·1–0·3M $HClO_4$ in aqueous medium. The rate increases with increase in H^+ concentration (Table 4). A plot of log k_{obs} *vs* log$[H^+]$ has a slope of 0·38 while a plot of $1/k_{obs}$ *vs* $1/[H^+]$ is found to be linear with a definite Y-intercept (Fig 3).

The dependence of rate on pH over the range 1–6 was studied in the absence of initially added chloride ion at constant alcohol concentration. It was observed that while the rate constants at pH = 1 and 2 were identical, thereafter the rate sharply increased with increase in pH. While the increased rate with increase in H^+ could be traced to increased protonation of NCS thereby increasing the positivity of the halogen in NCS, the increase in rate with increase in pH may be due to the forma-

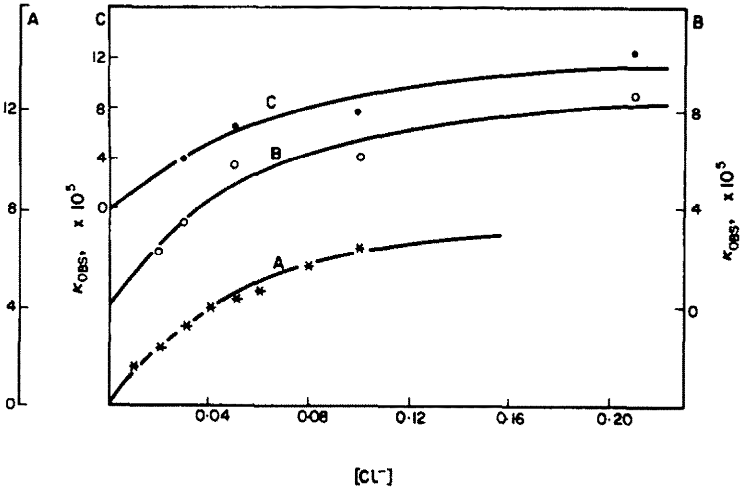


Fig 2. Plot of k_{obs} *vs* $[Cl^-]$ for NCS-propan-2-ol system: A—at 0·1M $HClO_4$; B—at 0·2M $HClO_4$; C—at 0·3M $HClO_4$.

Table 3. Dependence of rate on alcohol concentration in the presence of added chloride ion
$[HClO_4] = 0{\cdot}1M$ $\mu = 0{\cdot}3$ $[Cl^-] = 0{\cdot}05M$ $[NCS] = 0{\cdot}0015M$

Temp.	Solvent	Alcohol	Alcohol (M)	$k_{obs} \times 10^5$ sec^{-1}
55°C	100% H_2O	Propan-2-ol	0·01166	4·39
			0·02332	4·42
			0·03498	4·39
			0·04664	4·39
55°C	100% H_2O	Propan-2-ol	0·01261*	10·1
			0·02332*	9·86
			0·03217*	10·2
			0·04628*	9·95
55°C	100% H_2O	Butan-2-ol	0·01216	4·29
			0·02350	4·30
			0·03240	4·32
			0·04113	4·31
55°C	100% H_2O	Pentan-2-ol	0·01124	4·39
			0·02315	4·40
			0·03146	4·38
			0·04211	4·38
45°C	50% HOAc	Propan-2-ol	0·01124	6·62
			0·03221	6·51
45°C	50% HOAc	Fluoren-9-ol	0·005210	6·71
			0·03429	6·65
45°C	50% HOAc	Fluoren-9-ol-α-d	0·005221	6·51
45°C	50% HOAc	Benzhydrol	0·005169	6·64
			0·03224	6·52
45°C	50% HOAc	Benzhydrol-α-d	0·005126	6·62

*At 0·2M Cl^-.

Table 4. Variation of rate with $HClO_4$
[Propan-2-ol] = 0·023M $[Cl^-] = 0{\cdot}05M$ $[NCS] = 0{\cdot}0015M$
Temp. 55°

$HClO_4$ (M)	$k_{obs} \times 10^5$ sec^{-1}
0·1	4·42
0·2	5·80
0·3	6·66
1·0	8·91
1·5	14·2
2·0	19·2
2·5	27·4
3·0	36·3

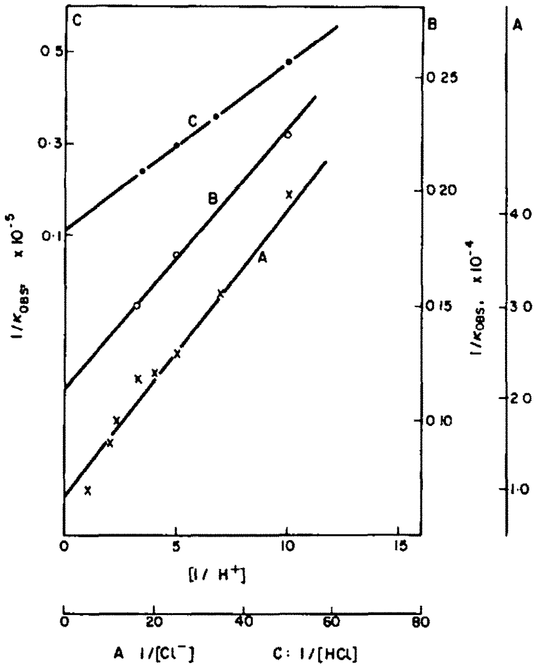


Fig 3. Double reciprocal plots of A—k_{obs} and [Cl^-]; B—k_{obs} and [H^+]; C—k_{obs} and [HCl] for NCS-propan-2-ol system.

tion of HOCl formed by the hydrolysis of NCS or $\overset{+}{N}CSH$.

The observed data on the dependence of rate at higher acidities (1·0–3·0M $HClO_4$) at constant alcohol and chloride concentrations (Table 4) were cast into a Bunnett plot. The slope 'ω' obtained was 6·25. The high positive 'ω' indicates that a water molecule acts as a proton transfer agent.[5]

Dependence on [HCl]. As the rate of the reaction is influenced by both [Cl^-] and [H^+], the dependence of rate on [HCl] was studied over the range 0·02–0·08M HCl. The rate of the reaction was found to increase with increasing [HCl]. As the first order rate constant at 0·1M and 0·01M $HClO_4$ are identical, the variation in rate with HCl may, as an approximation, be taken as a variation in rate with [Cl^-]. A plot of $1/k_{obs}$ *vs* 1/[HCl] (Fig 3) is found to be linear with a Y-intercept. The equilibrium constant obtained from the slope-intercept relationship is 13·7 which is nearly the same (K = 14·0) as that obtained from $1/k_{obs}$ *vs* 1/[Cl^-] plot.

Dependence on ionic strength. The effect of variation of the ionic strength of the medium was studied over the range 0·2–0·5M. The reaction is not susceptible to this change ($k_1 = 4{\cdot}41 \times 10^{-5}\ sec^{-1}$ at μ = 0·2 and $k_1 = 4{\cdot}35 \times 10^{-5}\ sec^{-1}$ at μ = 0·5 under otherwise identical conditions).

Dependence on [*succinimide*]. The effect of added succinimide on the rate of the reaction was studied at constant concentrations of alcohol and chloride (Table 5). The rate of the reaction decreases markedly with increase in succinimide concentration.

Rate law and mechanism. These results lead to the view that in an acid medium, in the presence of Cl^-, the rate of the reaction is governed by the rate of interaction between $\overset{+}{N}CSH$ and Cl^- to produce a steady small concentration of molecular chlorine which is consumed by the alcohol in a rapid stage.

$$NCS + H^+ \overset{k_1}{\rightleftharpoons} \overset{+}{N}CSH \qquad (i)$$

$$\overset{+}{N}CSH + Cl^- \xrightarrow{slow} Succinimide + Cl_2 \qquad (ii)$$

$$Cl_2 + R{-}CHOH{-}R' \xrightarrow{fast} R{-}CO{-}R' + 2HCl \qquad (iii)$$

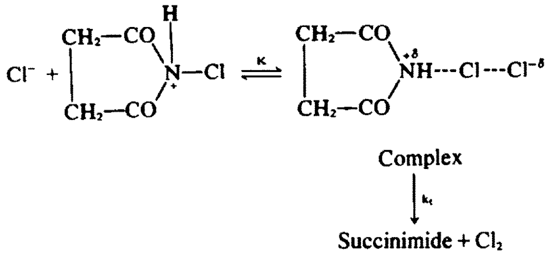
Table 5. Variation of rate with succinimide
[Propan-2-ol] = 0·02369M [Cl^-] = 0·1M [NCS] = 0·0015M Temp. 55°

$HClO_4$ (M)	Succinimide (M)	$k_{obs} \times 10^5\ sec^{-1}$
0·1	0·005742	2·27
	0·008	1·53
	0·01111	1·36
	0·0140	0·928
	—*	6·40
0·2	0·005	1·97
	0·01	1·43
	—*	6·06
0·3	0·005	2·44
	0·01	1·77
	—*	7·67

*no succinimide was added.

This scheme would account for the first order dependence on NCS, the zero order dependence on alcohol, the increased rate with increase in acidity and the absence of kinetic isotope effect.

Modifying equation (ii) as



and on the assumption that NCS is reacting essentially as $\mathrm{N\overset{+}{C}SH}$,

$$\frac{-d[\mathrm{N\overset{+}{C}SH}]}{dt} = k_{obs}\,[\mathrm{N\overset{+}{C}SH}]$$

$$[\mathrm{Complex}] = \frac{K\,[\mathrm{N\overset{+}{C}SH}]_{\mathrm{Total}}\,[\mathrm{Cl}^-]}{1 + K\,[\mathrm{Cl}^-]}$$

assuming $[\mathrm{Cl}^-] - [\mathrm{Complex}] \simeq [\mathrm{Cl}^-]$

$$\frac{-d[\mathrm{N\overset{+}{C}SH}]}{dt} = k_{obs}[\mathrm{N\overset{+}{C}SH}] = k_t[\mathrm{Complex}]$$

$$= \frac{k_t K[\mathrm{N\overset{+}{C}SH}]_{\mathrm{Total}}[\mathrm{Cl}^-]}{1 + K[\mathrm{Cl}^-]}$$

where

$$k_{obs} = \frac{k_t\,K\,[\mathrm{Cl}^-]}{1 + K\,[\mathrm{Cl}^-]}$$

It follows that

$$\frac{1}{k_{obs}} = \frac{1}{k_t} + \frac{1}{k_t\,K[\mathrm{Cl}^-]}$$

which is realised experimentally.

It was observed that while the reaction tended to exhibit a first order dependence on $[\mathrm{H}^+]$ at higher acidities, the dependence is of a fractional order at lower acidities. It was assumed earlier that NCS is reacting essentially and wholly as $\mathrm{N\overset{+}{C}SH}$. However the concentration of NCS would be appreciable at lower acidities and the deprotonation of $\mathrm{N\overset{+}{C}SH}$ may become significant. The true formation constant $\bar{K}$, for the complex could then be calculated as follows:

$$\mathrm{N\overset{+}{C}SH + H_2O \overset{K_h}{\rightleftharpoons} NCS + H_3O^+}$$

$$\mathrm{N\overset{+}{C}SH + Cl^- \overset{\bar{K}}{\rightleftharpoons} Complex}$$

Assuming

$$[\mathrm{NCS}]_{\mathrm{Total}} = [\mathrm{NCS}] + [\mathrm{N\overset{+}{C}SH}] + [\mathrm{Complex}],$$

$$[\mathrm{Cl}^-]_{\mathrm{Total}} \gg [\mathrm{NCS}]_{\mathrm{Total}}$$

and

$$([\mathrm{Cl}^-]_{\mathrm{Total}} - [\mathrm{Complex}]) \simeq [\mathrm{Cl}^-]_{\mathrm{Total}} \simeq [\mathrm{Cl}^-]$$

$$[\mathrm{Complex}] = \frac{\bar{K}[\mathrm{H}^+][\mathrm{Cl}][\mathrm{NCS}]_{\mathrm{Total}}}{[\mathrm{H}^+] + K_h + \bar{K}[\mathrm{H}^+][\mathrm{Cl}^-]}$$

$$\frac{-d[\mathrm{NCS}]_{\mathrm{Total}}}{dt} = k_{obs}\,[\mathrm{NCS}]_{\mathrm{Total}} = k_t[\mathrm{Complex}]$$

where

$$k_{obs} = \frac{k_t\bar{K}[\mathrm{H}^+][\mathrm{Cl}^-]}{\bar{K}[\mathrm{H}^+][\mathrm{Cl}^-] + [\mathrm{H}^+] + K_h}$$

Reshuffling,

$$\frac{1}{k_{obs}} = \frac{1}{k_t} + \frac{1}{k_t\bar{K}[\mathrm{Cl}^-]} + \frac{K_h}{k_t\bar{K}[\mathrm{Cl}^-][\mathrm{H}^+]}.$$

This equation predicts a linearity between $1/k_{obs}$ *vs* $1/[\mathrm{Cl}^-]$ at constant $[\mathrm{H}^+]$ and a linear relationship between $1/k_{obs}$ *vs* $1/[\mathrm{H}^+]$ at constant chloride concentration and these have been realised experimentally. $\bar{K}$ and K_h calculated from this relationship are 78·4 and 0·46 respectively.

The observed retardation in rate by added succinimide is probably due to a reaction between $\mathrm{Cl_2}$ and succinimide becoming significant thus opposing the breakdown of the complex.*

The high positive 'ω' value of 6·25 observed indicates that a water molecule is acting as a proton transfer agent in the rate-determining step of the reaction. It is difficult to visualise the participation

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*An alternative and simpler explanation suggested by the referee to explain the observed kinetics is the following mechanism:

$$\mathrm{NCS + H_3O^+ \rightleftharpoons N\overset{+}{C}SH + H_2O}$$

$$\mathrm{N\overset{+}{C}SH + Cl^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SH + Cl_2\ (SH = succinimide)}$$

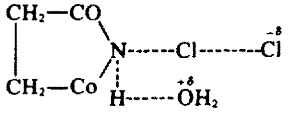
$$\mathrm{Cl_2 + ROH \xrightarrow{k_2} Products}$$

for which the rate-expression will be of the form

$$\frac{d[\mathrm{Products}]}{dt} = \frac{k_1\,k_2\,[\mathrm{ROH}]\,[\mathrm{Cl}^-]\,[\mathrm{NCS}]}{k_1\,[\mathrm{Cl}^-] + k_{-1}[\mathrm{SH}] + k_2[\mathrm{ROH}]}$$

However this rate-law demands a dependence on ROH at least in certain concentration ranges which has not been observed over a wide range. The rate is also not a function of [ROH] even at a higher chloride concentration. However this scheme is in accord with the observed retardation with added succinimide. The authors thank the referee for his suggestion.

of a water molecule as a base in the strict Bunnett sense. However, the following transition state may by visualised, in which



the proton transfer is considered to be concerted with the breaking of the N—Cl bond. Analogies for this scheme are found in the general acid catalysed hydrolysis of piperazine-2, 5-dione[5] and of ortho esters.[6,7]

A relevant and immediate comparison of the above behaviour of NCS in the oxidation of alcohols is the transformation of N-chloroacetanilide to ortho and para-chloroacetanilides (the familiar Orton rearrangement[8]). It is known that the rate-determining step in this reaction is the reaction between HCl and the chloramine to produce chlorine, followed by a rapid interaction between chlorine and acetanilide.

$$C_6H_5\text{—NClAc} + HCl \xrightarrow{\text{slow}} C_6H_5NHAc$$

$$+ Cl_2 \xrightarrow{\text{fast}} (o,\, p)\ Cl\text{—}C_6H_4\text{—NHAc} + HCl$$

More significantly the transformation in presence of chlorine consumers like, phenol, *p*-cresol and acetanilide, has the same rate and is unaffected by the amount of substrate[9,10] thus paralleling the NCS oxidation of alcohols.

However, the kinetics of oxidation of alcohols by NCS exhibit certain significant differences from those of the oxidation of alcohols by NBS in the presence or Br^-. Thiagarajan and Venkatasubramanian[2,3] have shown recently that the NBS oxidation of alcohols exhibits a first order dependence on both NBS and the alcohol. The reaction is also accelerated by added bromide ions and by mineral acids. Oxidation by NBS in the absence of Br^- (the Br^- generated as a product being complexed by Hg(II) ions) is essentially a slow reaction between the $N\overset{+}{B}SH$ molecule and the alcohol. Oxidation by NBS in presence of Br^- (as happens when no steps are taken to keep back the Br^- produced in the reaction or when Br^- is initially added) is essentially a slow oxidation by molecular bromine which exhibits a direct dependence of rate on the concentration of alcohol and NBS. Thus oxidation by NCS in the presence of Cl^-, though conceived as passing through molecular chlorine differs significantly from NBS oxidations. A mechanism for NBS oxidation analogous to the scheme written for NCS oxidations could be

$$NBS + H_3O^+ \rightleftharpoons N\overset{+}{B}SH + H_2O \qquad \text{(i)}$$

$$N\overset{+}{B}SH + Br^- \xrightarrow{\text{fast}} Br_2 + \text{succinimide} \qquad \text{(ii)}$$

$$Br_2 + R\text{—CHOH—}R' \xrightarrow{\text{slow}} \text{Products} \qquad \text{(iii)}$$

The difference presumably arises from the fact that NBS molecule has the more positive halogen $(>\overset{-\delta}{N}\text{—}\overset{+\delta}{Br})$ than the NCS molecule (due to the electronegativity differences between the halogens[11]) and a protonation of these two molecules makes the rupture of a N—Br bond faster and more facile than that of a N—Cl bond. Consequently, step (ii) becomes a slow and rate-determining step in NCS oxidations and is fast in NBS oxidations. The difference in the strengths of the N—X bonds would thus be responsible for the zero order dependence on alcohol.

EXPERIMENTAL

Benzhydrol-α-d. In a two necked 200 ml flask fitted with a $CaCl_2$ guard tube were taken D_2O (6 gms) and pure dry ether (30 ml) and stirred magnetically. Freshly cut Na pieces (2 g) were gradually added so that the temp of the mixture did not rise appreciably. After complete addition of Na, pure dry benzophenone (2 g) were added and stirred for about 3 hr. The filtrate was shaken with HCl diluted with D_2O (5 ml). The ether layer is separated and evaporated to give the crude solid benzhydrol-α-d. This was purified with a column of neutral alumina. The yield of deuterated benzhydrol (m.p. 63–65°C) was 65%. Mass spectrometry and NMR confirm that the isotopic purity of the sample is 99%.

Fluoren-9-ol-α-d was prepared by a similar procedure. The crude sample (Yield 60%) was twice recrystallised from dry CCl_4. Fluoren-9-ol-α-d (m.p. 150°) is of 99·0% isotopic purity as confirmed by Mass spectrometry and NMR studies.

The liquid organic compounds were of the extra pure variety (Fluka AG) and were purified further by distillation from an all-glass apparatus. 50 ml each of the oxidant and the substrate were mixed after thermostating them for 2 hr in a vessel wrapped in aluminium foil. All the kinetic experiments were carried out in a dark room where only a yellow incandescent bulb was used. 5 ml aliquots were quenched in 5% KI containing 0·3M $NaHCO_3$ and liberated I_2 was then titrated against standard $Na_2S_2O_3$ soln to starch end point.

Secondary alcohols are known to be oxidised by NCS to ketones.[1] The products of oxidation of propan-2-ol (85%) and butan-2-ol (72%) were identified and estimated as DNP derivatives and also by iodoform method. The yields of ketones are given in the parentheses.

Acknowledgement—The authors thank Dr. C. N. Pillai, Department of Organic Chemistry, Indian Institute of technology, Madras and Mr. V. M. Sadagoparamanujam, Research Scholar, Vivekananda College, Madras for their help in Mass spectrometry and NMR analysis of benzhydrol-α-d and fluoren-9-ol-α-d.

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