Oxidations of Cyclohexane, 1-Octyl Trifluoroacetate, Heptane, and Decane Which Stop at the Alcohol Stage

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Abstract: Cyclohexane, 1-octyl trifluoroacetate, heptane, and decane are oxidized by Fe(II)-Et$_2$NOH or Fe(II)-Et$_3$NO in CF$_3$COOH. The trifluoroacetates are formed with no evidence of further oxidation. Polar selectivity is shown by 72% selectivity for oxidation of 1-octyl trifluoroacetate in the 7 position. Steric selectivity is shown by the relative yields of decyl and heptyl trifluoroacetates from oxidations with Et$_3$NO compared to oxidations with Et$_2$NOH. The selectivity is attributed to H abstraction by R$_3$N·$^+$ to produce an alkyl radical. Further, it is suggested that the alkyl radical is converted into the ester product *via* an encumbered carbonium ion, produced by Fe(III) oxidation.
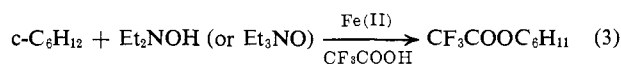
Free radical chlorinations with *N*-chloroammonium ions are proving to be highly selective for the introduction of chloro functions into a chain of closely similar CH$_2$ groups.[1-6] Exemplifying the polar effect is the chlorination of 1-octanol to 7-chloro-1-octanol with 92% selectivity.[1] Exemplifying the sensitivity to small steric differences is the 11:1 ratio of 2-chloro- to 3-chloropentane in the chlorination of pentane with *N*-chloro-2,2,6,6-tetramethylpiperidine.[2] An added bonus is the high selectivity for monochlorination.[1-6]

The present study started with the concept that since *N*-chloroammonium ions chlorinate alkanes, *N*-hydroxyammonium ions might be able to hydroxylate alkanes. However, there was reason to doubt that an exactly analogous mechanism (eq 1 and 2) would prevail be-

$$R'_2NH \cdot^+ + RH \longrightarrow R'_2NH_2^+ + R \cdot \qquad (1)$$

$$R \cdot + R'_2NHOH^+ \longrightarrow ROH + R'_2NH \cdot^+ \qquad (2)$$

cause of the lack of precedent for the radical displacement on oxygen in eq 2.

Cyclohexane was oxidized by equimolar Et$_2$NOH or Et$_3$NO in CF$_3$COOH. The only product detected (boiling point, gc, nmr) was cyclohexyl trifluoroacetate (eq 3). In particular, no cyclohexanone could be de-

$$\text{c-C}_6\text{H}_{12} + \text{Et}_2\text{NOH (or Et}_3\text{NO)} \xrightarrow[\text{CF}_3\text{COOH}]{\text{Fe(II)}} \text{CF}_3\text{COOC}_6\text{H}_{11} \qquad (3)$$

tected by gc. Distillation produced a 25% yield of cyclohexyl trifluoroacetate, which was identical in boiling point, nmr, and gc retention time with an authentic sample.

The yields of cyclohexyl trifluoroacetate and recovered cyclohexane were determined by gc using aliquots of an ether extract and 3-hexyl trifluoroacetate as an internal standard. These two yields accounted for >90% of the cyclohexane initially used. The data in Table I show that (1) yields based on Et$_2$NOH are

(1) N. Deno, W. E. Billups, R. Fishbein, C. Pierson, R. Whalen, and J. C. Wyckoff, *J. Amer. Chem. Soc.*, **93**, 438 (1971).
(2) N. Deno, D. G. Pohl, and H. J. Spinelli, *Bioorg. Chem.*, **3**, 66 (1974).
(3) F. Minisci, *Synthesis*, 1 (1973).
(4) G. Sosnovsky and D. J. Rawlinson, "Advances in Free Radical Chemistry," Vol. 4, G. H. Williams, Ed., Academic Press, New York, N. Y., 1972, p 203.
(5) N. Deno, "Methods in Free-Radical Chemistry," Vol. 3, E. S. Huyser, Ed., Marcel Dekker, New York, N. Y., 1972, p 135.
(6) N. Deno, K. Eisenhardt, R. Fishbein, C. Pierson, D. Pohl, H. Spinelli, R. C. White, and J. C. Wyckoff, *Proc. Int. Congr. Pure Appl. Chem.*, *23rd, Boston, 1971*, **4**, 155 (1972).
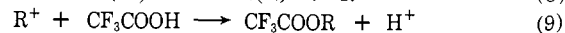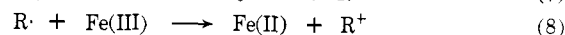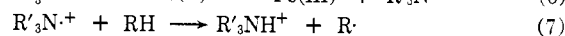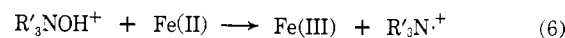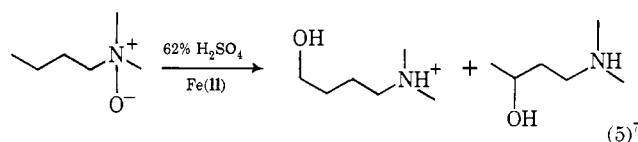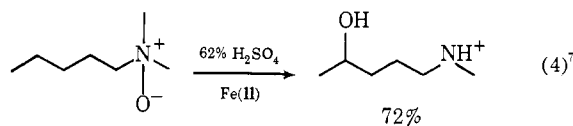
Table I. Gc Yields of Cyclohexyl Trifluoroacetate from the Oxidation of 10 mmol of Cyclohexane in 40 ml of CF$_3$COOH at 72°

Oxidizing agent	Oxid. agent, mmol	FeSO$_4$· 7H$_2$O, mmol	Time, hr	Yield, %
Et$_2$NOH	3	10	24	8
	5	10	24	12
	10	10	24	31
	10	10	48	38
	10	20^a	48	34
	20^a	10	48	52
Et$_3$NO	3	10	24	6
	5	10	24	11
	10	10	24	15

^{a} Half was added at the start and the other half after 24 hr.

30–40%, (2) FeSO$_4$·7H$_2$O is not a limiting reagent at equimolar levels, and (3) the conversion of cyclohexane into cyclohexyl trifluoroacetate can be increased to 52% by a second equimolar treatment with Et$_2$NOH and apparently could be further increased by repetitive treatments.

During the course of this work, a most interesting paper appeared which reported eq 4 and 5.[7] The mechanism of eq 5 was studied using the 4,4,4-tri-

$$R'_3NOH^+ + Fe(II) \longrightarrow Fe(III) + R'_3N \cdot^+ \qquad (6)$$

$$R'_3N \cdot^+ + RH \longrightarrow R'_3NH^+ + R \cdot \qquad (7)$$

$$R \cdot + Fe(III) \longrightarrow Fe(II) + R^+ \qquad (8)$$

$$R^+ + CF_3COOH \longrightarrow CF_3COOR + H^+ \qquad (9)$$

deuteriobutyl group in place of butyl. It was found that the 3-hydroxybutyldimethylamine consisted of

(7) J. R. L. Smith, R. O. C. Norman, and A. G. Rowley, *J. Chem. Soc., Perkin Trans. 1*, 566 (1973).

Table II. Bistrifluoroacetates of 1,*x*-Octanediols from the Oxidation of 1-Octyl Trifluoroacetate

Reagent	Relative yields (gc), x =						
	2	3	4	5	6	7	8
Et₃NO[a]	0	0	1	5	22	72	0
Et₂NOH[a,b]	0	0	2	9	31	58	0
Relative retention times[c]	1.21	1.34	1.42	1.65	1.81	1.98	2.56

[a] A small (5% with Et₃NO, 10% with Et₂NOH) unidentified band appeared at relative retention time of 3.77. [b] Two unidentified bands at ~2.0 relative retention time had a total area that was 15% of the bistrifluoroacetates. [c] 1-Octyl trifluoroacetate was 1.00.

Table III. Heptyl Trifluoroacetates from Heptane and Decyl Trifluoroacetates from Decane

Reactant	Reagent	% conversion[a]	Relative yields (gc)			
			1	2	3	4 or 4 + 5
Heptane	Et₂NOH	40	0	42	41	17
	Et₃NO	55	0	51	37	12
Relative retention times[b]			3.58	2.55	2.41	2.30
Decane	Et₂NOH	23	0˙	27	26	47
	Et₃NO	35	0	36	28	36
Relative retention times[b]			2.05	1.81	1.73	1.58

[a] The % conversion of the alkane to the alkyl trifluoroacetates using a 2.5 mol excess of reagent. Presumably this could be increased by a greater excess of reagent or by repetitive treatment. [b] The alkane was 1.00.

equal amounts of dideuterio and trideuterio product. This along with the results of BrCCl₃ trapping experiments led to the proposal that carbonium ions were intermediates.[7]

Equations 6–9 are the Smith–Norman–Rowley mechanism[7] translated to the intermolecular case and to CF₃COOH as the solvent. Such a mechanism suggests that the remarkable selectivities which have been demonstrated for eq 1 and R₂NCl chlorinations[1–6] would not be found in the hydroxylations and trifluoroacetoxylations because of rearrangements in intermediate carbonium ions. This question was tested in the following experiments.

1-Octyl trifluoroacetate was oxidized with a 2.5 molar excess of Et₃NO. The conversion into bistrifluoroacetates was 10%. High (72%) selectivity was found for oxidation at C-7 to produce the bistrifluoroacetate of 1,7-octanediol (Table II). This polar selectivity is comparable to that found in chlorination of 1-octanol and octanoic acid by R₂NCl species.[1] The selectivity for C-7 was greater with Et₃NO than with Et₂NOH. This is attributed to a steric hindrance effect pyramided onto the polar effect. This steric effect favoring attack at the penultimate carbon has been demonstrated in the chlorinations of pentane,[2] 2,2-dimethylbutane,[2] isopentane,[2] and 2,2-dimethylpentane[8] with sterically hindered R₂NHCl⁺ species[2] and R₃NCl⁺ species.[8]

A similar steric effect is demonstrated in the oxidation of heptane to heptyl trifluoroacetates and decane to decyl trifluoroacetates (Table III). Again, Et₃NO gives a higher proportion of attack at the penultimate carbon (C-2 in this case).

Since the polar and steric selectivities closely resemble those found in the R₂NCl and R₃NCl⁺ chlorinations, it is concluded that carbonium ion rearrangements are not involved in the reactions in Tables I–III. It remains to bring this fact into harmony with the studies on eq 5,[7] which provide a strong precedent for carbonium ion intermediates.

(8) Unpublished results.

The propensity of carbonium ions to rearrange depends on the degree of freedom or encumbrance of the carbonium ion.[9] Carbonium ions which are formed in highly exothermic processes undergo both isoenergetic and exothermic rearrangements. These are termed free.[9] Encumbered carbonium ions are characteristic of solvolysis reactions where solvent relaxes about the ion concurrent with its formation. Rearrangement in encumbered ions is limited to highly exothermic types.[9]

The studies on eq 5 and the data in Tables I–III can now be reconciled. The intermediate carbonium ions are encumbered, either by solvent relaxation during formation or a Fe–R⁺ interaction. In the reactions in Tables I–III, only secondary carbonium ions are involved because secondary radical formation is highly preferred in eq 1 and 7. No rearrangements occur. In contrast, in eq 5 a primary carbonium ion is formed and a primary to secondary rearrangement is possible and takes place.[7] From the data reported,[6] it can be calculated that this rearrangement is only 64% complete. The fact that this highly exothermic primary to secondary carbonium ion rearrangement is only partially completed is the strongest evidence that the intermediate carbonium ion was encumbered. Although the above interpretation is satisfying, the mechanism is not regarded as established. More stringent tests are necessary and these are in progress.

The oxidations in Tables I–III appear to have more potential for selective oxidation of alkanes and alkyl chains than any yet reported.[10] They also more nearly

(9) J. T. Keating, Ph.D. Thesis, The Pennsylvania State University, 1968; J. T. Keating and P. S. Skell, "Carbonium Ions," Vol. II, G. A. Olah and P. v. R. Schleyer, Ed., Wiley-Interscience, New York, N. Y., 1970, pp 573–646.

(10) For reviews on alkane oxidations, see N. M. Emanuel, "The Oxidation of Hydrocarbons in the Liquid Phase," Macmillan, New York, N. Y., 1965; N. M. Emanuel, E. T. Denisov, and Z. K. Maizus, "Liquid-Phase Oxidation of Hydrocarbons," Plenum Press, New York, N. Y., 1967; I. V. Berezin, E. T. Denisov, and N. M. Emanuel, "The Oxidation of Cyclohexane," Pergamon Press, New York, N. Y., 1966; "Oxidation of Organic Compounds," Advan. Chem. Ser. No. 76–78 (1968).

duplicate the remarkable specific biological hydroxylations of which there are abundant examples.[11-13]

Experimental Section

Analyses by Gas Chromatography. All gas chromatograms (gc) were obtained on a Barber-Colman Series 5000 instrument equipped with a flame ionization detector. The fuel gas was a mixture of hydrogen and air, and the carrier gas was nitrogen. The glass U columns were 0.25 in. × 6 ft.

For the cyclohexane and cyclohexyl trifluoroacetate analyses, 3% SE 30 on 45-60 Gas Chrom W was used at 90° with 3-hexyl trifluoroacetate (bp 128-129°) as an internal standard. For the detection of cyclohexanone, an EGSS-X column was used as well as the SE-30 column. For the decyl trifluoroacetates and the bistrifluoroacetates of 1,x-octanediols, 20% SE 30 on 80-100 Gas Chrom W was used at 150°. Flow rates were 23 ml min⁻¹.

Gc Standards for Bistrifluoroacetates of 1,x-Octanediols. Mixtures of chloro-1-octanols were available from a previous study.[1] These were converted into a mixture of octanediols by refluxing with 10% aqueous KOH for 3 days. The octanediols were converted into diacetates by treatment with acetic anhydride at 100°. The diacetates had retention times on SE-30 in the same order as the chloro-1-octyl acetates[1] and with the same relative band areas. This shows that the mixture retained the same proportions during hydrolysis. Part of the octanediol mixture was converted into the bistrifluoroacetates, and their relative retention times are summarized in Table II. Identification rested on identity of gc retention times, separately and in mixtures.

Heptyl Trifluoroacetate Gc Standards. 1-Heptanol was commercially available and was converted into the trifluoroacetate by mixing with CF₃COOH. The three heptanones (2, 3, and 4) were commercially available. They were reduced to the alcohols with NaBH₄ in ethanol and the alcohols converted into the trifluoroacetates. Relative retention times are listed in Table III. Identification rested on identity of gc retention times, separately and in mixture. No trace of heptanones could be detected by gc in the heptyl trifluoroacetate products.

Decyl Trifluoroacetate Gc Standards. All five decanols were

commercially available and were converted into the trifluoroacetates by mixing with CF₃COOH. Relative retention times are listed in Table III. Identification rested on identity of gc retention times, separately and in mixtures.

Triethylamine Oxide. This was prepared by a procedure similar to that reported.[14,15] To a solution of 20 g (0.20 mol) of Et₃N in 20 ml of methanol, 45 ml (0.40 mol) of cold 30% H₂O₂ was slowly added. An ice bath was used to keep the temperature below 25°. After standing for 24 hr, excess H₂O₂ was destroyed by adding MnO₂ and stirring until O₂ evolution ceased. The solution was filtered to remove MnO₂, extracted with diethyl ether to remove Et₃N, and concentrated to a syrup under vacuum. The nmr spectrum of Et₃NO consists of a quartet at δ 3.18 and a triplet at 1.17. Also present was a singlet at δ 4.90 due to H₂O. This decreased with pumping. The reagent used for the oxidations had the composition Et₃NO·1.1H₂O.

Oxidation of Cyclohexane. A heterogeneous mixture of 10 mmol of cyclohexane, 10 mmol of Et₂NOH (or Et₃NO), 10 mmol of FeSO₄·7H₂O, and 40 ml of CF₃COOH was stirred and heated at 65-72° for 24 hr. The product was isolated by addition of the reaction mixture to water, ether extraction, washing the extract with water and 10% aqueous Na₂CO₃, and distillation. Several such runs were combined to give a 25% yield of distilled cyclohexyl trifluoroacetate. This was identified by boiling point (identical with the 148-149° reported),[16] gc retention time, and nmr spectrum which was identical in every detail [broad band δ 4.97 (α-H); complex multiplet 0.7-1.3 (10 H)] with that of a sample prepared from cyclohexanol and CF₃COOH.

Oxidations of 1-Octyl Trifluoroacetate, Heptane, and Decane. These were conducted in a manner identical with that used with cyclohexane except that 25 mmol of Et₂NOH or Et₃NO was used. It was important to conduct the isolation rapidly and cold to avoid hydrolysis. Any alcohols arising from hydrolysis could be converted back into trifluoroacetates by addition of a little trifluoroacetic anhydride.

(11) C. W. Bird and P. M. Molton, "Topics in Lipid Chemistry," Vol. 3, F. D. Gunstone, Ed., Elek Science, London, 1972, p 125.

(12) D. F. Jones and R. Howe, *J. Chem. Soc.*, 2801 (1968).

(13) G. S. Fonken and R. A. Johnson, "Chemical Oxidations with Microorganisms," Marcel Dekker, New York, N. Y., 1972.

(14) J. P. Ferris, R. D. Gerwe, and G. R. Gapski, *J. Org. Chem.*, **33**, 3493 (1968).

(15) S. N. Lewis, "Oxidation," Vol. I, R. L. Augustine, Ed., Marcel Dekker, New York, N. Y., 1969, p 248.

(16) H. A. Staab and G. Walther, *Angew. Chem.*, **72**, 35 (1960).

Substituent Effects in Acetal Hydrolysis

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Abstract: The rates of acid-catalyzed hydrolysis of five para-substituted 2-phenyl-2-methyl-1,3-dioxolanes have been measured in aqueous HCl solution at 25°. The rate constants correlate well with the Yukawa-Tsuno equation, giving $\rho = -2.9$ and $r = 0.3$. On the basis of these values, an explanation is advanced to account for the fact that an anomalously small rate increase is observed for 2-phenyl-2-methyl-1,3-dioxolane hydrolysis over 2-methyl-1,3-dioxolane hydrolysis.

The mechanism of the acid-catalyzed hydrolysis of acetals and ketals has been the subject of numerous investigations as this process is an excellent model for the action of lysozyme and other glycosidases. In spite of the fact that the main features of the overall mechanism are well understood,[1] there are many aspects which have not as yet been satisfactorily explained.

(1) E. H. Cordes, *Progr. Phys. Org. Chem.*, **4**, 1 (1967).
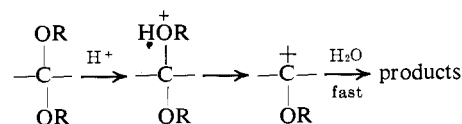
A particularly perplexing set of observations is the effect of phenyl substitution at the pro-acyl carbon.[2]

(2) The term pro-acyl carbon has been proposed by Kresge[3] to refer to the carbon atom which becomes the acyl carbon after hydrolysis.

(3) Y. Chiang, A. J. Kresge, P. Salomaa, and C. I. Young, *J. Amer. Chem. Soc.*, **96**, 4494 (1974).