PHOTOCHEMICAL TRANSFORMATIONS---- IVª

OXYFUNCTIONALIZATION OF SOME SATURATED HYDROCARBONS WITH HYDROXYL RADICALS (1)^{D,C}

S.N. SHARMA^d, H.R. SONAWANE AND SUKH DEV^{*e}

National Chemical Laboratory, Pune 411 008, India

(Received in UK 30 January 1985)

Abstract — It is shown that hydroxylation of saturated hydrocarbons by hydrogen peroxide occurs under the influence of light. This reaction has been investigated on acyclic, monocyclic and bicyclic hydrocarbons. These reactions were also studied using performic acid as the source of hydroxyl radicals and results compared with those obtained with peracetic acid. As expected, the preferred attack was on tertiary centres, followed by secondary and then primary.

Functionalization of a non-activated carbon in organic compounds is a reaction of considerable practical and theoretical interest, and has been extensively investigated.¹ Usually, the methods employed exploit radical pathways and have embraced thermal, photochemical and metal-catalyzed reactions. Olah and co-workers² have studied in detail, oxygenation of alkanes with ozone and hydrogen peroxide in super acid media under typical electrophilic conditions.

- a Part III: Tetrahedron 39, 2999 (1983)
- ^b Communication No. 3678, National Chemical Laboratory, Pune, India
- ^C Abstracted from Ph.D. thesis of S.N. Sharma, Poona University (1976)
- ^d Present address: Dept of Rockets and Missiles, Sena Bhavan, New Delhi
- e Present address: Malti-Chem Research Centre, Nandesari, Vadodara, India.

We now wish to report oxyfunctionalization of certain representative saturated hydrocarbons by hydroxyl radicals generated by photolysis of hydrogen peroxide or per acids.

At the time this work was undertaken two reports^{3,4,5} on photohydroxylation of a few saturated hydrocarbons (cyclohexane, <u>cis</u>-decalin, and admantane) using essentially anhydrous peracetic acid in ethyl acetate were available. Explicit in the mechanism proposed for this reaction by Heywood <u>et al</u>.³, is homolytic decomposition of peracetic acid, generating hydroxyl radicals. Hydrogen peroxide (UV absorption: 195-400 nm)⁶ on photolysis is known to generate hydroxyl radicals⁷ and this system has been exploited for hydroxylation of aromatic compounds⁸.

In view of this, oxyfunctionalization of saturated hydrocarbons with this system appeared worth investigating. Reaction was first studied with cyclohexane to essentially optimize reaction conditions. Ethyl acetate was found to be the most appropriate solvent, while using 0.1 mole equivalent of 180% H₂0₂ aq, for every one mole equivalent of cyclohexane. Reactions of other substrates were then investigated under these conditions without any further attempts at optimization. Comparative studies were also carried out with 35% HC000H ag and 40% CH3COOOH aq as source of hydroxyl radicals. In each case it was ascertained that there was no dark reaction. Also, irradiation of substrates in moist ethyl acetate failed to give any functionalization, thus indicating that water present in hydrogen peroxide or per acids does not contribute to any product development.

RESULTS

Cyclohexane, cyclododecane, n-octane

Reaction of cyclohexane with H_2O_2 under the above conditions resulted in ~45% yield (based on H_2O_2) of a product consisting of cyclohexanol (56%), cyclohexanone (2%), cyclohexyl acetate (9%), besides unidentified products (33%). The unidentified products evidently arise from further known⁹ photochemistry of cyclohexanone, and their formation could be substantially reduced by using a 9700 Corex filter (cut-off wavelength 254 nm) (Table 1). Cyclohexyl acetate clearly arises from participation of ethyl acetate solvent at some stage; this is borne out by the fact that when ethyl formate replaced ethyl acetate as solvent, cyclohexyl formate was produced. These results, together with other relevant data and results of comparative studies with HCOOOH and CH₃COOOH are summarized in Table 1.

Reaction products from reactions of cyclododecane and n-octane were analyzed after hydrolysis. Results (Table 1) are similar to those described above for cyclohexane. In the case of cyclododecane, <u>cis</u>-bicyclo (8.2.0)dodecan-1-ol (<u>1</u>), arising from known¹⁰ photochemistry of cyclododecanone, constituted some 20% of the product, both with hydrogen peroxide and peracetic acid.

Methylcyclohexane, p-menthane

With methylcyclohexane as the substrate, photoreaction with H₂0₂ gave a product in ~22% yield (based on H₂O₂) containing some 25% acetates (IR, PMR). Hydrolysis of the product gave a material essentially free from ketones. Similar results were obtained when peracetic acid was used in place of H_2O_2 . In each case, the hydrolyzed product consisted of tert. alcohol 2 and sec. alcohols 3-8. These results are shown in Table 2. Compound 2 was isolated by preparative GLC and characterized by comparison (GLC, IR, PMR) with an authentic sample. The secondary alcohols were identified

									UI (12,13)	6
Product composition [Increasing GLC relative retention time] ^f	re)			İ	UI-3	28	6	6	Octanol-1	10
	UI ^g (mixtu 33	5 C C	I	9	₹ 	45	58	62	UI(8-10)	16
	इ-⊖ ३	78	40	06	J.	20	22	16	Octanol-2	24
	o=() ^	4 00	6	I	% 57	4	11	12	Octanol-3	20
	ğ.⊖ •	~ ~	42	4	UI-2	2	e	1	Octano1-4	16
	§.∽ ,	ı ı	12	I	UI-1	I	3	£	UI (1-4)	ŝ
Yield ^e (%)	ų.	50	45	50		25	17	42		- 20
Reaction time ^d (hr)	=	25	10	12		ŝ	17	12		5
Reagent	Ċ	^{E202} H202 ^C	нооон	сн ³ сооон		H202	H202 ^C	сн ₃ сооон		H202
Substrate		\bigcirc								n-octane ^b

Table 1. Photohydroxylation of cyclohexane, cyclododecane and n-octane^a

Reaction mixture consisted of 0.80 mole substrate, 0.08 mole reagent and 350 ml EtOAc Product compositions after hydrolysis; c) Irradiation using a Corex filter Time taken for disappearance of ROOH; e) Based on alcohol expected from ROOH used 20% diethylene glycol polysuccinate as stationary phase UI = unidentified.

ଜନ୍ତିକ୍ରିକ

Photooxidation of methylcyclohexane and **p-menthane^a** Table 2.

Substrate	Reagent	Reaction timed (hr)	Yield ^c (%)		T	Product c 8 [Increasing GLC re	omposition lative retent	tion time}		
- ~ _ ~	H ₂ 02 Сн ₃ сооон	10 10	22 33	RRT [£]		50 1.68 0H 2.0 2.0 1.68 1.68	HO JI Jep	₩ ₩ ₩ ₩ ₩ ₩ ₩ ₩		ſ_⌒₅ぁ
~~~~	H2 ⁰ 2 СН ₃ Сооон	12 14	22 39	RRTG	°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°°		33 <b>2</b> → → →	20 21 20 br>20 20 20 20 20 20 20 20 20 20 20 20	2 I I I I I I I I I I I I I I I I I I I	1.80 23 <b>35</b> >
a) Reaction	mixture co	nsisted of (	0.80 mole	substi	rate, 0.08 m	ole reagent and 3	50 ml EtOAc;	p-menthane	e was a mixtur	te of

c) Product composition after hydrolysis followed by  $CrO_3$  oxidation e) Based on alcohol expected from ROOH used 9) Column B , programmed GLC (80-1300,40/min), 60 ml  $H_2/min$ .

- cis/trans isomers (1/1.5)Product composition after hydrolysis Time taken for disappearance of ROOH Column C, temp.  $100^{\circ}$ , 60 ml H₂/min. GLC resolution unsatisfactory.

  - ፚ፞፞፞ቒ፞፞፞፞፝፝

by their identical behaviour on three different GLC columns (columns A,B, and C) with authentic samples. The exact percentages of 5-8 could not be computed as their resolution was not satisfactory enough. When subjected to Cr03 oxidation, sec. alcohols in the reaction mixture were transformed into the corresponding ketones, which were also identified by their mixed GLC with authentic samples of ketones on two different columns (columns A,C).

Photoreaction of p-menthane (cis/ trans: 1/1.5) with either  $H_2O_2$  or peroxyacetic acid in EtOAc furnished a product, which after saponification gave a material consisting of at least 12 components. This was then subjected to Cr03 oxidation and the GLC of the product, thus obtained, revealed it to

be a mixture of seven compounds, as summarized in Table 2. The mixture was chromatographed on  $Al_20_3$  and the components corresponding to RRT 1.00, 1.23, 1.23, 1.53 and 1.67 were isolated and characterized as 9, 10, 11, 12 and 14 respectively by comparison of their spectral data with those of authentic samples. The other components with RRT 1.57 and 1.80 were identified as 13 and 15 respectively by mixed GLC with authentic samples on two different columns (columns A, B).

# cis-Pinane

Photoirradiation of cis-pinane in EtOAc was carried out following closely the methodology described above. The hydrolyzed reaction product on GLC analysis was found to be a mixture of

Product	RRT	% (GLC)				
		H ₂ O ₂ reac. ^b	CH ₃ COOOH reac ^C			
OH H H H	1.00	12	6			
17	1.20	37	8			
	1.72	20	46			
Unidentified		31	40			

Table 3. Photohydroxylation of cis-pinane^a

a)See footnotes to Table 1; product composition after hydrolysis b) Reaction time 18 hr, yield ~26% c) Reaction time 22 hr, yield ~30%

at least 13 components. Fractionation followed by chromatography over  $Al_20_3$ afforded the three major components in pure state. These were identified as <u>trans</u>-pinan-2-ol (<u>16</u>), <u>cis</u>-pinan-2-ol (<u>17</u>) and  $\alpha$ -terpineol (<u>18</u>) by comparison (IR, PMR, GLC) with authentic samples. The remaining compounds could not be isolated in a pure enough state for identification. These results have been collected in Table 3.

# DISCUSSION

The above results show that photooxidation of saturated hydrocarbons by  $H_2O_2$  can be carried out effectively, but invariably a complex product is obtained. From the results it is also clear that a tert.C-H bond reacts faster than a sec. C-H bond, which, in turn, is more susceptible than the primary C-H linkage. Thus, for example, in the hydroxylation of methylcyclohexane with  $H_20_2$ , the ratio of secondary to tertiary hydroxylated products is 1.0 : 3.5 per relevant C-H bond; the ratio is still lower (1.0 : 9.5) with peracetic acid. This is as expected in terms of the well-known relative stabilities of different carbon radicals.¹¹ However, the higher discrimination in the reaction with peracetic acid must then be attributed to the free energy difference of the transition state for attack of alkyl radical on CH₃COOOH as compared to that on  $H_2O_2$ .¹² From

pattern of hydroxylation of n-octane, it is evident that the reaction proceeds with little regioselectivity. However, in the case of p-menthane regioselectivity seen in the formation of <u>13</u> and <u>14</u> is noteworthy, and clearly a steric factor is indicated.

#### EXPERIMENTAL

All m.ps and b.ps are uncorrected. All solvent extracts were finally washed with brine before drying over Na₂SO₄.

IR spectra were recorded as smears (liquids) or Nujol mulls (solids), on a Perkin-Elmer Infracord model 137E. PMR spectra were taken in 10-15% soln in CCl₄ on a Varian T-60 spectrometer, with TMS as internal standard. Mass spectra were recorded on a CEC mass spectrometer, model 21-110B, using an ionization potential of 70 eV.

Alumina for chromatography was made neutral (HN03 method)¹³, activated at 400° (8-10 hr) and then graded according to Brockmann.¹⁴ GLC analysis were carried out on "Aerograph" model A-350-B using Al columns (300 cm x 0.6 cm) packed with 20% diethyleneglycol polysuccinate (col. A), or 20% Hyprose (col.B), or 20% FFAP (free fatty acid phase; col. C) on Chromosorb W (60-80 mesh). For preparative GLC 300 cm x 1.0 cm Al column packed with 30% Carbowax-20M or 30% Hyprose on 30-60 mesh Chromosorb W was used. Hydrogen was used as carrier gas. A spinning-band column (46 cm x 6 mm; 23 plates) supplied

by Balthen International, Philadelphia, U.S.A., was employed for fractional distillation.

# Materials and authentic samples

Ethyl acetate used in photoirradiation was washed with water and rapidly dried over fused-CaCl₂; it was then distilled through a Vigreux column and the fraction b.p. 75-77^o collected. Cyclohexane (Sarabhai M. Chemicals, India), methylcyclohexane (B.D.H., UK), and n-octane (B.D.H., UK) were GLC pure samples and were freshly distilled before use. Cyclododecane was obtained by hydrogenating cyclododecatriene over 5% Pd-C. <u>p-Menthane¹⁵ (cis/trans</u>: 1/1.5), and (+)-<u>cis</u>-pinane¹⁶ were prepared by hydrogenation of dipentene, and  $\alpha$ -pinene ( $\alpha_{\rm D}$  + 21.0^o) respectively over Raney Ni.

Hydrogen peroxide (0.85%) was obtained by slow removal of water from 30% H₂0₂ aq. under reduced pressure (30 mm) at 45-50[°]. Performic acid (0.35% aq.) and peracetic acid (0.40% aq.) were freshly prepared by known methods.¹⁷

Authentic samples of 1-methylcyclohexanol,¹⁸ <u>cis</u>- and <u>trans</u>-2-,3-, 4-methylcyclohexanols,¹⁹ and isocarvomenthone²⁰ were prepared following known procedures. Octanol-3 and octanol-4 were also synthesized.²¹ Menthone, isomenthone, <u>cis</u>- and <u>trans</u>-pinan-2-ols, carvomenthone  $\alpha$ -terpineol, octanol-1 and octanol-2 were already available in the laboratory. For other products spectral data were compared with those reported in the literature.

#### General procedure for photooxidation

Photoirradiation was carried out with an Hanovia medium-pressure mercury vapour lamp (200 W), suspended in a double-walled, water-cooled, clear-fuzed quartz well, without filter (unless stated to the contrary). It was fitted into a cylindrical reactor containing a soln. of substrate (0.8 mole) and ROOH (0.08 mole) in EtOAc (350 ml). A minute steady flow of N2 was bubbled through the soln throughout the course of reaction. The course of the reaction was monitored by the presence of ROOH, as judged qualitatively by KI-AcOH test. When ROOH had essentially disappeared, the reaction mixture was worked up by washing with Na₂S₂O₃ aq., followed by water. Solvent was carefully removed through a Vigreux column, and the residue fractionated to first remove unreacted hydrocarbon and then collect the product under reduced pressure. In the case of cyclohexane, methylcyclohexane and n-octane, the unreacted hydrocarbon was removed along with the solvent fraction.

The above product (1.0 g), in each case, was taken in 5% methanolic-KOH (25 ml), refluxed for 4 hr, and then worked up in the usual way to get total hydrolyzed product.

# Separation/identification of products

(a) <u>Products from cyclohexane</u>. Cyclohexanol, cyclohexanone, cyclohexyl
formate and cyclohexyl acetate were

isolated by preparative GLC (Hyprose column,  $140^{\circ}$ , 90 ml H₂/min) and identified by comparison of spectral data (IR, PMR) with those of authentic samples.

(b) <u>Products from cyclododecane</u>. Hydrolyzed product (1.5 g) from peracetic acid reaction was chromatographed on  $Al_20_3/II$  (54 cm x 1.8 cm), while monitoring with GLC (col.A). Elution with light petrol and light petrol containing increasing quantities of benzene (5%, 10%, 20%, 40%, 60% and 100%) furnished pure <u>1</u> (107 mg eluted with light pet./benzene: 60/40), and pure cyclododecanol (350 mg eluted with further quantities of light pet/ benzene: 60/40; m.p. 78-80°, IR, PMR).

<u>cis</u>-Bicyclo $\{8.2.0\}$  dodecan-1-ol (<u>1</u>) was crystallized from light pet., m.p.  $47-48^{\circ}$  (Lit.¹⁰, m.p.  $47-49^{\circ}$ ) and identified by comparison of its IR and PMR with the data reported in the lit.¹⁰ Mass: m/z 182[°] (M⁺, 6%), 111 (100%), 58(96%), 71(80%), 41 (65%), 55(59%), 98(53%), 97(44%), 43(37%).

(c) <u>Products from p-menthane</u>. The total hydrolysis product, b.p.  $80-115^{\circ}/35$  mm was oxidized with  $Cr0_3^{22}$ , and the product (20.2 g) systematically chromatographed on  $Al_20_3/II$  (64 cm x 5.2 cm) and 105 fractions (of 500 ml each) with solvents of increasing polarity (light pet. with increasing amounts of benzene, then benzene with increasing amount of ethyl acetate) were collected. Following fractions yielded compounds <u>9</u> to <u>12</u> and <u>14</u>. A mixture (560 mg) of menthone ( $\underline{9}$ ) and isomenthone ( $\underline{10}$ ) was eluted with light pet./benzene: 95/5 (500 ml x 2) and the compounds recognized by GLC and PMR.

Isocarvomenthone (14; 285 mg) was next obtained with further elution with light pet./benzene: 95/5 (500 ml x 2) and was identified by GLC, IR & PMR.

Elution with light pet./benzene: 85/15 (500 ml x 5) furnished <u>cis-p-</u> menthan-4-ol (<u>11</u>; 146 mg) (IR, PMR), while <u>trans-p-menthan-1-ol</u> (<u>12</u>; 380 mg) was eluted with light pet./benzene: 50/50 (500 ml x 12).

(d) Products from cis-pinane. The total product from hydrogen peroxide reaction was hydrolyzed and this material (22.0g, b.p.  $80-110^{\circ}/18$  mm) carefully fractionated on spinning-band column (reflux ratio, 1:15), while monitoring with GLC (col. C). The appropriate fractions were further purified by chromatography over silica gel/IIA, and the compounds 16 to 18 identified by comparison of their IR & PMR with those of authentic samples.

### REFERENCES AND NOTES

1 For reviews: H. Kropf, Houben-Weyl: Methoden der organischen Chemie, 6/1a (part 1), 10 (1979); Y. Mazur, Pure Appl. Chem. 41, 145 (1975); M. Fischer, Angew. Chem. Intern. Edit. 17, 16 (1978); R. Breslow, Acc. Chem.Res. 13, 170 (1980).

- ²G.A. Olah, D.G. Parker and N. Yoneda, <u>Angew. Chem. Intern. Edit</u>. <u>17</u>, 909 (1978).
- ³D.L. Heywood, B. Phillips and H.A. Stansbury, <u>J. Org. Chem</u>. <u>26</u>, 281 (1961); D.L. Heywood, H.A. Stansbury and B. Phillips, U.S. Patent
- 3,182,008 May 4, 1965.
- ⁴P. von R. Schleyer and R.D. Nicholas, <u>J. Am. Chem. Soc. 83</u>, 182 (1961).
- ⁵ Since then, another report describing hydroxylation of two steroidal acetates by peracetic acid under irradiation by light, has appeared: A Rotman and Y. Mazur, <u>J. Am. Chem. Soc</u>. <u>94</u>, 6228 (1972).
- ⁶ The spectrum is a rising continuum from  400  to  195  nm, with no maximum or fine structure: <u>Organic Peroxides</u> (Editor, D. Swern), vol. II, p. 678. Wiley-Interscience, New York (1971).
- ⁷ See e.g.: J.G. Calvert and J.N. Pitts, <u>Photochemistry</u>, p. 202. John Wiley, New York (1966).
- ⁸ For review: T. Matsuura and K. Omura, <u>Synthesis</u> 173 (1974).
- ⁹ See e.g.: J.G. Calvert and J.N. Pitts, <u>Photochemistry</u> p. 389. John Wiley, New York (1966).
- ¹⁰ K. Matsui, T. Mori and H. Nozaki, <u>Bull. Chem. Soc. Japan</u> <u>44</u>, 3440 (1971)
- ¹¹ See e.g.: D.S. Nonhebel, J.M. Tedder and J.C. Walton, <u>Radicals</u>, p. 8. Univ. Press, Cambridge (1979).

- ¹² cf. J.H. Baxendale and J.A. Wilson, Trans. Faraday Soc. <u>53</u>, 344 (1957)
- ¹³ D.D. Evans and C.W. Shoppee, <u>J. Chem</u> <u>Soc</u>. 543 (1953).
- 14 H. Brockmann and H. Schodder, <u>Ber. Dtsch</u>. Chem. Ges. <u>74</u>, 73 (1941).
- ¹⁵ V. Tzukamoto, S. Nonomura and H. Sakai, <u>Agri. Biol. Chem</u>. <u>39</u>, 617 (1975)
- ¹⁶ W. Cocker, P.V.R. Shannon and P.A. Staniland, <u>J. Chem. Soc.(C)</u> 41 (1966).
- ¹⁷ F.P.G. Span, <u>J. Am.Chem.Soc</u>. <u>68</u>, 907 (1946).
- 18 J.J. Uebel and H.W. Goodwin, <u>J. Org.</u> <u>Chem.</u> <u>33</u>, 3317 (1968).
- ¹⁹ J.W. Huffman and J.T. Charles, <u>J. Am. Chem. Soc</u>. <u>90</u>, 6486 (1968).
- ²⁰ M.M. Badoche, <u>Bull. Chim.Soc. Fr</u>. 190 (1951).
- ²¹ By Grignard reaction.
- ²² H.C. Brown and C.P. Garg, <u>J. Am. Chem.</u> <u>Soc.</u> <u>83</u>, 2952 (1961).