Tetrahedron Vol. 34, pp. 135 to 139. Pergamon Press 1978. Printed in Great Britain

OXIDATION OF N-ALKYL-N'-TOSYLHYDRAZINES TO HYDROPEROXIDES[1]

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(*Received in UK 27 June 1977; Accepted for publication 7 July 1977*)

Abstract—N-Alkyl-N'-tosylhydrazines upon treatment with H_2O_2 and Na_2O_2 give with high yields the corresponding aliphatic hydroperoxides. A discussion on the possible reaction mechanism which involves the formation of an "ion pair" intermediate, is reported. The reaction of tosylhydrazones carried out under simular conditions to give dihydroperoxides and other compounds is also described.

Within the general context of the study of the tosylhydrazine derivatives, the treatment of N-alkyl-N'-tosylhydrazine by different oxidizing agents has been considered.

These studies are correlated with preceding works on tosylazoalkenes and analogous compounds.[2]

Recently, in particular, the behaviour of this class of compounds with SeO_2, HgO and CrO_3 in different solvents has been studied.[3]

Under these conditions, high yields of alkane sulphinic esters have been obtained. The chemical behaviour of N-alkyl-N'-tosylhydrazine with hydrogen peroxide, has been studied in the present work.

RESULTS AND DISCUSSION

N-Alkyl-N'-tosylhydrazines can be easily oxidized, with high yields (90–95%), into hydroperoxides with hydrogen peroxide and sodium peroxide, according to the following general scheme:

$$R{-}NH{-}NH{-}Ts \xrightarrow[THF\ r.t.]{H_2O_2/Na_2O_2} R{-}OOH.$$

The original N-alkyl-N'-tosylhydrazines were obtained through reduction of the corresponding tosylhydrazones or tosylhydrazides.[4]

N - (5α - Cholestan - 3β - yl) - N' - tosylhydrazine (**5**) and N - (2 - methylcyclohexyl) - N' - tosylhydrazine (**4**) in particular, have been obtained through repeated crystallizations of the reaction compounds.

The structure of the described tosylhydrazines has been determined on the basis of analytical data and spectroscopic results. The NMR of N - (5α - cholestan - 3β - yl) - N' - tosylhydrazine (**5**), in particular, shows a multiplet signal at δ 2.57 with $W_{1/2}$ = 20 Hz, assigned to C_3–H; furthermore the amplitude value of the signal is in excellent accord with the one of the C_3–H in α position.[5] On the contrary, the corresponding C_3–H in β position shows $W_{1/2}$ = 7 Hz.

Oxidation results on the different substrates are summarized in Table 1.

The reaction described above, was followed by means of HPLC in order to ascertain the most suitable conditions and to evaluate yields. Pure samples of the hydroperoxides were obtained by chromatographic separation on an open column (SiO_2 0.040–0.063; eluent: hexane, and subsequently hexane/ethyl acetate 80/20 v/v).

The hydroperoxides were characterized on the basis of the analytical data (C, H and O) of the IR data (ν_{H-O} 3450, ν_{-O-O-} 830–890 cm^{-1})[9,10] and of the ^1H NMR signal spectrum. In fact, the characteristic signal of the hydroperoxidic proton with chemical shift within fields ranging between 8 and 9 δ is always present in the latter.[10]

The configurational isomers were characterized, whenever necessary, on the basis of the value of the chemical shift and of the J of the proton on the α-carbon with respect to the hydroperoxidic group ($\rangle C^{\alpha}H{-}OOH$) similarly to what was previously observed with regard to the corresponding N - alkyl - N' - tosylhydrazines.[5,11] In the particular case of **5a** and **5b**, they had to be reduced to the corresponding alcohols, with LAH, and checked against authentic samples.

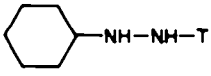
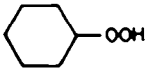
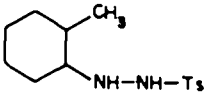
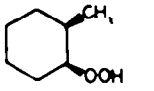
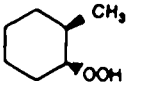
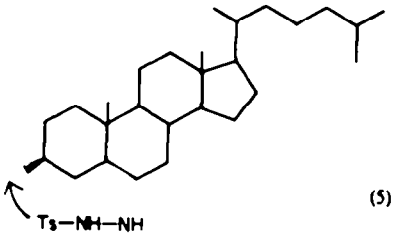
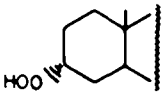
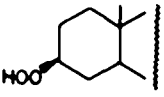
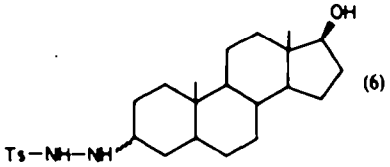
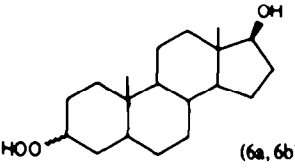
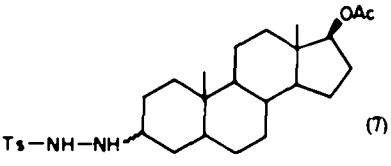
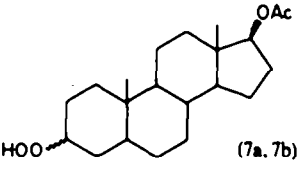
The possibility of the formation of an intermediate carbocation was first evaluated by studying the oxidation of N - (5α - cholestan - 3β - yl) - N' - tosylhydrazine (**5**). By this process of oxidation a mixture of the isomer 3α (**5a**) and 3β (**5b**), in a ratio of approximately 1/1 (Table 1), was obtained. This result may be interpreted as a racemization of the asymmetric center to which the tosylhydrazinic residue is bound.

Furthermore a mixture of the hydroperoxide isomer *cis*-**4a** and *trans*-**4b** (Table 1) was obtained by the oxidation of the N - (2 - methylcyclohexyl) - N' - tosylhydrazine (**4**), while no significant amount of the product of transposition: 1-methylcyclohexyl hydroperoxide, which could result from the intermediate formation of a carbocation, was observed.

Further evidence to exclude intermediate formation of a carbocation is obtained from the oxidation reaction of N - alkyl - N' - tosylhydrazine in a methanol containing solution. In such reactions, as a matter of fact, negligible methanol incorporations are noted.

In order to reveal the possible formation of an intermediate diazo compound A (Scheme 1), oxidation of N -

Table 1.

N-Alkyl-N'-tosylhydrazines		m.p.	Alkylhydroperoxides		m.p.	Yield (%)	
t-Bu—CH_2—NH—NH—Ts	(1)	82–4°	t-Bu—CH_2—OOH	(1a)	oil		87
$C_{15}H_{31}$—CH_2—NH—NH—Ts	(2)[2]		$C_{15}H_{31}$—CH_2—OOH	(2a)[7]			95
	(3)[6]			(3a)[8]			92
	(4)	106–8°		(4a)	oil	43%[a]	90 (85)[b]
				(4b)	oil	57%[a]	
	(5)	127–30°		(5a)	158–60°	57%[a]	95 (88)[b]
				(5b)	104–5°	43%[a]	
	(6)			(6a, 6b)	166–8°		93
	(7)			(7a, 7b)	124–7°		95

[a]Relative percentages.
[b]Yields obtained in the "one-step" process.

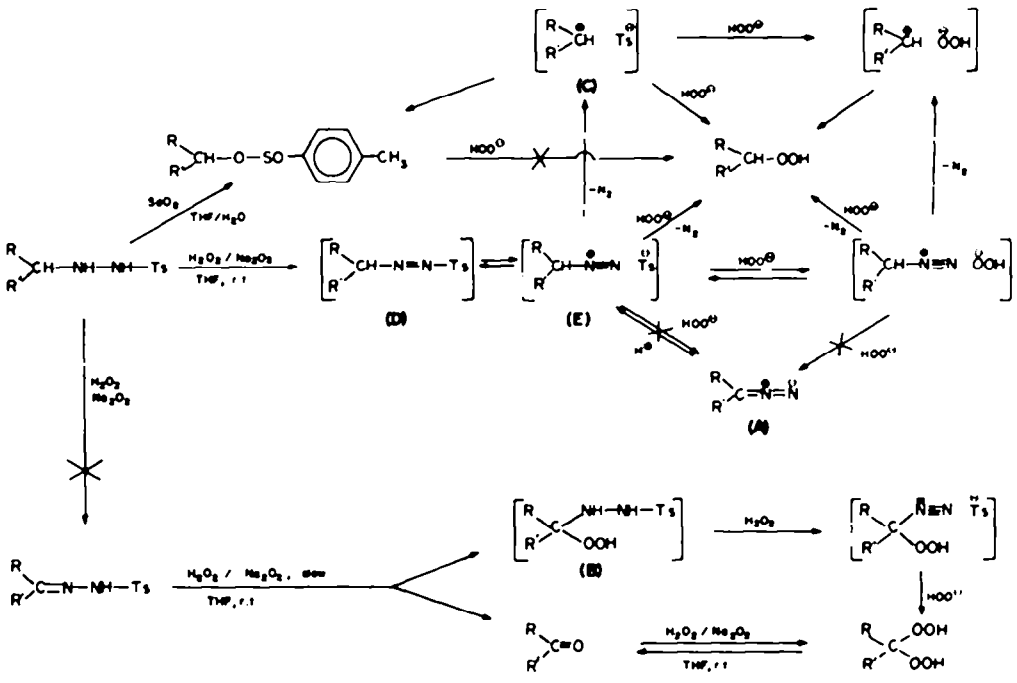
(2 - methyl - 1 - deuterocyclohexyl) - N' - tosylhydrazine, obtained by reduction with $NaBD_4$ of the related tosylhydrazone of 2-methylcyclohexanone, was carried out in the described conditions. The hydroperoxides obtained from this reaction present a high content of deuterium. This result, therefore, confirms that the diazo compound is not the intermediate responsible for the formation of hydroperoxides. In fact, the diazo compound would determine an exchange with the protons of the medium.

The formation of the hydroperoxide from the corresponding sulfinic ester can be ruled out since a pure sample of sulfinic ester in the same conditions does not give significant amount of hydroperoxide.

Furthermore, the formation of the corresponding intermediate tosylhydrazones is to be excluded since oxidation of the latter, through independent means, and under similar conditions, leads to the formation of corresponding dihydroperoxides, in accordance with Scheme 1 given herein, together with large quantities of the corresponding hydrolysis-derived ketone.

Formation of dihydroperoxide can be accounted for by two alternative processes: one, as demonstrated, contemplates the attack of $HOO^{\ominus}$ ion, on the double bond C=N, with subsequent formation of the intermediate (B), which similarly to what happens to the N - alkyl - N' - tosylhydrazine seen above, decomposes into the corresponding dihydroperoxide; the other implies preliminary hydrolysis of tosylhydrazone to the corresponding ketone, which is subsequently transformed into dihydroperoxide. This last hypothesis is supported by the fact that, through HPLC analysis, the presence of the corresponding ketone has been emphasized.

On the basis of the results obtained, the existence of the ion pair (C) as an intermediate, has been supposed.



Scheme 1.

To confirm such hypothesis N - (5α - cholestan - 3β - yl) - N' - tosylhydrazine (5) was oxidized with SeO_2 in THF/H_2O, which, as previously described,[3] causes the formation of the corresponding sulphinic esters. In this reaction the 5α - cholestan - 3β - yl - *p* - toluenesulphinic ester and the isomer 3α- in the relative ratio of 7:1, with high configuration retention, have been isolated. Such result tallies with the fact that in processes involving ion pairs, configuration retention frequently occurs.[13]

On the basis of data obtained, therefore, the existence of a process allowing for the formation of the intermediate tosylazoalkane (D), obtained by direct oxidation of N - alkyl - N' - tosylhydrazine, which can, in the reaction medium, be present as ion pair and cause the equilibria reported in Scheme 1, can be surmised.

Furthermore the intermediate (E) can loose nitrogen, bringing forth the ion pair (C) which can, in turn, either rearrange to the corresponding sulphinic ester with high configuration retention directly, or alternately, and in relation to the experimental conditions, interact with the $HOO^{\ominus}$ ions present, to produce corresponding hydroperoxides with high racemization percentages. Other possible interactions, amongst the various ones present in solution, are set forth in the scheme.

However contributions of radicals (possible "cage effects") or concerted pathways related to undissociated tosylazoalkane (D), cannot be excluded.

It is interesting to note, at last, from a synthetic point of view, that the same hydroperoxides may be obtained directly from tosylhydrazides or tosylhydrazones, without isolating the intermediate N-alkyl-N'-tosylhydrazines.

In this case, tosylhydrazone or tosylhydrazide is reduced with either B_2H_6, or with $NaBH_4$, to the corresponding N - alkyl - N' - tosylhydrazine; the reaction mixture is subsequently treated with methanol and evaporated in order to yield a crude product, the oxidation of which is carried out by a similar process to the one previously described.

The yields related to the hydroperoxides obtained through this one-step procedure are reported in brackets in Table 1.

The above described method points to a new way of synthetizing the primary and secondary hydroperoxides, starting from ketonic or aldehydic compounds or carboxylic acids under mild conditions and high yields.

Such a synthetic method may be considered convenient and may offer an alternative to the methods of preparation of hydroperoxides already described.[7,8,14,15]

EXPERIMENTAL

Equipment. IR spectra were recorded as film or KBr pellets with a Perkin-Elmer Model 337 and Model 621 grating spectrophotometers. NMR spectra were obtained with a Varian T-60 and Jeolco 60-HL spectrometers. The chemical shifts are expressed in δ values (ppm) relative to a Me_4Si internal standard. All m.ps reported are uncorrected. Analytical data (% C, H, N and S) were obtained from Mikroanalytisches Lab., Dr. F. Pascher, Bonn (Germany). Liquid chromatography was performed on a Waters Ass. ALC/GPC 202/R401 Model equipped with a 6000M reciprocating pump and RI400 detector.

N-*Alkyl*-N'-*tosylhydrazines*

The N - alkyl - N' - tosylhydrazines were prepared by reduction of the corresponding tosylhydrazones and of the N - acyl - N' - tosylhydrazines as previously reported.[4]

N - (2 - *Methylcyclohexyl*) - N' - *tosylhydrazine* (4) obtained by reduction with diborane of 2-methylcyclohexyl tosylhydrazone. Pure sample of 4 was isolated from the reduction mixture by recrystallization from CH_2Cl_2/hexane; m.p. 106–8° (dec); IR (Nujol): 3230–3180 (ν_{NH}) 1308, 1195 (ν_{SO_2}) cm^{-1}. ^1H NMR: ($CDCl_3$) δ, 7.57 (q, 4H, AA'BB', J = 8 Hz, *p*-C_6H_4), 2.76 (m, 1H, $-CH-NH-$, $W_{1/2}$ = 12 Hz), 2.40 (s, 3H, $CH_3-C_6H_4-$), 2.20–0.50 (m, 7H, $-CH-(-CH_2)_5-$), 0.80 (d, 3H, CH_3-CH-, J = 8 Hz) ppm; (Found: C, 59.49; H, 7.92; N, 10.13; S, 11.20. $C_{14}H_{22}N_2O_2S$ requires: C, 59.55; H, 7.85; N, 9.92; S, 11.33%).

N - (5α - *Cholestan* - 3β - *yl*) - N' - *tosylhydrazine* (5) obtained by recrystallizations of the crude product of reduction with diborane of 3-cholestanone tosylhydrazone, m.p. 127–30° (dec)

from CH_2Cl_2/hexane; IR (Nujol): 3310–3180 (ν_{-NH-}), 1320, 1160 (ν_{-SO_2-}), 1600, 815 cm^{-1}. ^1H NMR: ($CDCl_3$), 7.57 (q, 4H, AA'BB', J_{AB} = 8 Hz, p-C_6H_4), 2.57 (m, 1H, $-CH-N-N-$, $W_{1/2}$ = 20 Hz), 2.42 (s, 3H, CH_3-Ar), 2.25–0.50 (m, remaining steroidical protons) ppm; (Found: C, 73.25; H, 10.36; N, 5.11; S, 5.74. $C_{34}H_{56}N_2O_2S$ requires: C, 73.34; H, 10.14; N, 5.03; S, 5.74%).

Oxidation of N-alkyl-N'-tosylhydrazines: alkylhydroperoxides (1a–7a,b)

General procedure. The following sample is typical of the method employed to obtain the alkylhydroperoxides (1a–7a, b).

To a soln of 3 (1.00 g, 3.73 mmol) in THF (100 ml), 42.3 ml of 30% H_2O_2 (373 mmol) and 436 mg Na_2O_2 (5.59 mmol) were added, at room temp. and under magnetic stirring. The mixture was allowed to react for 24 hr, then diluted with water (200 ml), acidified with 2 N HCl and extracted with CH_2Cl_2. The extract was dried (Na_2SO_4) and evaporated under reduced pressure to give a colourless oily residue which was analyzed by High Performance Liquid Chromatography (HPLC) (eluent: isooctane/ethyl acetate, 85/15, v/v; column: Hibar SiO_2-60, 7 μ, 25 cm; flow: 1.0 ml/min; detector: RI. The yield (92%) was calculated by the external standard method using as reference an authentic specimen previously prepared.

The oily residue was purified by column chromatography (Silica gel, 0.040–0.063 mm) eluting with hexane to remove a small amount of the corresponding hydrocarbon which is a minor product of the reaction. Further elution with ethyl acetate/n-hexane 20/80 gave pure hydroperoxide.

Neopentylhydroperoxide (1a; 87% yield). IR (liquid film): 3400 (ν_{H-O_2}), 840 (ν_{-O-O-}) cm^{-1}. ^1H NMR: ($CDCl_3$) δ, 8.90 (bs, 1H, H–O_2, removed by D_2O exchange), 3.80 (s, 2H, HO_2-CH_2-), 0.97 (s, 9H, $-C(CH_3)_3$) ppm; (Found: C, 57.82; H, 11.61. $C_5H_{12}O_2$ requires: C, 57.82; H, 11.61%).

Hexadecylhydroperoxide (2a; 95% yield). IR (Nujol): 3430 (ν_{H-O_2}, s), 920 (ν_{-O-O-}, m) cm $^{-1}$. ^1H NMR: ($CDCl_3$) δ, 8.40 (bs, 1H, H–O_2, removed by D_2O exchange), 4.00 (t, 2H, J = 6 Hz, HO_2-CH_2-), 1.28 (m, 28H, $-(CH_2)_{14}-$), 0.90 (t, 3H, $-CH_3$) ppm; (Found C, 74.45; H, 13.33. $C_{16}H_{34}O_2$ requires: C, 74.36; H, 13.26%). The physico-chemical properties were identical with those of an authentic sample.[7]

Cyclohexylhydroperoxide (3a; 92% yield). IR (liquid film): 3400 (ν_{H-O_2}, s), 840 (ν_{-O-O-}, m) cm^{-1}.[8] ^1H NMR: ($CDCl_3$) δ, 8.00 (bs, 1H, H–O_2, removed by D_2O exchange), 3.97 (m, 1H, $-O_2-CH-$, $W_{1/2}$ = 18 Hz), 2.15–1.05 (m, 10H, $-(CH_2)_5-$) ppm. The other physico-chemical properties were identical with those of an authentic sample.[8]

cis- *and* trans-2-*Methylcyclohexylhydroperoxide* (4a, 4b). From the reaction of the N - (2 - methylcyclohexyl) - N' - tosylhydrazine with H_2O_2 and Na_2O_2, as described in the general procedure, both isomeric hydroperoxides were obtained. The relative amounts of the isomers (Table 1) were determined by HPLC (general procedure) and they have been isolated by column chromatography (Silica gel) eluting with hexane/EtOAc 90/10.

cis-2-*Methylcyclohexylhydroperoxide* (4a; 39% yield). IR (liquid film): 3400 (ν_{H-O_2}), 840 (ν_{-O-O-}) cm^{-1}. ^1H NMR: ($CDCl_3$) δ, 8.20 (bs, 1H, H–O_2, removed by D_2O exchange), 4.03 (m, 1H, $-O_2-CH-$, $W_{1/2}$ = 11 Hz), 2.50–0.70 (m, 9H, $-(CH_2)_4-CH-$), 0.93 (d, 3H, J = 6 Hz, CH_3) ppm.

trans-2-*Methylcyclohexylhydroperoxide* (4b; 51% yield). IR (liquid film: 3400 (ν_{H-O_2}), 840 (ν_{-O-O-}) cm^{-1}. ^1H NMR: ($CDCl_3$) δ, 8.20 (bs, 1H, H–O_2, removed by D_2O exchange), 3.50 (m, 1H, HO_2-CH-, $W_{1/2}$ = 20 Hz), 2.50–0.70 (m, 9H, $-(CH_2)_4-CH-$), 0.98 (d, 3H, J = 5 Hz, CH_3) ppm.

3α- *and* 3β-*Cholestanylhydroperoxide* (5a–5b). The relative per cent ratio of the two isomers was calculated by HPLC using conditions described in the general procedure and eluting with isooctane/EtOAc (90/10, v/v).

The two isomers were separated by column chromatography (Silica gel, 0.040–0.063) eluting, after washing with hexane, with hexane/EtOAc (85/15).

3α-*Cholestanylhydroperoxide* (5a; 54% yield), m.p. 158–60° (dec) from CH_2Cl_2–hexane; $[\alpha]_D^{20}$ = + 26° ($CHCl_3$, c = 0.0124 g/ml); IR (Nujol): 3400 (ν_{H-O_2}), 850 (ν_{-O-O-}) cm^{-1}. ^1H NMR: ($CDCl_3$) δ, 7.95 (bs, 1H, H–O_2–, removed by D_2O exchange), 4.17 (m, 1H, $-O_2-CH-$, $W_{1/2}$ = 7 Hz), 2.25–0.50 (m, remaining steroidical protons) ppm.

3β-*Cholestanylhydroperoxide* (5b, 41% yield), m.p. 104–5° (dec) from CH_2Cl_2–hexane; $[\alpha]_D^{20}$ = + 23° ($CHCl_3$, c = 0.0144 g/ml); IR (Nujol): 3400 (ν_{H-O_2}), 850 (ν_{-O-O-}) cm^{-1}. ^1H NMR: ($CDCl_3$) δ, 8.00 (bs, 1H, H–O_2–, removed by D_2O exchange), 3.90 (m, 1H, $-O_2-CH-$, $W_{1/2}$ = 22 Hz), 2.25–0.50 (m, remaining steroidical protons) ppm. Analyses: Found for 3α-cholestanylhydroperoxide: C, 80.31; H, 12.08; O, 7.98%. Found for 3β-cholestanylhydroperoxide: C, 78.97; H, 11.94; O, 8.90%. $C_{27}H_{46}O_2$ requires: C, 80.14; H, 11.96; O, 7.91%.

3α- *and* 3β-*Androstanyl-17*β-*ol hydroperoxide* (6a–6b; 93% yield).

It was not possible, as for 3α- and 3β-cholestanylhydroperoxide, to isolate the two isomers by means of open column chromatography, but an HPLC analysis has confirmed that the mixture contains about equal parts of the two isomers, m.p. 166–8° (dec) from CH_2Cl_2–hexane; IR (Nujol): 3450 (ν_{H-O_2}, s), 3230 (ν_{H-O-}, s), 1050 (ν_{HO-CH-}, s), 860 (ν_{-O-O-}, m) cm^{-1}. ^1H NMR: ($CDCl_3$) δ, 10.00 (bs, 2H, H–O_2–, H–O–, removed by D_2O exchange), 4.05 (m, 1H, HO_2-CH-), 3.60 (t, 1H, HO–CH–, J = 8 Hz), 2.30–0.50 (m, remaining steroidical protons) ppm; (Found: C, 73.70; H, 10.50. $C_{19}H_{32}O_3$ requires: C, 73.98; H, 10.46%).

3α- *and* 3β- - *Androstanyl* - 17β - *acetoxy* - *hydroperoxide* (7a–7b; 95% yield).

Also in this case, we have obtained a mixture of two isomers, which were not separated, m.p. 124–7° (dec) from CH_2Cl_2–hexane; IR (Nujol): 3450 (ν_{H-O_2}), 1710 ($\nu_{C=O}$), 860 (ν_{-O-O-}) CM^{-1}. ^1H NMR: ($CDCl_3$) δ, 8.70 (bs, 1H, H–O_2–, removed by D_2O exchange), 4.63 (t, 1H, $-CH-OAc$, J = 8 Hz), 4.10 (m, 1H, HO_2-CH-), 2.06 (s, 3H, $-CO-CH_3$), 2.30–0.50 (m, remaining steroidical protons) ppm; (Found: C, 71.76; H, 9.89. $C_{21}H_{34}O_4$ requires: C, 71.96; H, 9.78%).

One-step transformation of cholestanone tosylhydrazone into cholestanylhydroperoxides

Cholestanone tosylhydrazone (0.89 mmol, 0.50 g) in THF (6 ml) were treated with 8 ml of 1 M diborane in THF for 30' at room temp. and under N_2. The 20 ml of MeOH were added and after 20 min the solvent was distilled at room temp. and under reduced pressure. The mixture was dissolved in THF (60 ml) and H_2O_2 (10 ml) and Na_2O_2 (104 mg) were added. The reaction was carried out at room temp. for 24 hr, then the mixture was diluted with water (100 ml), acidified with 2 N HCl and extracted with CH_2Cl_2. The extract was dried (Na_2SO_4) and evaporated under reduced pressure to give a solid residue, in a 88% yield. The yield was calculated by HPLC (external standard method). The mixture was purified by column chromatography (silica gel), as previously described.

One-step transformation of 2-methylcyclohexanone tosylhydrazone into 2α- *and 2*β-*methylcyclohexylhydroperoxide*

The reaction was carried out as above described starting from 2-methylcyclohexanone tosylhydrazone (3 g, 10.71 mmol). The mixture was chromatographed on a silica gel column (0.04–0.06 mm) eluting with EtOAc/n-hexane (20/80). (Total yield of the two isomeric hydroperoxides: 1.03 g, 7.92 mmol, 85%).

Reduction of 3α- *and* 3β-*cholestanylhydroperoxide with* LAH

3α(3β)-Cholestanylhydroperoxide (50 mg) in diethyl ether

(10 ml) were treated with 30 mg of LAH at room temp. After 30 min, 5 ml of EtOAc and then 30 ml water were added. The organic layer was separated, dried and evaporated giving a solid residue, consisting, by comparison with an authentic sample, only of the 3α(3β)-cholestanol.

Reaction of N-(5α-*cholestan*-3β-*yl*)-N'-*tosylhydrazine with* H_2O_2 *in methanol*

N - (5α - cholestan - 3β - yl) - N' - tosylhydrazine (170 mg) in THF (3 ml) were treated with 10 ml MeOH and 0.8 ml of 30% H_2O_2, for 24 hr at room temp. to yield a mixture of 3α- and 3β-cholestanylhydroperoxides. No considerable amounts of the 3α and 3β-metoxycholestane were detected.

Oxidation of N - (5α - *cholestan* - 3β - *yl*) - N' - *tosylhydrazine*[5] *with* SeO_2

To 600 mg of N - (5α - cholestan - 3β - yl) - N' - tosylhydrazine (1.08 mmol) in THF (3 ml), 120 mg (1.08 mmol) of SeO_2 were added and the mixture was stirred at room temp. for 2 hr. The soln was filtered, the solvent removed and the oily residue was chromatographed on silica with hexane/EtOAc (95/5) as eluant giving the two isomeric sulphinic esters (total conversion yield, 67%; 3β : 3α relative ratio, 88 : 12%).

3β-p-*Toluensulphinylcholestane*, m.p. 136–9° (dec) from CH_2Cl_2–hexane; IR (Nujol): 1130 (ν_{S-O}) cm^{-1}. ^1H NMR: ($CDCl_3$) δ, 8.0–7.2 (q, 4H, AA'–BB', J_{AB} = 8 Hz), 4.26 (m, 1H, –CH–OSOAr, $W_{1/2}$ = 20 Hz), 2.45 (s, 3H, CH_3–Ar), 2.25–0.50 (m, remaining steroidical protons) ppm.

3α-p-*Toluensulphinylcholestane*, m.p. 132–6° (dec) from CH_2Cl_2–hexane; IR (Nujol): 1130 (ν_{S-O}) cm^{-1}. ^1H NMR: ($CDCl_3$) δ, 8.0–7.2 (q, 4H, AA'BB', J_{AB} = 8 Hz), 4.66 (m, 1H, –CH–OSOAr, $W_{1/2}$ = 8 Hz), 2.44 (s, 3H, CH_3–Ar), 2.25–0.50 (m, remaining steroidical protons) ppm; (Found: for 3α isomer C, 77.25; H, 10.12; S, 5.89%. for 3β-isomer C, 76.98; H, 10.09; S, 5.87. $C_{34}H_{54}O_2S$ requires: C, 77.52; H, 10.33; S, 6.07%).

Reaction of cyclohexanone tosylhydrazone with H_2O_2/Na_2O_2

The reaction of 1.00 g of cyclohexanone tosylhydrazone (3.76 mmol) in THF (20 ml) was treated with 43 ml (376 mmol) of 30% H_2O_2 and 440 mg (5.64 mmol) of Na_2O_2 was carried out at 25° for 15 days. Then the mixture was neutralized with 1N HCl and extracted with 100 ml of CH_2Cl_2. The extract, dried and evaporated under reduced pressure, gave a colourless oily residue, which by HPLC analysis shown to contain cyclohexanone and cyclohexylidenhydroperoxide (~20%). This latter compound was isolated from the mixture by column chromatography (silica gel) eluting with n-hexane/EtOAc (80/20) and identified by comparison with an authentic sample.[16]

Reaction of 3-*cholestanone tosylhydrazone with* H_2O_2/Na_2O_2

3,3-*Dihydroperoxycholestane*. The reaction was carried out as above described. Column chromatography with N-hexane/EtOAc (80/20) as eluant of the mixture gave pure 3,3-dihydroperoxycholestane (22%), m.p. 151–5° (dec) from CH_2Cl_2–hexane; IR (Nujol): 3320–3460 (ν_{O-H}), 1020–930 (ν_{C-O}), 850 (ν_{O-O-}) cm^{-1}. ^1H NMR: ($CDCl_3$) δ, 8.93 (bs, –OOH, 2.0–0.5 (m, remaining steroidical protons) ppm; (Found: C, 74.45; H, 11.23; O, 14.61. $C_{27}H_{48}O_4$ requires: C, 74.31; H, 11.01; O, 14.68%).

Reaction of 3-*cholestanone with* H_2O_2/HCl

3,3-*Dihydroperoxicholestane*. 3-Cholestanone (1.0 g, 2.59 mmol) in THF (10 ml) was treated with 2.6 ml 30% H_2O_2 (22.9 mmol) and 0.1 ml 37% HCl and the reaction was carried out at 25° for 3 hr. Then 50 ml water were added and the mixture was extracted with 100 ml CH_2Cl_2. The extract dried and evaporated under reduced pressure gave a solid residue from which dyhydroperoxide was isolated by column chromatography (silica gel) with n-hexane/EtOAc (80/20) as eluant (94% yield).

Reaction of 3-*cholestanone tosylhydrazone with* H_2O_2/HCl

3,3-*Dihydroperoxycholestane*. The reaction was carried out as above described, starting from 3-cholestanone tosylhydrazone to give 3,3-dihydroperoxicholestane in 91% yield.

Reduction of 3,3-*dihydroperoxicholestane with* LAH

The dihydroperoxide (50 mg) in diethyl ether (5 ml) was treated with 30 mg of LAH at room temp. for 20 min. Then AcOEt and water was added and the mixture was extracted with CH_2Cl_2. The extract, dried and evaporated, gave a solid residue which resulted to consist of 3α- and 3β- cholestanol.

Reaction of 3,3-*dihydroperoxicholestane with* KI

A soln of 3,3-dihydroperoxicholestane in diethyl ether was shaken in a funnel together with a soln of KI. The organic layer dried and evaporated gave a solid crystalline residue which resulted to consist of 3-cholestanone.

Acknowledgement—We thank Mrs. Giovanna Cancelliere for her helpful assistance, and the National Research Council (C.N.R.) for financial support.

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