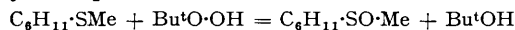


**634.** *The Use of Radioactive Sulphur [<sup>35</sup>S] in a Study of the Oxidation of cycloHexyl Methyl Sulphide with tert.-Butyl Hydroperoxide.*

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*cyclo*Hexyl methyl [<sup>35</sup>S]sulphoxide has been synthesised from methane-<sup>35</sup>S]thiol and has been used to show the irreversibility of the primary oxidation step in the conversion of *cyclo*hexyl methyl sulphide into the corresponding sulphoxide by *tert.*-butyl hydroperoxide.

OVER a wide range of experimental conditions the oxidation of *cyclo*hexyl methyl sulphide to *cyclo*hexyl methyl sulphoxide by *tert.*-butyl hydroperoxide in benzene is stoichiometrically represented by the equation :



In a kinetic study of this oxidation made by Dr. K. R. Hargrave in these laboratories (unpublished work) a strong, auto-retardative effect due to the sulphoxide has been observed. It is a reasonable assumption that, whatever the detailed reaction mechanism, the formation of sulphoxide from sulphide occurs in one individual step, although for the present purpose the mechanism of this oxygen transfer is of no consequence. The reversibility of this oxidation step is one possibility which would account for the observed retardation and the present work was undertaken to verify or disprove this.

The principle of the investigation can be stated as follows. A relatively large excess of *cyclo*hexyl methyl sulphide is caused to react with *tert.*-butyl hydroperoxide in benzene

in the presence of sulphoxide labelled with  $^{35}\text{S}$ , under conditions which allow of the major utilisation of the hydroperoxide. The residual sulphide is then rigorously separated from sulphoxide and its activity determined. The absence of activity in this sulphide will demonstrate the irreversibility of the primary oxidation process.

*cyclo*Hexyl methyl [ $^{35}\text{S}$ ]sulphide was prepared from methane[ $^{35}\text{S}$ ]thiol and *cyclo*hexene and oxidised, without isolation, to *cyclo*hexyl methyl [ $^{35}\text{S}$ ]sulphoxide with *tert.*-butyl hydroperoxide. The overall yield indicated by a trial synthesis was 83%. Purification was achieved by fractional distillation, and traces of *cyclo*hexyl methyl [ $^{35}\text{S}$ ]sulphide were finally removed by a chromatographic procedure.

The necessarily rigorous separation of sulphide from sulphoxide after oxidations carried out in the presence of labelled sulphoxide was best achieved by fractional elution from alumina. The results of control experiments in which *tert.*-butyl hydroperoxide was replaced by *tert.*-butanol, and of actual oxidation runs, are given below, the activities of the isolated samples of sulphide being expressed as the counts per minute of an "infinitely thick" layer of *cyclo*hexyl methyl sulphone assayed under standard conditions. This final counting form was superior, for low-activity samples, to the standard "infinitely thick" precipitates of benzidine sulphate, chiefly because of increased sensitivity. We have used the latter method for samples of higher activity and have found that, by suitable

TABLE I. Activities of products assayed as *cyclo*hexyl methyl sulphone.

Compound	Activity (counts/min.)	Activity due to possible reversibility of oxidation step (counts/min.)	% of maximum activity *
<i>cyclo</i> Hexyl methyl [ $^{35}\text{S}$ ]sulphoxide ...	261,000	—	—
<i>cyclo</i> Hexyl methyl sulphide from :			
(i) Control A .....	29	—	—
(ii) Control B .....	25		
(iii) Oxidation A .....	57	30	0.064
(iv) Oxidation B .....	60	33	0.071

\* If equilibration of sulphide and [ $^{35}\text{S}$ ]sulphoxide were complete, activities of sulphides from oxidations A and B would be 46,860 counts/min. and 46,590 counts/min. respectively.

refinement of techniques, errors due to non-uniformity of the precipitate and geometry of presentation to the counter can be reduced. With a negligibly small counting error the reproducibility amongst replicates has a standard deviation of about 1%.

The difference in activity between sulphide samples isolated from control and oxidation experiments is thus so slight that it can be concluded that the oxidation step involving oxygen transfer to the sulphide is irreversible under the conditions studied and, moreover, that there is no entity produced during the reaction which is capable of reducing sulphoxide to sulphide.

#### EXPERIMENTAL

*Preparation of Inactive Materials.*—*cyclo*Hexyl methyl sulphide was prepared by ultraviolet irradiation of a mixture of methanethiol and *cyclo*hexene (Barnard, Fabian, and Koch, *J.*, 1949, 2442). The pure sulphide (yield 84%) had b. p. 62.2—62.6°/13 mm.,  $n_D^{20}$  1.4945 (Found : C, 64.4; H, 10.75; S, 24.6. Calc. for  $\text{C}_7\text{H}_{14}\text{S}$  : C, 64.6; H, 10.8; S, 24.6%). *cyclo*Hexyl methyl sulphoxide, prepared by Barnard and Hargrave's method (*Analyt. Chim. Acta*, 1951, 5, 536), had b. p. 88.3°/0.05 mm.,  $n_D^{20}$  1.5119 (yield 77%) (Found : C, 57.5; H, 9.75; S, 22.1. Calc. for  $\text{C}_7\text{H}_{14}\text{OS}$  : C, 57.5; H, 9.65; S, 21.9%). Analysis of the sulphoxide by Barnard and Hargrave's method (*loc. cit.*) indicated a purity of 99.0%. Commercial *tert.*-butyl hydroperoxide was purified by Barnard and Hargrave's method (*ibid.*, p. 476), to give a material, b. p. 28.8°/10 mm., assaying as 99.7% pure.

*Assay of Samples for  $^{35}\text{S}$ .*—(i) The activities of "infinitely thick" samples were determined with a G.E.C. mica end-window Geiger-Müller counter (Type E.H.M.2S). With the high-activity samples sufficient counts were taken to give a standard error of less than  $\pm 1\%$ . With the low-activity samples having activities of <60 counts/min. sufficient counts were taken to give a standard error of less than  $\pm 2.5\%$ . All count-rates recorded have been corrected for the resolving time of the counter, background (<10 counts/min.), variations in counter efficiency, decay, and sample dilution.

(ii) *Assay as benzidine sulphate.* Samples were oxidised to sulphate ion by the standard

micro-combustion technique and, after suitable dilution with inactive potassium sulphate to give an "infinitely thick" sample, were precipitated as benzidine sulphate according to the method of Henriques, Kistiakowsky, Margnetti, and Schneider (*Ind. Eng. Chem., Anal.*, 1946, 18, 349). The resulting samples (diam. 2.3 cm.), on a Whatman No. 2 filter, were placed on a duralumin support and adjusted by means of a levelling device to obtain a constant height between sample surface and counter window. This adjustment was previously found to be an important factor in obtaining reproducible count-rates with samples of a given thickness. To minimise the effects of non-uniformity at the edge of the precipitate samples were covered with a mask having an aperture of diam. 1.8 cm. Results (Table 2) of the assay of representative samples indicate the order of reproducibility attained.

TABLE 2. Assay of [<sup>35</sup>S] as benzidine sulphate.

Volume of 0.0497M-K <sub>2</sub> SO <sub>4</sub> (~20 μc/l. <sup>35</sup> S) (ml.)	Mean sample thickness (mg./cm. <sup>2</sup> )	Corrected count rate (counts/min.)	Mean corr. count rate (counts/min.)
8.0	27.2	2415	2426 ± 9 *
"		2419	
"		2443	
10.0	33.7	2403	2428 ± 6 *
"		2444	
"		2433	
"		2441	
"		2422	
"	2427		
13.0	43.8	2406	2429 ± 17 *
"		2418	
"		2463	

\* Error given as standard error of the mean.

(iii) Assay as liquid cyclohexyl methyl sulphone. Samples were counted in a polished duralumin cup, of internal diam. 2.52 cm. and depth 0.75 cm., which was covered with a mask having an aperture of diam. 1.8 cm. The physical characteristics of the sulphone were suitable for obtaining samples of reproducible geometry; the liquid flows easily, does not creep, and is non-hygroscopic and involatile. Table 3 records the count-rates for different weights of sul-

TABLE 3. Assay of [<sup>35</sup>S] as cyclohexyl methyl sulphone.

Wt. (g.)	0.3580	0.4245	0.5112	0.5995	0.6860	0.8061
Sample thickness (mg./cm. <sup>2</sup> )	71.7	85.1	102	120	138	162
Corr. count rate (counts/min.)	703	693	706	704	716	733

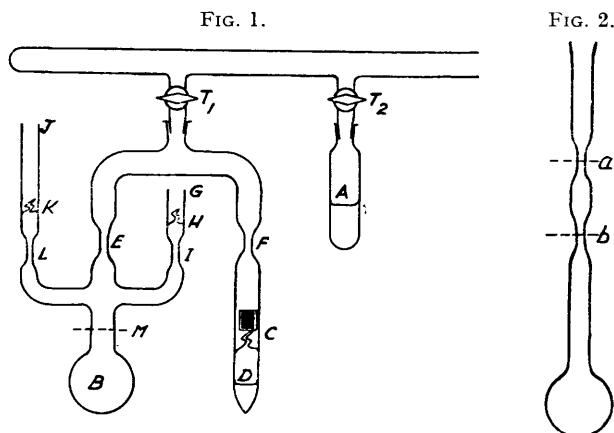
phone assayed under an accurately reproducible geometry, except for variation in height between sulphone surface and counter-window. The results show that all the sample weights used lie within the "infinite thickness" range and that variation in the sulphone weight from ca. 0.36 to 0.80 g. causes <5% increase in the count rate. Activities of [<sup>35</sup>S]sulphone samples obtained in the experiments to be described below were obtained on samples of weight ca. 0.52—0.53 g. within which range there will obviously be negligible variation in count rate for any given sample.

*Synthesis of cycloHexyl Methyl [<sup>35</sup>S]Sulphoxide.*—The apparatus used is shown in Fig. 1. Methane[<sup>35</sup>S]thiol (1.15 g., ~12.0 mc) was supplied by The Radiochemical Centre, Amersham. cycloHexene (3.934 g., 100% excess; freshly chromatographed on alumina under nitrogen) and "AnalaR" acetone (0.10 ml.) contained in the tube *A* were degassed on the vacuum-manifold and then transferred *in vacuo* to the 50-ml. flask *B*. *T*<sub>1</sub> was closed and, with *B* cooled in liquid air, the seal at *C* was broken and the methane[<sup>35</sup>S]thiol distilled *in vacuo* from *D* into the flask *B* which was then sealed off at the constriction *E*. Tube *D* was cooled in liquid air and sealed off at the constriction *F*. The reactants in *B* were irradiated with ultra-violet light, with water-cooling, for 16.0 hr. *B* was re-attached to the vacuum-manifold at *G* and then, with *B* cooled in liquid air, the seal at *H* was broken and a mixture of previously degassed *tert.*-butyl hydroperoxide (2.300 g., 6% excess based on 100% yield of sulphide) and redistilled absolute methanol (25.0 ml.) was distilled *in vacuo* into *B*, and the apparatus sealed off at the constriction *I*. The reactants were heated at 50.0° ± 0.1° for 64 hr. after which time the apparatus was re-attached to the vacuum-manifold at *J* in conjunction with a tube with a seal-off constriction. After evacuation of the apparatus, the latter tube was cooled in liquid air, the seal at *K* broken and about 10 ml. of low-boiling material were distilled *in vacuo* from *B* into the tube which was then

sealed off. This was done to trap any unchanged [ $^{35}\text{S}$ ]thiol before opening of *B* to the air. The main apparatus was sealed off at the constriction *L* until required. The flask *B* was broken at *M*, and the contents were transferred to a Vigreux distillation unit (150-ml., a pear-shaped flask). *B* was washed out with successive portions of inactive cyclohexyl methyl sulphoxide (total, 40.1 g.), followed by a little methanol, the total washings being transferred to the distillation unit. After removal of the low-boiling material, the cyclohexyl methyl [ $^{35}\text{S}$ ]sulphoxide was distilled *in vacuo* ( $10^{-3}$  mm.), to give (i) a small forerun (7.0 g.) and (ii) the main fraction (35.4 g.) (Found: S, 22.0. Calc. for  $\text{C}_7\text{H}_{14}\text{OS}$ : S, 21.9%). The latter fraction had an activity as sulphone of 265,400 counts/min. and as benzidine sulphate of 181,700 counts/min.

The same synthesis with inactive materials gave an 83% yield of cyclohexyl methyl sulphoxide, b. p.  $65^\circ/0.01$  mm.,  $n_D^{20}$  1.5122. The oxidation of cyclohexyl methyl sulphide to the corresponding sulphoxide was shown to be 96.1% complete after 24.0 hr. at  $50^\circ$ .

*Oxidation of cycloHexyl Methyl Sulphide to cycloHexyl Methyl Sulphone.*—The sulphide (1.00 g.) in "AnalaR" benzene (2.0 ml.), light petroleum (b. p.  $<40^\circ$ ; 2.0 ml.), and "AnalaR" acetic acid (20 ml.) was oxidised with hydrogen peroxide (2.73 ml., assayed as 8.45 mole/l.). The temperature rose to about  $40^\circ$  and was then slowly raised to refluxing temperature (bath at  $130^\circ$ ) and held there for 3.0 hr. After removal of the solvents and excess of peracetic acid



the residue was distilled in a small molecular-still, to give the pure sulphone,  $n_D^{20}$  1.4918 (1.07 g., 86%) (Found: C, 51.45; H, 8.8; S, 19.75. Calc. for  $\text{C}_7\text{H}_{14}\text{O}_2\text{S}$ : C, 51.8; H, 8.7; S, 19.7%).

*Chromatographic Separation of cycloHexyl Methyl Sulphide and cycloHexyl Methyl [ $^{35}\text{S}$ ]sulphoxide.*—A mixture of inactive sulphide (1.128 g.) and [ $^{35}\text{S}$ ]sulphoxide (0.5079 g.), in "AnalaR" benzene (1.0 ml.) and light petroleum (25 ml.; b. p.  $<40^\circ$ ), was chromatographed on alumina (20 g.;  $15 \times 1.3$  cm.). Successive fractions were eluted with (i) light petroleum (50 ml.), (ii) light petroleum (50 ml.), and (iii) chloroform (125 ml.). The sulphide obtained from the first eluate by removal of most of the petroleum through a gauze-packed column was oxidised to the sulphone (1.22 g., 86.7%) having an activity of 706 counts/min.

The [ $^{35}\text{S}$ ]sulphoxide, recovered from eluate (iii) by removal of the solvent, was mixed with more inactive sulphide (1.13 g.), and the mixture rechromatographed as above. The sulphide now obtained from the first eluate gave a sulphone having an activity of 25 counts/min. The low activity of the latter sulphone sample indicates the effectiveness of the separatory method, whilst the comparatively high activity of the first sulphone sample suggests the presence of some cyclohexyl methyl [ $^{35}\text{S}$ ]sulphide as impurity in the original [ $^{35}\text{S}$ ]sulphoxide. The assay results indicate a maximum percentage of [ $^{35}\text{S}$ ]sulphide impurity of 0.05%. This maximum value assumes that the chromatographic procedure is 100% efficient and that in the synthesis of the [ $^{35}\text{S}$ ]sulphoxide yields are theoretical.

*Purification of cycloHexyl Methyl [ $^{35}\text{S}$ ]sulphoxide.*—A mixture of the impure [ $^{35}\text{S}$ ]sulphoxide (6.73 g.) and inactive sulphide (3.0 ml.) in light petroleum (b. p.  $<40^\circ$ , 80 ml.) and benzene (5 ml.) was separated on alumina (120 g.;  $31 \times 2.3$  cm.). The sulphide was eluted with light petroleum (75 ml.). More inactive sulphide (3.0 ml.) in light petroleum (5 ml.) was added to the column and eluted with light petroleum (145 ml.). The [ $^{35}\text{S}$ ]sulphoxide was eluted with chloroform (450 ml.) until no further activity could be detected in the eluate. Removal of the solvent and molecular-distillation of the residue from a horizontal pot-still (bath-temp.  $45^\circ$ )

gave pure cyclohexyl methyl [<sup>35</sup>S]sulphoxide (5.6 g.) (Found: S, 22.0. Calc. for C<sub>7</sub>H<sub>14</sub>OS: S, 21.9%), having an activity as sulphone of 261,000 counts/min. and as benzidine sulphate of 175,600 counts/min.

Chromatographic separation of inactive sulphide (1.1448 g.) and the purified [<sup>35</sup>S]sulphoxide (0.5274 g.) as described above gave a sulphide fraction having an activity, as sulphone (1.14 g.) (Found: S, 19.6%), of 18 counts/min. This result confirms (i) that the [<sup>35</sup>S]sulphoxide has been purified from the [<sup>35</sup>S]sulphide impurity and (ii) that the chromatographic method is suitable for the rigid separation of sulphide-sulphoxide mixtures.

*Oxidation of cyclohexyl Methyl Sulphide with tert.-Butyl Hydroperoxide in the Presence of cyclohexyl Methyl Sulphoxide.*—(1) *Trial oxidations.* These experiments were done to determine the conditions favouring a maximum of any possible reversible reaction, and to test the stoichiometry of the oxidation over an extensive reaction range. Sulphide (3.4383 g., 0.02645 mole), sulphoxide (0.8388 g., 0.00575 mole), and *tert.*-butyl hydroperoxide (0.4997 g., 0.00555 mole) were well mixed in previously degassed benzene (25.0 ml.) and then immediately pipetted into tubes (4 at 6.0 ml. and 1 at 3.0 ml.), degassed, sealed *in vacuo*, and heated at 50.0° ± 0.1° for the appropriate times. The product was analysed for sulphoxide and hydroperoxide by Barnard and Hargrave's method (*Analyt. Chim. Acta*, 1952, 6, 23). The results (Table 4) confirm that the equation is obeyed up to 85.6% reaction.

TABLE 4. Reaction of cyclohexyl methyl sulphide with *tert.*-butyl hydroperoxide in the presence of cyclohexyl methyl sulphoxide at 50.0° ± 0.1°.

Time (hr.) .....	0	6.0	26.0	43.5	97.5
Sulphoxide (mole) .....	0.00585	—	0.00856	0.00934	0.0104
Hydroperoxide (mole) .....	0.00546	0.00447	0.00245	0.00156	0.00075

(2) *Control experiments.* To a mixture of purified cyclohexyl methyl [<sup>35</sup>S]sulphoxide (0.4942 g.) and inactive cyclohexyl methyl sulphide (1.3141 g.) contained in the apparatus shown in Fig. 2 was added, by distillation *in vacuo*, a mixture of previously degassed "AnalaR" benzene (10.0 ml.) and *tert.*-butanol (0.1648 g.), the latter replacing the hydroperoxide of the actual oxidation experiments. The flask was sealed *in vacuo* at the constriction (a), and the contents were heated at 50.0° ± 0.1° for 96.0 hr. After freezing in liquid air, the flask was opened and stannous chloride solution (25 ml.; 0.112N) was cautiously added. The flask was sealed at the constriction (b), then warmed to room temperature, and the contents were shaken occasionally for 1 hr. The flask was opened and the benzene layer, contained in the narrow neck of the flask, carefully pipetted into a second tube where, together with benzene washings (2 × 5 ml.) from the aqueous phase, it was shaken with potassium dichromate solution (3.0 ml.; 0.05N) to remove the last traces of stannous chloride solution. The benzene layer, together with benzene washings (15 ml.), was pipetted into a third tube, washed with water (8 ml.), and dried by passage through a filter pad of anhydrous magnesium sulphate. The latter was extracted with benzene washings (3 × 5 ml.) of the water phase, followed by pure benzene (5 ml.). After removal of the benzene through a spiral gauze column the product was fractionally eluted from alumina (20 g.) as previously described, to give a sulphide fraction having an activity, as sulphone (1.24 g.), of 29 counts/min. In a duplicate control experiment the sulphide fraction had an activity, as sulphone, of 25 counts/min. These results show (i) the absence of thermal exchange between sulphoxide and sulphide at 50° under the given experimental conditions, and (ii) that the stannous chloride [used to reduce unchanged hydroperoxide in experiment (3)] does not reduce [<sup>35</sup>S]sulphoxide to [<sup>35</sup>S]sulphide to any significant extent.

(3) *Oxidations in the presence of cyclohexyl methyl [<sup>35</sup>S]sulphoxide.* The purified [<sup>35</sup>S]sulphoxide (0.3382 g.), inactive sulphide (1.3771 g.), and hydroperoxide (0.1998 g.) in benzene (10.0 ml.) were heated at 50.0° ± 0.1° for 96.0 hr. under conditions identical with those of the trial oxidations and control experiments. Similar working up gave a sulphide fraction which had an activity, as sulphone (0.90 g.), of 57 counts/min.

In a second experiment, with [<sup>35</sup>S]sulphoxide (0.3361 g.), sulphide (1.3775 g.), and hydroperoxide (0.1997 g.), there was obtained a sulphide fraction which had an activity, as sulphone, of 60 counts/min.

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