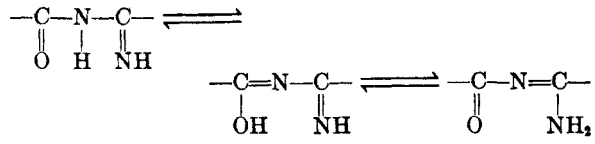

which would be prevented by replacement of the *N*-hydrogen atoms by butyl groups.

EXPERIMENTAL

The compounds were prepared by heating equimolar amounts of reactants to reflux in either methyl ethyl ketone or the ethanol-methanol solvent for 3–38 hr. Analytical samples were purified by recrystallization from ethanol. All melting points are uncorrected. The ultraviolet absorption spectra were determined in ethanol using a Beckman DK-2 recording spectrophotometer.

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Organic Sulfur Compounds. II.[1] Synthesis of Indanyl Aryl Sulfides, Sulfoxides, and Sulfones

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Cracked petroleum distillates contain indene and aromatic thiols[2,3] and it is possible that an addition reaction between these compounds can occur. Therefore, a study of these compounds was undertaken with emphasis on the ease with which addition is accomplished and to determine the properties of the resulting indanyl aryl sulfides.

It was found that aromatic thiols readily add to indene even in the absence of any added peroxide catalyst. The addition yielded the same sulfides in the presence or absence of peroxide catalyst. It is assumed, therefore, that thiol-indene addition reactions normally proceed by a radical mechanism. The addition products are formulated as 2-indanyl derivatives, since the ionic addition of acids gives 1-indanyl derivatives.[4,5] The 2-indanyl aryl sulfides obtained are white crystalline compounds soluble in hydrocarbons. An aliphatic thiol, *n*-butanethiol, reacted with indene at a much slower rate than aromatic thiols. The reaction product, 2-indanyl butyl sulfide, is a colorless liquid.

As expected, these sulfides can be oxidized by hydrogen peroxide to the corresponding sulfoxides and sulfones which are less soluble in hydrocarbons in the order mentioned. 2-Indanyl-4-tolyl sulfoxide was also prepared by adding equivalent amounts of 4-toluenethiol and cumene hydroperoxide to an *n*-heptane solution of indene. In this case, the hydroperoxide at first acted as a catalyst for addition, and then as an oxidizing agent for the sulfide formed. Some physical properties and analytical data of the compounds synthesized are shown in Table I.

1-Indanyl aryl sulfides were also synthesized by treating 1-chloroindane[6] with sodium thiophenolates in benzene–isopropyl alcohol. The 1-indanyl, phenyl, and tolyl sulfides prepared were colorless liquids. They had slightly lower boiling points at 2 mm. pressure than the corresponding 2-indanyl aryl sulfides. The main absorption peaks in the spectra of I–II and III–IV, shown in Table I, were the same. However, triplets between 5.2 and 5.6 μ had peaks at slightly different wave length. To get a more convincing proof of the difference between the 1- and 2-indanyl derivatives, the 1-indanyl sulfides were oxidized to the corresponding sulfones. The latter were white crystalline compounds melting at slightly lower temperatures than their 2-indanyl isomers. Mixed melting-point determinations of the isomers gave a definite depression.

EXPERIMENTAL

Materials. The indene and mercaptans used in the experiments were vacuum distilled under nitrogen before use. The hydrogen peroxide was a Merck reagent (Superoxol) in the form of a 30% aqueous solution. The solvents were C.P. reagents.

Synthesis of 2-indanyl aryl sulfides. A 15–100% solution of 0.1 mole of aromatic mercaptan in n-heptane was added to 11.6 g. (0.1 mole) of freshly distilled indene. Although the initial reaction was exothermic, it was necessary, after a few nours, to heat the mixture on a water bath to complete the addition. The products were recrystallized from *n*-heptane or alcohol. The yields and some physical and analytical data are listed in Table I.

The experimental procedure described above was repeated with 4-chlorothiophenol and indene in the presence of 0.76 g. (0.05 mole) of cumene hydroperoxide (added to the indene before the thiophenol). The same sulfide was obtained in a yield similar to the experiment without the hydroperoxide. This latter experiment supports a radical mechanism of the mercaptan addition to indene.[7]

Synthesis of 2-indanyl aryl sulfoxides. The 2-indanyl aryl sulfide (0.1 mole) was dissolved in a mixture of 40 ml. acetic anhydride and 20 ml. acetic acid. To the solution, 0.1 mole

(1) For the preceding communication of this series, see *J. Org. Chem.*, **24**, 443 (1959).

(2) A. N. Sachanen, *The Chemical Constituents of Petroleum*, Reinhold Publishing Corp., New York, N. Y., 1945, p. 265.

(3) G. S. Windle, *Petroleum Refiner*, **23**, No. 2, 83 (1944).

(4) W. J. Pope and J. Read, *J. Chem. Soc.*, **101**, 758 (1912).

(5) R. Weissgerber, *Ber.*, **44**, 1436 (1911).

(6) 1-Chloroindane was synthesized according to Weissgerber[5] by the introduction of hydrogen chloride into cool indene. It was observed that at the low temperature, 1 mole of indene adsorbed about 2 moles of hydrogen chloride while the mixture turned red. (Details in Experimental.)

(7) E. Müller, *Methoden der organischen Chemie* (Houben-Weyl), G. Thieme Verlag, Stuttgart, W. Germany, 1955, Vol. 9, p. 120.

TABLE I

INDANYL SULFIDES, SULFOXIDES, AND SULFONES
'Indanyl-SO_x—R'

No.	-Indanyl	X	R	Formula	Yield,[a] %	M.P.[b]	B.P.[b] (2 mm.)	Calc. C	Calc. H	Calc. S
I	2	0	Phenyl	$C_{15}H_{14}S$	86	46–47	135–137	79.65	6.20	14.1
II[c]	1	0	Phenyl	$C_{15}H_{14}S$	67	...	127–128	79.65	6.20	14.1
III	2	0	4-Tolyl	$C_{16}H_{16}S$	90	86–86.5	140–142	80.00	6.67	13.3
IV[d]	1	0	4-Tolyl	$C_{16}H_{16}S$	69	...	135–136	80.00	6.67	13.3
V[e]	2	0	4-Chlorophenyl	$C_{15}H_{13}ClS$	89	90–91	...	69.08	5.02	12.3
VI	2	0	2-Naphthyl	$C_{19}H_{16}S$	91	99–100	...	82.61	5.79	11.6
VII[f]	2	0	*n*-Butyl	$C_{13}H_{18}S$	93	...	118–119	75.67	8.79	15.5
VIII	2	1	4-Tolyl	$C_{16}H_{16}OS$	89	107–108	...	75.00	6.25	12.5
IX[g]	2	1	4-Chlorophenyl	$C_{15}H_{13}OClS$	87	97–98	...	65.08	4.73	11.6
X	2	2	Phenyl	$C_{15}H_{14}O_2S$	91	107–108	...	68.77	5.46	12.4
XI	1	2	Phenyl	$C_{15}H_{14}O_2S$	84	105–106	...	68.77	5.46	12.4
XII	2	2	4-Tolyl	$C_{16}H_{16}O_2S$	94	134.5–135.5	...	70.59	5.88	11.8
XIII	1	2	4-Tolyl	$C_{16}H_{16}O_2S$	98	132–133	...	70.59	5.88	11.8
XIV[h]	2	2	4-Chlorophenyl	$C_{15}H_{13}O_2ClS$	95	137.5–138.5	...	61.53	4.47	10.9
XV	2	2	2-Naphthyl	$C_{19}H_{16}O_2S$	97	140–141	...	73.99	5.23	10.4
XVI	2	2	*n*-Butyl	$C_{13}H_{18}O_2S$	89	61–62	...	65.51	7.61	13.4

[a] Without the use of any catalyst. [b] Uncorrected. [c] n_D^{20} 1.6306. [d] n_D^{20} 1.6193. [e] Calcd.: Cl, 13.6. Found: Cl, 13.8. [f] n_D^{20} 1.5475. [g] Calcd.: Cl, 12.8. Found: Cl, 12.7. [h] Calcd.: Cl, 12.1. Found: Cl, 12.3.

of hydrogen peroxide was added in the form of an aqueous 30% solution. The reaction mixture was allowed to stand for 3 days at room temperature. After the oxidation was complete, the solution was diluted with water which precipitated the crude sulfoxide. The 2-indanyl sulfoxides obtained in this manner were purified by recrystallization from alcohol. The yields, physical and analytical properties of the compounds so obtained, are shown in Table I.

In another experiment, the addition of 12.4 g. (0.1 mole) of 4-toluenethiol to 11.6 g. (0.1 mole) of indene was followed by a mixture of *t*-butyl hydroperoxide (about 18 g., 0.2 mole) and di-*t*-butylperoxide (about 6 g.) prepared according to Milas and Surgenor.[8] After the addition of the peroxide, the reaction mixture was heated on a steam bath for 3 min., which caused gas evolution and color change. The heating was, therefore, discontinued, and the mixture was cooled to room temperature, where it was allowed to stand. After 3 days, the low boiling compounds (di-*t*-butylperoxide, *t*-butyl alcohol) were removed by distillation on a steam bath at 10 mm. Then the residue crystallized to a red mass, which after repeated recrystallizations from benzene–*n*-heptane and alcohol gave 12 g. (49.5%) colorless 2-indanyl-4-tolyl sulfoxide (m.p. 106.5–107.5°).

Synthesis of 2-indanyl aryl sulfones. An acetic anhydride–acetic acid solution of 0.1 mole of indanyl aryl sulfide and 0.2 mole of hydrogen peroxide, was heated on a water bath for 15 min. The reaction mixture was then diluted with water to precipitate the raw 2-indanyl aryl sulfone, which was purified by recrystallization from alcohol. The yields, physical and analytical properties of the compounds are tabulated.

The addition of n-butanethiol to indene. (a) *In the absence of peroxide catalyst.* A mixture of 11.6 g. (0.1 mole) of indene and 9 g. (0.1 mole) of *n*-butanethiol in a round-bottom flask was purged with nitrogen. Then the flask was closed, and the reaction mixture allowed to stand for 10 days. A mercaptan determination of the mixture, after 3 and 10 days, showed 75.7 and 68.1% of the original mercaptan concentration. After 10 days, the reaction mixture was fractionated *in vacuo*. After the removal of the unchanged *n*-butanethiol and indene, 6.1 g. (93% based on the amount of converted butanethiol) of indanyl butyl sulfide, b.p. 218–219° (2 mm.), n_D^{20} 1.5475, was obtained. Some further analytical data of the product are shown in Table I.

(8) N. A. Milas and D. M. Surgenor, *J. Am. Chem. Soc.*, **68**, 205 (1946).

(b) *In the presence of peroxide catalyst.* To the mixture of indene and *n*-butanethiol described in (a), 0.7 g. (0.005 mole) of cumene hydroperoxide was added. The resulting mixture became warm after 2 hr. standing. A mercaptan determination of the reaction mixture after 3 days showed 26.7% of the original mercaptan still present. A subsequent vacuum distillation yielded 13.5 g. (89% based on the amount of converted butanethiol) of indanyl butyl sulfide, b.p. 216–218° (1.9 mm.), n_D^{20} 1.5474. The infrared spectrum of this product was identical with the product obtained without any added peroxide catalyst under (a).

The peracetic acid oxidation of both sulfide products resulted in 2-indanyl *n*-butyl sulfone, m.p. 61–62°, in 89 and 87% yield, respectively. A mixed melting-point determination of the two products gave no depression. Their infrared spectra were identical. Some of the analytical data obtained are shown in Table I.

Synthesis of 1-chloroindane. Gaseous hydrogen chloride was introduced into 58 g. (0.5 mole) of cool indene; a method used by Weissgerber,[5] except that a Dry Ice–acetone mixture instead of salt-ice was used for cooling. The indene was cooled as low as possible without freezing it. During the introduction of the hydrogen chloride, the freezing point of the mixture decreased and finally a viscous red liquid resulted at −60° which had adsorbed about 36.5 g. (1 mole) of hydrogen chloride. This liquid, on coming to room temperature, released about 18.2 g. (0.5 mole) of hydrogen chloride and became almost colorless. On vacuum distillation, it yielded 68.7 g. (90%) 1-chloroindane, b.p. 103° (20 mm.). About 7.5 g. of viscous, orange liquid remained as a distillation residue.

Anal. Calcd. for C_9H_9Cl: Cl, 23.1. Found: Cl, 22.8.

Synthesis of 1-indanyl aryl sulfides. An aromatic thiol (0.1 mole), was dissolved in 1:1 benzene–isopropyl alcohol and allowed to react with 2.3 g. (0.1 mole) of sodium. To the resulting sodium thiophenolate was added 15.3 g. (0.1 mole) of 1-chloroindane in 50 ml. of benzene. The precipitation of sodium chloride from the reaction mixture started at room temperature. To complete the reaction, the mixture was refluxed for 6 hr. Then it was washed with water, 5% aqueous sodium hydroxide and water, dried, and distilled in vacuo. After the removal of benzene, the 1-indanyl aryl sulfides were obtained as colorless liquids. Some of the physical and analytical data of the products are shown in Table I.

Synthesis of 1-indanyl aryl sulfones. 1-Indanyl aryl sulfide (0.05 mole) was dissolved in a mixture of 30 ml. of acetic

TABLE I (*Continued*)

INDANYL SULFIDES, SULFOXIDES, AND SULFONES
'Indanyl-SO_x—R'

No.	Found C	Found H	Found S	Infrared Absorption Peaks (Microns)								
I	80.11	6.25	13.9	5.27	5.44	6.3	5.58			9.2	9.38	9.78
II[c]	79.18	6.24	14.0	5.22	5.33	6.3	5.53			9.2	9.38	9.78
III	80.72	6.67	13.3	5.27	5.46	6.25	5.60			9.18		9.84
IV[d]	79.56	7.02	13.4	5.25	5.55	6.25				9.18		9.84
V[e]	68.79	5.17	11.9	5.26	5.43	6.35				9.15		9.9
VI	83.23	5.89	11.2	5.24	5.43	6.15, 6.3	5.57			9.15		9.8
VII[f]	75.47	8.97	15.4	5.24	5.42	6.21, 6.27	5.57			9.13		9.76
VIII	74.89	6.34	12.8			6.25	7.68	7.87		9.25	9.75	9.9
IX[g]	64.64	4.83	11.4			6.3	7.6	7.85		9.2	9.7	9.9
X	69.01	5.83	11.8			6.3	7.65	7.8	8.75	9.23		9.8
XI	68.94	5.53	12.9			6.21, 6.28	7.65	7.75	8.85	9.25	9.79	10.01
XII	70.41	5.91	11.3			6.25	7.7		8.8	9.25		9.9
XIII	70.01	5.95	11.4									
XIV[h]	61.73	4.75	10.9			6.3	7.6	7.85	8.75	9.25		9.9
XV	74.08	5.51	9.7			6.15, 6.3	7.65	7.8	8.75	9.35		
XVI	65.73	7.69	12.8			6.21, 6.3	7.60	7.78	8.85	8.95		

anhydride and 10 ml. of acetic acid. Aqueous 30% hydrogen peroxide (11.4 g., 0.01 mole) was added to the sulfide solution at 5°. Then the reaction mixture was kept at that temperature for 24 hr., and at room temperature for an additional 48 hr. After the completion of the reaction, the crystalline 1-indanyl aryl sulfone was precipitated by careful addition of crushed ice. The crude crystalline product was filtered and twice recrystallized from 90% aqueous ethanol. The yields obtained and some of the physical and analytical data of the products obtained are shown in Table I.

When 1-indanyl aryl sulfides were oxidized with the same reagents on a water bath, a smaller yield of the sulfones was realized due to some decomposition.

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Carcinogenic Amine Derivatives Containing Nitrogen-15[1,2]

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Several carcinogens have been found to bind to the protein of tissues in which they cause cancer. Since some chemically related noncarcinogens have also been found to bind to protein, this interaction may well be a necessary but not sufficient requirement for the production of tumors.[3]

In order to study this further, the synthesis of three carcinogens labeled with nitrogen-15 was undertaken. These were 4-acetylaminobiphenyl-N^{15}, 4'-fluoro-4-acetylaminobiphenyl-N^{15}, and *N*-(7-hydroxy-2-fluorenyl)acetamide-N^{15}, a weakly carcinogenic metabolite of the strong carcinogen, *N*-2-fluorenylacetamide.

2-Nitrofluorene-N^{15} had been prepared previously in this laboratory[4] by nitrating fluorene with aqueous nitric acid-N^{15} using acetic anhydride to remove the excess water. No reaction occurred when this method was used with biphenyl. When the reaction was carried out in sulfuric acid solvent or when potassium nitrate-N^{15} and sulfuric acid were used as the source of nitric acid, the material either failed to react or was sulfonated. The only effective nitrating agent proved to be 100% nitric acid-N^{15}. The procedure used for nitrating the biphenyl derivatives was based on the method of Maki and Obayashi.[5] The desired *para* isomers were separated from the *ortho* isomers and unchanged hydrocarbon by trituration with hexane, in which the *para* isomers are not soluble. 2-Acetoxyfluorene was nitrated by a modification of the procedure described by Bryant and Sawicki.[6] The nitro compounds were reduced and acetylated by the usual methods as described in the Experimental section.

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(2) Presented before the Meeting-in-Miniature, Florida Section, American Chemical Society, St. Petersburg, Fla., May 8–9, 1959.

(3) For detailed discussion see E. K. Weisburger and J. H. Weisburger, *Advances in Cancer Research*, Vol. 5, J. P. Greenstein and A. Haddow, editors, Academic Press, Inc., New York, 1958, p. 382.

(4) M. F. Argus and F. E. Ray, *Cancer Research*, 11, 423 (1951).

(5) T. Maki and K. Obayashi, *J. Chem. Soc. Japan, Ind. Chem. Soc.*, 54, 375 (1951); *Chem. Abstr.*, 48, 2011 (1954).

(6) H. Bryant and E. Sawicki, *J. Org. Chem.*, 21, 1322 (1956).