Registry No.—IV, 32979-47-8; IV polymer, 33029-40-2; V, 32979-49-0; V polymer, 33029-41-3; 2,6-diphenyl-4-bromoanisole, 20104-39-6; 2,6-diphenyl-4-(2,6-dimethylphenoxy)anisole, 32979-46-7; 2,6-dimethyl-4-(2,6-diphenylphenoxy)anisole, 32979-48-9; copolymer of 2,6-dimethylphenol and 2,6-diphenylphenol, 26006-43-9.

Acknowledgment.—The authors are indebted to R. A. Kluge for assistance in the interpretation of the dsc and nmr results.

Nonstereospecific Oxidative Addition of Benzenethiol to Indene[1]

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The oxidative addition of benzenethiol to indene produces a mixture of three isomeric 2-phenylsulfinylindanols that contains 14–18% of the *cis*-hydroxy sulfoxide contrary to previous claims that this reaction leads stereospecifically only to trans addition products. The fourth isomeric 2-phenylsulfinylindanol (cis-syn) was prepared by the oxidation of the sulfide precursor. The examination of the concentration dependence of hydrogen bonding, of the nmr spectra, and of the relative yields permits the assignment of the configurations at the sulfur atom in all four isomers.

Results and Discussion

The four isomeric 2-phenylsulfinylindanols (trans-anti, trans-syn, cis-anti, and cis-syn)[4] have been described in the literature, but unfortunately the reports are inconsistent and incomplete. Thus, Ford and coworkers[5] claimed that direct cooxidation of indene and thiophenol produces only traces (0.25% maximum) of the cis products and described two trans isomers of mp 149.5-150.5 and 99°, respectively. The cis isomers were prepared in a roundabout fashion *via* 2-bromoindanone and were described as solids of mp 158 and 122–123°, respectively. Later Oswald[6] repeated the cooxidation reaction and reported the isolation of *three* isomeric hydroxy sulfoxides of this series of melting points 158–159, 148–150, and 132–135°, respectively. More recently, however, the same investigator[7] stated that only *trans*-2-phenylsulfinylindanols are produced, and the stereospecificity of this reaction has been assumed[8] in the consideration of the bridged nature of the intermediate olefin–thiyl radical adduct.[9] In view of this confusion, and also since "the relationship between the four isomers with respect to the orientation about the sulphur atom is not known,"[5] the cooxidation of indene and thiophenol was reinvestigated with care. The preparation of the cis isomers from 2-bromoindanone was also repeated.

Extensive application of thin layer chromatography (tlc) to the products of the cooxidation of indene and thiophenol showed that the reaction produced three isomers, namely two trans isomers of mp 158 and 101°, respectively, and a high-melting cis isomer (mp 158°). The relative yields of these three isomers were determined by careful column chromatography and by characterization of each fraction by tlc. Regardless of whether the cooxidation was carried out in benzene or hexane, the cis isomer of mp 158° was obtained in 14–18% yield[10] while the yields of the high- and low-melting trans isomers were 24–29 and 56–60%, respectively. In order to obtain information on the relative rates of formation of the three hydroxy sulfoxides during the cooxidation reaction, samples of the reaction mixture were subjected to tlc, and it was found that the cis isomer and the low-melting trans isomer were formed in approximately equal amounts during the early stage of the reaction, while the high-melting trans isomer did not begin to accumulate until later.

The missing cis hydroxy sulfoxide was synthesized in the manner previously described except that sodium borohydride, rather than lithium aluminum hydride, was used in the reduction of 2-phenylmercaptoindanone. It is of interest to note that while the latter reducing agent gave a ratio of hydroxy sulfides 4.6:1 in favor of the trans isomer, the use of the borohydride produced a 15:1 ratio in favor of the cis isomer. The difference in these results is due, in part, to the alkaline conditions of the sodium borohydride reduction, which are known[5] to bring about the decomposition of the *trans*-2-phenylmercaptoindanol. Thus, while the lithium aluminum hydride results are based on essentially quantitative yields of hydroxy sulfides, the total yield of hydroxy sulfides using sodium borohydride was only 33%. However, even if we assume that the loss of the missing hydroxy sulfide is due to the decomposition of the trans hydroxy sulfide, the ratio of trans:cis reduction products is only 2.2:1 in the case of the sodium borohydride. The fate of the *trans*-2-phenylmercaptoindanol during the alkaline decomposition was not ascertained by Ford and coworkers.[5] We have isolated essentially all of the missing phenylmercapto portion of the initial 2-

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[3] The Puerto Rico Nuclear Center is operated by the University of Puerto Rico for the U. S. Atomic Energy Commission under Contract AT-(40-1)-1833.

[4] The names, in accord with the nomenclature employed by Ghersetti and coworkers, *J. Chem. Soc.*, 3718 (1963), refer, in the first place, to the relative orientation of the hydroxyl and sulfoxide functions, and, secondly, to the orientation of the oxygen of the sulfoxide relative to the benzene ring of indan when the conformation of the sulfoxide group is such that its phenyl group points away from the indan ring.

[5] J. J. Ford, R. C. Pitkethly, and V. O. Young, *Tetrahedron*, **4**, 3251 (1958).

[6] A. Oswald, *J. Org. Chem.*, **26**, 842 (1961).

[7] A. A. Oswald and T. J. Wallace in "Organic Sulfur Compounds," Vol. 2, N. Kharasch and C. Y. Myers, Ed., Pergamon Press, Elmsford, N. Y., 1966, p 224.

[8] P. D. Readio and P. S. Skell, *J. Org. Chem.*, **31**, 759 (1966).

[9] P. S. Skell in "Organic Reaction Mechanism," Special Publication No. 19, The Chemical Society, London, 1965, p 143.

[10] H. H. Szmant and J. J. Rigau, *Tetrahedron Lett.*, 3337 (1967).

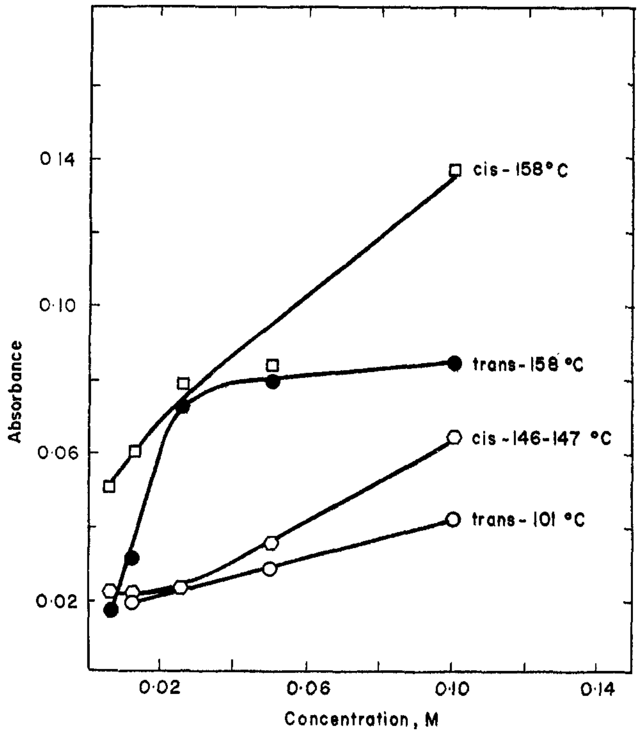


Figure 1.—*Absorbance of "bound" O–H as a function of dilution.*

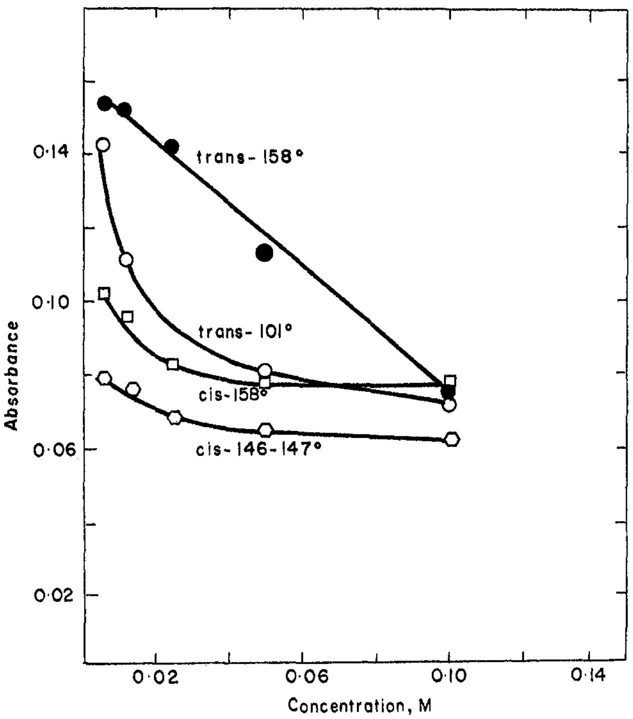


Figure 2.—Absorbance of "free" O–H as a function of dilution.

phenylmercaptoindanone as phenyl disulfide and the diphenyl thioacetal of 1-indanone.

The isomeric *cis*- and *trans*-2-phenylmercaptoindanols were also prepared by the Oswald modification of the oxidative addition of thiols to olefins in the presence of tertiary amines.[11]

The oxidation of *cis*-2-phenylmercaptoindanol with 30% hydrogen peroxide or *m*-chloroperbenzoic acid gave a mixture of two sulfoxides and the latter were separated by column chromatography (rather than by fractional crystallization employed by previous investigators) to give the missing isomer of mp 146° (and not 122–123°),[5] as well the isomer of mp 158° obtained in the cooxidation reaction. Similarly, *trans*-2-phenylmercaptoindanol was oxidized by *m*-chloroperbenzoic acid to the two sulfoxides of mp 158 and 101° also isolated from the cooxidation reaction, and as in the case of the latter, the low-melting isomer again predominated.

The cis or trans structure of each isomeric hydroxy sulfoxide was checked by conversion to the known[5] hydroxy sulfones. The identity of the *cis*- and *trans*-2-phenylsulfonylindanols was confirmed by means of their infrared spectra and the pronounced intramolecular hydrogen bonding[12] in the case of the first-mentioned isomer.

The assignment of the stereochemistry about the sulfur atom in each pair of isomeric hydroxy sulfoxides is based mainly on the concentration dependence of hydrogen bonding followed by infrared spectroscopy, and differences in the nmr spectra.

Hydrogen bond formation as a function of solute concentration was followed while the total number of solute molecules was maintained constant throughout a set of determinations. The concentration dependence of the absorption intensities of the "free" and "bound" hydroxyl bands is shown in Figures 1 and 2. The "free" hydroxyl band refers to the stretching frequency of the hydroxyl group when it is solvated by carbon tetrachloride or when it is subject to the weak interaction with the π system of indene.[11] The "bound" hydroxyl absorption refers, on the other hand, to the hydroxyl group that interacts rather strongly with the sulfoxide function and produces a large displacement (200–280 cm^{-1}) in the H–O stretching frequency. Examination of Figure 1 shows that the cis isomer of mp 158° is the only isomer that retains a relatively high absorbance with dilution, and, on this basis alone, we can assign to it the cis-anti structure that is conducive to intramolecular hydrogen bonding. This configurational assignment agrees with the fact that this is the only cis isomer obtained in the cooxidation reactions. It is known[13] that the hydroperoxide–sulfide is the intermediate in this reaction, and it stands to reason that its intramolecular disproportionation should give exclusively the cis-anti hydroxy sulfoxide. The configuration of the cis hydroxy sulfoxide of mp 158° finds additional support in the observation that the *m*-chloroperbenzoic acid oxidation of the cis hydroxy sulfide gives 80% of the high-melting sulfoxide and only 20% of the cis hydroxy sulfoxide of mp 146°. The stereoselectivity in the oxidation of sulfide to sulfoxide by peracids induced by the presence of a vicinal hydroxyl group was observed in the oxidation of thioxanthen-9-ol,[14] and is reminiscent of the induced stereoselectivity in epoxidation.[15]

Since in the course of the infrared examinations the number of solute molecules in the light path remains constant while their concentration is being changed, a horizontal plot in Figures 1 and 2 signifies that the given hydroxyl group absorption is unperturbed by changes in the opportunities for solute molecules to

(11) A. A. Oswald, F. Noel, and G. Fisk, *J. Org. Chem.*, **26**, 3974 (1961).

(12) H. H. Szmant and J. J. Rigau, *ibid.*, **31**, 2288 (1966).

(13) A. A. Oswald, *ibid.*, **24**, 443 (1959).

(14) A. L. Ternay, Jr., D. W. Chasar, and M. Sax, *ibid.*, **32**, 2465 (1967).

(15) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, p 115.

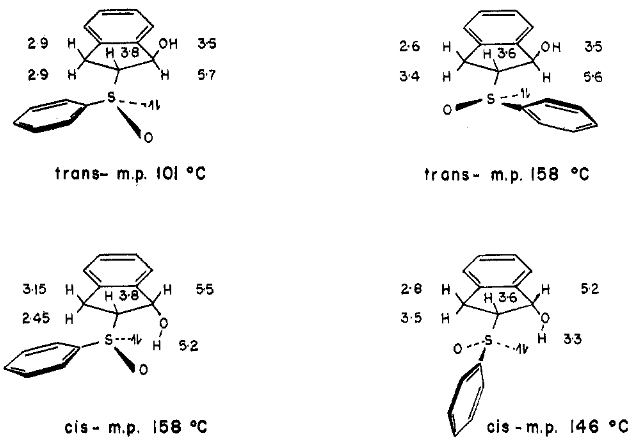
associate. The positive slope of the "bound" hydroxyl absorption plots given by three isomers (Figure 1) indicates that the increasing concentration induces the formation of hydrogen-bonded aggregates. The rise in the effective absorption is expected in view of the recognized[16] greater absorption intensity of intermolecular hydrogen bonds as compared to that of intramolecular hydrogen bonds, and especially that of the "free" hydroxyl band. The steep initial slope followed by the nearly horizontal plot given by the trans isomer of mp 158° reveals that this substance is prone to give polymeric, hydrogen-bonded aggregates, and that even at the low concentration of 0.02 *M* the association has progressed very far. Such a behavior can be expected of the trans-syn isomer, since this structure is most favorable for the formation of chainlike aggregates. The "free" hydroxyl plots shown in Figure 2 are consistent with the above conclusions. The leveling of the decrease in the "free" hydroxyl absorption reflects a relative reluctance to association in all the isomers except the last mentioned high-melting trans compound. The latter seems to form chainlike aggregates in a constant fashion over the range of concentrations investigated here. However, while the "free" hydroxyl absorption disappears regularly, the increase in the "bound" hydroxyl absorption cannot quite keep up and this discrepancy can be explained by the weakening of the absorptivity of hydrogen bonds in the larger chain aggregates.

The greater tendency of the higher-melting trans isomer to associate, and hence the likelihood of its trans-syn structure, is clearly demonstrated by the larger apparent molecular weight as compared to that of the lower-melting trans isomer under equivalent conditions (see Experimental Section), and also its lower solubility in solvents that are poor acceptors in hydrogen bonding.

The nmr spectra of the four isomers provide further evidence in favor of the structural assignments discussed so far. The chemical shifts (δ TMS) in deuteriochloroform are given together with the assigned preferred conformations in Figure 3.

As expected, the cis isomer of *mp* 158° exhibits an exceptional chemical shift for the hydroxylic proton in accord with the intramolecularly hydrogen bonded cis-anti structure. This hydrogen bond forces the sulfoxide phenyl group into the proximity of the methylene group of the indan ring with the consequent large shielding of one of its protons. In the low-melting cis-syn isomer, on the other hand, one of the methylenic protons is deshielded by the sulfoxide oxygen while the hydroxylic proton is shielded by the nonbonding sulfur electrons.

The low-melting trans isomer, in accord with the assigned anti configuration, shows a deshielded proton at C-1 indicative of the proximity of the sulfoxide oxygen. The equivalence of the methylenic protons indicates that the preferred conformation of the sulfoxide group allows the phenyl group to rotate freely while pointing away from the indane ring. In the high-melting trans-syn isomer, on the other hand, the sulfoxide oxygen deshields one of the methylenic protons, and the fact that the proton C-1 is not affected by the sulfoxide phenyl group indicates that the preferred conformation again allows the phenyl group to rotate freely while pointing away from the indan ring.



trans- m.p. 101 °C

trans- m.p. 158 °C

cis- m.p. 158 °C

cis-m.p. 146 °C

Figure 3.—Proposed structures and nmr assignments of isomeric 2-phenylsulfinyl-1-indanols (δ from TMS in $CDCl_3$).

The isolation of *ca.* 14% of cis product in the cooxidation of thiophenol and indene reveals that, while not stereospecific, the reaction is still stereoselective. The relevance of this observation to the question of classical *vs.* bridged sulfur-containing radicals has been touched upon elsewhere[10] and will be dealt with in greater detail in future publications.

Experimental Section[17]

Cooxidation of Indene and Thiophenol.—Freshly distilled (under oxygen-free atmosphere) indene, 5.32 ml, and thiophenol, 4.53 ml, were dissolved in 150 ml of hexane and the solution was stirred in a constant-temperature bath maintained at 25°. The flask was connected to a gas burette that could be conveniently refilled from an oxygen reservoir. A rapid rate of oxygen absorption over the first 10 min was followed by a slower absorption over the next 80 min. The reaction mixture was stirred under oxygen for 24 hr to ensure the absorption of the calculated 1100 ml of oxygen, and then was allowed to stand for 6 days. A precipitate first appeared at the end of the initial 10-min period and accumulated gradually as the reaction mixture rested. Filtration yielded 9.647 g of white solid and evaporation of the filtrate produced 2.465 g of viscous oil.

An essentially quantitative separation of the constituents present in the solid cooxidation product was achieved by using a 3.25 ft × 1 in. column containing 290 g of Baker's chromatographic grade silica gel per 1.000 g of product. The eluent was anhydrous ethyl acetate and there were separated 33 fractions ranging in volume from 30 to 300 cc in accordance with information procured by simultaneous tlc of each fraction as it was eluted from the column.

The tlc technique employed 8 × 8 in. plates covered with silica gel (grade G supplied by E. Merck, Darmstadt), and activated overnight at 125°. The plates were eluted[18] with anhydrous ethyl ether (45 min) and developed in an iodine atmosphere.[19]

The results of the separation using a 1.000-g portion of the solid reaction product are shown in Table I.

The analogous cooxidation experiment in 150 ml of benzene gave a nearly complete absorption of oxygen in 90 min at a rapid and essentially uniform rate. The reaction mixture was allowed to rest for 6 days, but filtration yielded only 2.60 g of solid. Evaporation of the filtrate gave an additional 9.51 g of product. The products were combined by dissolving in chloroform, and an aliquot representing 1.50 g of the combined products was sub-

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[16] G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman, San Francisco, Calif., 1960, pp 95, 101, 170, 197.

[17] Microanalyses by Dr. Alfred Bernhardt, Mülheim, Ruhr, Germany. Melting points were determined in a Mel-Temp apparatus and are otherwise uncorrected.

[18] M. Brenner, A. Niedermieser, G. Pataki, and A. R. Fahmy, *Experientia*, **18**, 101 (1962).

[19] G. C. Barrett, *Nature (London)*, **194**, 1171 (1962).

TABLE I

Fraction	Solid, g[a]	Isomer (mp, °C)	R_f	Analysis found[b] C	H	S
10–13	0.267	trans (158)	0.26	69.88	5.46	12.31
14–23	0.511	trans (101)	0.17	69.92	5.53	12.27
28–32	0.130	cis (158)	0.08	69.84	5.52	12.49

[a] The remaining 0.092 g was subjected to infrared examination and found to exhibit absorption bands typical of ketones, sulfides, and sulfoxides. [b] Calcd: C, 69.77; H, 5.46; S, 12.40.

jected to chromatographic separation, as described above. A total of 1.012 g of solids was isolated consisting of 0.244 g of the trans isomer, mp 158° (fractions 11–14), 0.610 g of the trans isomer, mp 101° (fractions 15–20), and 0.158 g of the cis isomer, mp 158° (*fraction* 24).

The cooxidation was also repeated using only 50 ml of benzene as solvent. The relative yields of the products as a function of the solvent and solvent concentration are tabulated in Table II.

TABLE II

	Yields (in g)[a] of chromatographically pure *fractions as function of solvent in cooxidation* experiments		
2-Phenylsulfinylindanol (mp, °C)	Hexane, 150 ml	Benzene 150 ml	Benzene 50 ml
Trans (158)	0.213	0.163	0.190
Trans (101)	0.407	0.407	0.408
Cis (158)	0.103	0.105	0.134
Total	0.723	0.675	0.732

[a] On the basis of 1.000 g of crude solid reaction product.

While all three cooxidation conditions also gave rise to the formation of some *trans*-2-phenylmercapto-1-indanol, the last-mentioned experiment produced a remarkably high yield of the hydroxy sulfide, namely 0.211 g per 1.000 g of crude reaction product. This material was identical with the sample prepared by the reduction of the corresponding ketone (see below).

An additional cooxidation experiment was carried out using 300 ml of benzene as solvent in order to prevent precipitation of solid products and to decrease the rate of reaction. Small samples of the reaction mixture were subjected to tlc at intervals of 3–5 min. After a reaction time of 15 min, spots corresponding to the trans isomer of mp 101° and to the cis isomer of mp 158° began to appear, and the intensity of these spots seemed to increase at about the same rate. The spot that corresponds to the trans isomer of mp 158° did not appear until approximately 90 min from the start of the reaction.

Reduction of 2-Phenylmercaptoindanone.—A solution of 2.5 g of sodium borohydride in water containing 0.2% of sodium hydroxide (44% borohydride concentration) was added in small portions to a solution of 34 g of 2-phenylmercaptoindanone[5] in 100 ml of isopropyl alcohol while the temperature was maintained at 35–45°. The reaction mixture was stirred for 2 days in an inert atmosphere and then was extracted with benzene to give 27.4 g of solid product. The insoluble residue was decomposed with 5 *N* hydrochloric acid and extraction with benzene yielded an additional 2.65 g of product. The combined solid products were separated by chromatography using a silica gel column and the eluents ligroin, benzene, and chloroform, in that order. There were isolated 8.55 g of diphenyl disulfide (identified by melting point and microanalysis), 7.70 g of solid, mp 76–77°, identified tentatively as the diphenyl thioacetal of 1-indanone on the basis of its infrared spectrum and analysis (Calcd: C, 75.40; H, 5.42; S, 19.17. Found: C, 74.74; H, 5.47; S, 19.73), 0.8 g of unidentified oil, 1.30 g of impure cis hydroxy sulfide, 9.23 g of analytically pure cis hydroxy sulfide, mp 71–75°, and 0.73 g of analytically pure trans hydroxy sulfide, mp 101°.

Cooxidation of Indene and Thiophenol in the Presence of Triethylamine.—A solution of 37.46 g (0.34 mol) of thiophenol, 12.78 g (0.11 mol) of indene, and 0.01 mol of triethylamine (previously dried over phosphorus pentoxide for 2 min) was oxygenated for 6 hr at room temperature. The reaction mixture was extracted three times with 100-ml portions of 5% potassium hydroxide, washed with water, dried over magnesium sulfate, and concentrated under reduced pressure to give 32.30 g of product. Tlc on silica and using chloroform showed the presence of three components. A 10.200-g portion of the product was chromatographed on silica and 100-ml fractions of eluent were collected. The first ten fractions (benzene) and the following three fractions (chloroform) gave 5.228 g of pure diphenyl disulfide. Fractions 14–16 (chloroform) gave 0.311 g of *cis*-2-phenylmercaptoindanol. Fractions 17–24 (chloroform) gave 3.703 g of a mixture of trans and cis isomers, while fractions 25–28 (chloroform) gave 0.616 g of pure trans-2-phenylmercaptoindanol for a recovery of 9.858 g (96.6%) of sample subjected to column chromatography. The mixture of trans and cis isomers, 2.874 g, was subjected to a new chromatographic separation to give 0.153 and 1.001 g of pure cis and *trans* isomers, respectively, while 1.470 g was still recovered as a mixture.

Preparation of the Isomeric *cis*-2-Phenylsulfinylindanols.—The oxidation of *cis*-2-phenylmercaptoindanol was repeated as described in the literature[4] except that the products were separated by chromatography as described for the separation of the products of cooxidation. The two isomers were obtained in approximately equal amounts, and the higher-melting compound, mp 158°, was identical with the corresponding product isolated from the cooxidation reaction. The lower melting isomer, mp 146–147°, gave a R_f value of 0.17 (conditions described above), and gave correct analytical results (*Anal.* Calcd: C, 69.74; H, 5.46; S, 12.39. Found: C, 69.80; H, 5.34; S, 12.28). Both isomers were converted quantitatively to the identical sulfone,[4] mp 130–131°.

Oxidation of 2-Phenylmercaptoindanols with *m*-Chloroperbenzoic Acid.—A solution of 0.155 g (0.9 mmol) of *m*-chloroperbenzoic acid in 15 ml of methylene chloride was added dropwise to a stirred solution of 0.242 g (1 mmol) of the trans hydroxy sulfide in 10 ml of methylene chloride at 0°. After 12 hr the reaction mixture was filtered and the filtrate was washed with three 25-ml portions of aqueous sodium bicarbonate, dried over magnesium sulfate, and evaporated to give 0.192 g of product. The product was chromatographed (silica, ethyl acetate) to give 74.5 mg of unreacted hydroxy sulfide, and 35 and 67 mg of the *trans*-2-phenylsulfinylindanols of mp 158 and 101°, respectively.

An analogous experiment using 38 mg of *m*-chloroperbenzoic acid and 60 mg of cis hydroxy sulfide gave 23 mg of unreacted sulfide, and 2.4 and 9.6 mg of *cis*-2-phenylsulfinylindanols, mp 146 and 158°, respectively.

Determination of Infrared Spectra.—The spectra were determined by means of a Perkin-Elmer Model 237 spectrophotometer operating in a constant-temperature room. For the determination of the absorbance–concentration dependence, a variable thickness liquid absorption cell was employed, and special care was exercised to minimize changes in temperature during a given set of determinations. Limited solubility of the compounds required the use of dichloromethane (spectroquality) as the solvent, and did not permit the preparation of solutions of higher than 0.10 molar concentration (except in the case of the low-melting trans isomer where a 0.2 molar concentration could be attained). Starting with a 0.10 *M* solution and a 0.200 mm cell path, the dilution of the solutions and increase in the cell paths was carried out gradually until a solution of 0.00625 *M* was examined in the cell of 3.2 mm path length. The absorbances of the "free" and "bound" O–H stretching frequencies were determined at 3600 and 3350 cm^{-1}, respectively, and no significant changes in the positions of these bands were noticed as the concentration was varied. The results are shown in Figures 1 and 2 in which the absorbance of the "free" and "bound" O–H stretching frequencies is plotted as a function of concentration.

Nuclear Magnetic Resonance Spectra.—The nmr spectra were determined by the Spectroscopy Application Laboratories of Varian Associates at 60 Mcps using deuteriochloroform as a solvent. The assignments of some of the bands were checked by using a 100-Mcps spectrometer and pyridine as the solvent. The chemical shifts are shown in Figure 3.

Apparent Molecular Weight Determination.—The determination of apparent molecular weights by cryoscopy in benzene failed due to the limited solubility of the 2-phenylsulfinylindanols. Ebulliometric measurements were carried out in the case of the two trans isomers using benzene and a modified Cottrell apparatus. The trans isomer of mp 158° gave an apparent molecular weight of 363 at a molality of 0.0604, while the lower melting trans isomer showed an apparent molecular weight of only 269–311 at the higher molality of 0.0691–0.1159.

Registry No.—Benzenethiol, 108-98-5; indene, 95-13-6; trans,[20] mp 101°, 32819-87-7; trans,[20] mp 158°, 32819-88-8; cis,[20] mp 158°, 32819-85-5; cis,[20] mp 146°, 32785-03-8; diphenyl thioacetal of 1-indanone, 32819-86-6.

[20] See Figure 3.

α Anions of Carboxylic Acids. II. The Formation and Alkylation of α-Metalated Aliphatic Acids

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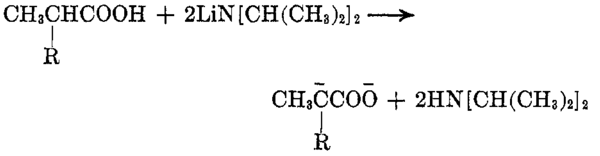
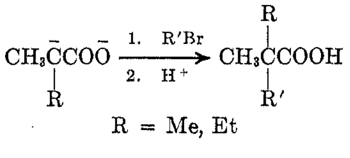
The degree to which α anions of straight chain and α-branched chain carboxylic acids are formed by reaction with lithium diisopropylamide in solutions of tetrahydrofuran (THF) and tetrahydrofuran containing hexamethylphosphoramide (HMPA) was established by deuteration and carbonation. The determinations indicate the extent of the metalations of straight and α-branched chain acids to be unaffected by HMPA. Straight chain acids are converted to α anions to the extent of 95% in either solvent system. HMPA assists the carbanion reactions by solubilizing insoluble dianions of straight chain acids and by accelerating their rate of alkylation in producing nearly quantitative yields of the α-branched acids. α-Branched chain acids are α metalated in both solvent media to the extent of 30–45% at −5 to 25° and to about 93% at 50°. The dianions of α-branched acids are soluble in THF without HMPA but the presence of HMPA is deleterious for these alkylations by inducing the elimination reaction between alkyl halide and the bases (unreacted amide and dianion). A steric effect in branched dianions increases olefin formation with increasing size of the alkyl substituents at the expense of alkylation. High conversions of α-branched acids to dianions are obtained in THF at 50°. The dianions alkylate to trialkylacetic acids in yields exceeding 90%. α lithiation of sodium and potassium alkanoates is less satisfactory, but alkylation of the dianions proceeds to high yields of α-branched acids. Carbonation and deuteration of α-lithiocarboxylates are recommended as a preparative synthesis of α-alkylmalonic acids and α-deuterioalkanoic acids, respectively. Monoolefinic acids containing isolated double bonds (oleic and undecylenic acids) α alkylate normally, but the more reactive double bonds in linoleic acid are altered by the strong base to produce a complex mixture of alkylated acids.

The direct introduction of a substituent into the α-carbon position in fatty acids has been limited to a few reactions, namely ionic halogenation,[2] sulfonation,[2] and free-radical substitution reactions.[3,4] An extensive series of classical, indirect reactions generally use the displacement of a facile leaving group at the 2 position, but these reactions require the initial introduction of the displaceable substituent at the designated site. Carbanions are highly reactive species that should provide the countervailing method for accomplishing α substitutions of fatty acids directly and propitiously. The unique opportunities α carbanions offer to derivatizations of fatty acids has not been exploited owing to the lack of adequate methods for generating this species.

Several groups of investigators have formerly undertaken the preparation of dianions of small chain carboxylic acids with limited success. In 1938, Morton, Fallwell, and Palmer[5] first demonstrated the intermediate formation of the α anion of sodium phenylacetate and sodium hexanoate using phenylsodium as the base for the abstraction of α-methylene protons. The presence of α anions as the reactive intermediates was demonstrated by carbonation that yielded phenylmalonic acid (60%) and butylmalonic acid (17%), respectively. Subsequently, other investigators have α metalated sodium phenylacetate with sodium (potassium) amide in liquid ammonia[6] and sodium acetate with sodamide at 200°.[7] The latter reaction was unsuitable in its application to propionic, *n*-butyric, and isobutyric acids.[7] Some of the preparative difficulties in these metalations were finally surmounted by Creger[8] who prepared α anions of isobutyric and 2-methylbutyric acids by means of lithium diisopropylamide in tetrahydrofuran (THF)–hexane (heptane) solution (eq 1). A single-step, high-yield synthesis



$$\mathrm{CH_3\underset{R}{C}HCOOH} + 2\mathrm{LiN[CH(CH_3)_2]_2} \longrightarrow \mathrm{CH_3\underset{R}{\bar{C}}CO\bar{O}} + 2\mathrm{HN[CH(CH_3)_2]_2} \quad (1)$$



$$\mathrm{CH_3\underset{R}{\bar{C}}CO\bar{O}} \xrightarrow[2.\ \mathrm{H^+}]{1.\ \mathrm{R'Br}} \mathrm{CH_3\overset{R}{\underset{R'}{C}}COOH} \quad (2)$$

$\mathrm{R = Me, Et}$

of trialkylacetic acids by α alkylation of the dianions (eq 2) provided Creger with an elegant demonstration of the utility of his method.

In our preliminary publication[9] we reported the limitations of Creger's method in its application to straight chain and α-branched chain carboxylic acids from which low yields (30–60%) of dialkyl and trialkyl acetic acids, respectively, were obtained. The metalated straight-chain acids were insoluble in THF, but readily dissolved by the addition of the highly dipolar

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