tion measurement indicates that these conditions lead to much more racemization than those of Nayak and Dev.[12]

Experimental

ω-Acetyllongifolene (Ib).—To 25 ml. of acetic anhydride and 31 ml. of boron trifluoride etherate, cooled and stirred in an ice bath, was added 10.2 g. of longifolene[13] during 5 min. The mixture slowly darkened and became almost homogeneous after an additional 5 min. at 0°. It was then added slowly to a mixture of ice and concentrated aqueous potassium hydroxide. This alkaline mixture was stirred as it warmed to room temperature. After 45 min. ether was added, the resultant emulsion was filtered from inorganic material and separated, and the aqueous phase was extracted with additional ether portions. In this way 12.0 g. of amber oil was obtained from the ether extract.

A rough separation of products was accomplished by chromatography on a column of 100 g. of silica gel to give: 3.07 g. of isolongifolene (infrared evidence) eluted with petroleum ether (b.p. 30–60°), 6.17 g. of crude Ib in the petroleum ether–ether (9:1 and 8:2) fractions, and about 1.5 g. of unidentified material in the petroleum ether–ether (7:3 and 6:4) eluates. Careful rechromatography of crude Ib on silica gel yielded 3.87 g. of product in fractions eluted with petroleum ether–ether (95:5) whose ultraviolet absorption maximum showed an $E\%$ in excess of 500.

The analytical sample was prepared from the semicarbazone (see below) by hydrolysis with 70% acetic acid at reflux for 22 hr., chromatography on silica gel, and evaporative distillation in a short-path still at 155° (20 mm.).

Anal. Calcd. for $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 83.17; H, 10.63.

This material was a single component on silica gel chromatoplates (R_f 0.63 in cyclohexane–ethyl acetate, 8:2, spotted with H_2SO_4). Vapor phase chromatography (2% SE-30, temperature 170°, retention time 21.5–23 min.) also showed this product to be a single component. Other data obtained on the analytical sample or material of comparable purity are as follows: λ_{max} 256 mμ (ε 15,000) (95% ethanol); λ_{max}^{neat} 5.95 and 6.19 μ (nearly equal intensities); the n.m.r. (Varian A-60 spectrometer) showed three sharp singlets at τ 9.00, 9.06, and 9.11 for the tertiary methyl groups (τ 9.01, 9.06, and 9.10 in longifolene), a three-proton singlet at τ 7.82 for the acetyl methyl, and a one-proton singlet at τ 4.13 for the vinylic proton, in deuteriochloroform; $[\alpha]D$ +52.2° ($CHCl_3$); circular dichroism $\Delta\epsilon_{332-328} = -0.17$ in dioxane.

Semicarbazone of ω-Acetyllongifolene.—To 1.0 g. of once-chromatographed Ib in 10 ml. of 95% ethanol was added 700 mg. of semicarbazide hydrochloride dissolved in 3 ml. of water to which 10 ml. of 95% ethanol had been added. After gentle warming for 15 min. and storage in an ice chest overnight, 630 mg. of crystals, m.p. 202–206° dec., was collected. Several recrystallizations from 95% ethanol yielded a sample: m.p. 203–206° dec.[14]; λ_{max} 272 mμ (ε 21,300); λ_{max}^{KBr} 2.90, 3.15, 5.89, 6.08 (weak), and 6.32 μ. The n.m.r. showed a three-proton singlet at τ 8.05 (CH_3CO) and a one-proton singlet at τ 4.47 (vinyl H), as well as the expected tertiary methyl groups at τ 9.0–9.1 in deuteriochloroform.

Anal. Calcd. for $C_{18}H_{29}N_3O$: C, 71.24; H, 9.63; N, 13.85. Found: C, 71.09; H, 9.68; N, 14.29.

ω-Carboxylongifolene (Ic).—To 125 mg. of Ib in 8 ml. of methanol was added 2.0 ml. of 1.53 M sodium hypochlorite solution. After an initial exothermic reaction the mixture was refluxed on a steam bath for 15 hr. It was cooled, water was added, and the mixture was extracted with ether. The ether extract was washed with aqueous sodium thiosulfate, dried, and concentrated to give 52 mg. of neutral product as an oil.

From the ether extract of the acidified initial aqueous phase 25 mg. of crystalline acid product was obtained. Recrystallization from ether–petroleum ether and then from 95% ethanol gave pure Ic, m.p. 223–224° (subliming slowly above 210°). This product was proved to be the same as ω-carboxylongifolene[11] by the identity of infrared spectra in chloroform and n.m.r. spectra in deuteriochloroform.

(13) We thank Dr. E. Klein (Dragoco, Holzminden) for the gift of longifolene used in this study.

(14) All melting points were taken on a Kofler micro hot stage.

The neutral product after chromatography on silica gel appeared to be ω-carbomethoxylongifolene (Id),[15] as evidenced by spectral data: λ_{max} 235 mμ, $E\%$ 528 (95% ethanol); methyl ester protons at τ 6.30 and a vinyl proton at τ 4.50. However, the optical rotation, $[\alpha]D$ +44.6° ($CHCl_3$), is quite different from that reported,[7] $[\alpha]D$ +104° (neat), for this compound by Dev and co-workers. There is, of course, the possibility of *cis–trans* mixtures.

Isolongifolene.—To 1.0 g. of longifolene in 5 ml. of sodium-dried ether was added 3 ml. of boron trifluoride etherate and the mixture was refluxed for 1 hr. on the steam bath. The resultant dark brown mixture was added cautiously to excess potassium hydroxide and ice. The mixture was stirred at room temperature for 1.5 hr., at the end of which time the ether phase became straw yellow in color. Separation, further extraction, water wash, and evaporation of ether left 980 mg. of light yellow oil. This material was essentially identical with authentic isolongifolene by infrared comparison, and vapor phase chromatography showed it to be about 90% pure isolongifolene. When this oil was passed through a column of 40 g. of silica gel the eluate contained 689 mg. of isolongifolene as a colorless oil, $[\alpha]D$ −14.9° (*c* 1.39, $CHCl_3$), in the first fraction and 143 mg., $[\alpha]D$ −3.9° (*c* 0.76, $CHCl_3$), in the second fraction.[12]

(15) We have been unable to find a precedent for this unusual esterification reaction in the presence of sodium hypochlorite.

N-Acylation of Cysteine

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Inconsistent yields and complex procedures characterize the indirect preparation[1-3] of N-acetyl-L-cysteine from L-cystine. Acetylation of two mercapto starting materials, L-cysteine ester[4] and anilide,[5] with acetic anhydride gave N,S-diacetyl derivatives. By acylating cysteine with acyl halides, good yields of S-acylated cysteines[6,7] and unspecified yields of N-acylated derivatives[8] were obtained.

We have prepared N-acetyl-L-cysteine in 65–80% yields directly from L-cysteine using 1 equiv. of acetic anhydride and a variety of acid acceptors in aqueous tetrahydrofuran. N-Propionyl and N-succinoyl derivatives were obtained in yields of 61 and 22%, respectively, by this simple, direct method.

Experimental[9]

N-Acetyl-L-cysteine.—A suspension of 35.2 g. (0.2 mole) of L-cysteine hydrochloride monohydrate in 87 ml. of 91% aqueous tetrahydrofuran (THF) was stirred under nitrogen at room temperature and treated with 54.4 g. (0.4 mole) of sodium acetate trihydrate. The sodium acetate addition lowered the internal temperature to 9° and produced a curdy mass. After

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(9) All melting points are uncorrected. The infrared spectra of all the described compounds were consistent with the assigned structures. We wish to thank Dr. Donald L. Timma and associates of these laboratories for the analytical and physical data. The sulfhydryl determination was performed potentiometrically with mercuric chloride using a gold indicating electrode [R. Cecil, *Biochim. Biophys. Acta*, **18**, 154 (1955)].

stirring for 20 min. at 9–15°, the mixture was cooled to 3–6° and treated, dropwise, with 20 ml. (20.8 g., 0.21 mole) of acetic anhydride. The resulting mobile suspension was stirred for 6 hr. at room temperature, allowed to stand overnight, and finally heated under reflux for 4 hr. Hydrogen chloride gas (8 g.) was then bubbled into the cooled reaction mixture at 5–10° to liberate the N-acetyl-L-cysteine from its sodium salt. The thick suspension was made mobile by the addition of THF and filtered to remove sodium chloride. The product was isolated by carefully concentrating the filtrate under reduced pressure at 40–50° and crystallizing the residual oil from 35 ml. of warm (45–50°) water: yield, 26.3 g. (80.6%) of white solid in two crops; m.p. 109–110°; pK_a = 3.2; $[\alpha]^{25}D$ +21.64° (*c* 5, dilute NaOH, pH 7), +4.07° (*c* 2.7, water); lit.[2] $[\alpha]^{21}_{546}$ +6.3° (*c* 2.7, water).

Anal. Calcd. for $C_5H_9NO_3S$: C, 36.80; H, 5.56; N, 8.58; SH, 20.2. Found: C, 36.78; H, 5.72; N, 8.54; SH, 19.9.

Yields of 65–77% were obtained when sodium hydroxide, ammonium hydroxide, or tribasic sodium phosphate was used as the acid acceptor in place of sodium acetate. The substitution of other reaction solvents for THF gave the following yields: methanol, 70%; 2-propanol, 78%; and water, 66%. Acetylation of L-cysteine base under anhydrous conditions in methanol, using 1 equiv. of sodium methoxide as the acid acceptor, gave a 67% yield.

When the above reaction was carried out with 2 equiv. of acetic anhydride, N,S-diacetyl-L-cysteine[10] was obtained in 34% yield.

N-Succinoyl-L-cysteine.—The use of 20 g. (0.2 mole) of succinic anhydride gave an oily product which was slurried with 150 ml. of anhydrous ether to yield 41.6 g. of crude solid, m.p. 131–132°. Two recrystallizations from water gave 9.7 g. (22%) of white solid, m.p. 141–142°, $[\alpha]^{25}D$ +4.5° (*c* 3, water).

Anal. Calcd. for $C_7H_{11}NO_5S$: C, 38.00; H, 5.01; N, 6.33; SH, 14.9. Found: C, 38.38; H, 5.08; N, 6.03; SH, 14.6.

N-Propionyl-L-cysteine.[8]—Propionic anhydride (26.4 g., 0.202 mole) was added slowly at 0–5° to a stirred suspension (under nitrogen) of 35.2 g. (0.2 mole) of L-cysteine hydrochloride monohydrate, 38.4 g. (0.4 mole) of sodium propionate, and 98 ml. of 80% aqueous THF. The reaction mixture was treated as described above, except that liberation of product was achieved by the slow addition of concentrated hydrochloric acid (18 ml.): yield, 21.7 g. (61%); m.p. 89–90°; $[\alpha]^{25}D$ +24.3° (*c* 5, dilute NaOH, pH 7).

Anal. Calcd. for $C_6H_{11}NO_3S$: C, 40.67; H, 6.26; N, 7.90; SH, 18.6. Found: C, 40.77; H, 6.24; N, 7.69; SH, 18.6.

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An Unusual Formation of a Benzothiophene Derivative

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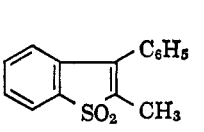
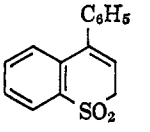
The cycloisomerization of allylbenzenes to hydrindenes is a well-known reaction; it is catalyzed by acids. In an attempt to use propenyl- instead of the isomeric allylbenzenes, the reaction of 1,1-diphenylpropene ($C_{15}H_{14}$) with sulfuric acid has been studied. It gave a well-crystallized product of the formula $C_{15}H_{12}O_2S$, which obviously arises from the reaction $C_{15}H_{14} + H_2SO_4 \rightarrow C_{15}H_{12}O_2S + 2H_2O$. The new compound contains a double bond, as hydrogenation gives the equally well-defined $C_{15}H_{14}O_2S$ and the infrared spectrum (KBr pellet) indicated the presence of a sulfone group; the peaks at 1300, 1176, and 1152 cm.$^{-1}$ correspond to the known infrared spectra of sulfones.[1] The ultraviolet spectrum shows a strong bathochromic shift in comparison with the starting material. It resembles somewhat that of indene: $C_{15}H_{12}O_2S$, 228 mμ (log ε 4.54), 254 (3.79, infl.), and 312 (3.38) (in ethanol); 1,1-diphenylpropene,[2] 235 mμ (log ε 3.87) and 248 (3.94) (in ethanol); indene,[3] 249 mμ (log ε 3.97) 279 (2.72), 285 (2.48), and 290 (2.26) (in ethanol).

These data establish for the compound $C_{15}H_{12}SO_2$ one of two possible formulas (I or II).

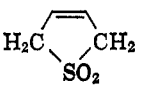


I

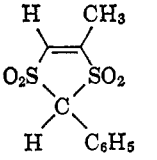


II

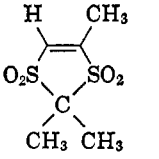
The choice between them has been based on the n.m.r. spectrum which consists of a very sharp signal at τ = 8.0 p.p.m. and a broad multiplet between τ = 2.35 and 3.1 p.p.m. The ratio of the two maxima is 2–3:9–10. Obviously, there is no vinyl hydrogen in the molecule (which would give a signal at about τ = 4.0 p.p.m.), and the comparison with the following examples indicates that the substance contains a methyl and not a methylene next to the sulfone group. The signal at



τ 6.26[4]



doublet at τ 7.62, 7.66[5]



doublet at τ 7.66, 7.70[5]

τ = 8 p.p.m. corresponds to the methyl, that at τ = 2.35–3.1 p.p.m. to the aromatic hydrogen atoms. Formula I of 2-methyl-3-phenyl-benzothiophene 1,1-dioxide is thus correct.

The n.m.r. spectrum of the dihydro derivative confirms these conclusions. It is composed of a doublet at τ = 9.15 p.p.m. (3 methyl protons), a quartet at τ = 6.62 p.p.m. (one proton at C-2), a doublet at τ = 5.91 p.p.m. (one proton at C-3), and a multiplet at τ = 2.3–3.4 p.p.m. (representing the nine protons of the aromatic rings).

Compound I is equally well obtained from ethyldiphenylcarbinol as from 1,1-diphenylpropylene, and substitution products appear to behave analogously. Thus, 1,1-di(*p*-chlorophenyl)propylene gives a product $C_{15}H_{10}Cl_2O_2S$ which has an infrared spectrum very similar to that of I and is thus very probably 5-chloro-3-(*p*-chlorophenyl)-2-methylbenzothiophene 1,1-dioxide.

This curious reaction recalls somewhat the observation of Kharasch[6] that styrene reacts with bisulfite in the presence of oxygen to give $C_6H_5 \cdot CHOH \cdot CH_2 \cdot$-

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