solid (6% over-all yield), m.p. 123–126°, but having mol. wt. 566. A methylene chloride extract of the crude product gave solid (12% over-all yield), m.p. *ca.* 50°, but having mol. wt. 518.

m-(**2-Aminoethyldithio**)**benzoic Acid Hydrochloride** (**15**). **A. From 2-Aminoethyl 2-Aminoethanethiolsulfonate Dihydrochloride** (**3**).—A solution at 50° of *m*-mercaptobenzoic acid[24] (2.00 g.) in ethanol (12 ml.) was added slowly over 15 min. to a stirred solution at 0° of the thiolsulfonate **3** (3.34 g.)[2] in water (8 ml.). The mixture was stirred for 3 hr. and then was chilled. The solid (1.55 g.) was collected; the infrared spectrum indicated that it contained considerable taurine. Numerous recrystallizations of this solid and other crops using water, alcohol, and acetone finally resulted in 1.16 g. (34%) of white solid, m.p. 187–190°, still containing taurine. Several recrystallizations from ethanol (below 40°) yielded the hydrochloride **15** having constant m.p. 191–193°.

Anal. Calcd. for $C_9H_{12}ClNO_2S_2$: C, 40.67; H, 4.55; N, 5.27; S, 24.13. Found: C, 40.50; H, 4.46; N, 5.10; S, 24.29.

Attempts to obtain a crystalline zwitterion **13** from this salt failed. Neutralization with 1 equiv. of sodium hydroxide precipitated no solid from concentrated solution; freeze drying gave only gum which resisted crystallization.

B. From *m*-**Carboxyphenyl** *m*-**Carboxybenzenethiolsulfonate** (**16**).—Thiolsulfonate **16** (14.8 g., m.p. 210–211° dec., finely ground) was added with stirring to 375 ml. of ethanol at 55°. After the mixture had cooled to 22°, 2-mercaptoethylamine hydrochloride (3.96 g.) in ethanol (80 ml.) under nitrogen was added dropwise over 80 min. with stirring. After 1 hr. more of stirring, the solution was concentrated (25°) to 160 ml. Solid was removed and the filtrate was concentrated to 90 ml. Dilution with ether (550 ml.), chilling, and one recrystallization from ethanol–ether below 40° gave 6.16 g. (67%) of the hydrochloride **15**, m.p. 191–193°; the infrared spectrum was identical with that of pure **15** described in A.

p-(**2-Aminoethyldithio**)**benzoic Acid** (**14**).—A mixture (9.0 g. of 4,4′-dithiodibenzoic acid, containing 30% (iodine titer) of *p*-mercaptobenzoic acid (0.018 mole),[25] and ethanol (50 ml.) was added rapidly to a stirred solution of the aminothiolsulfonate **3** (5.0 g.)[2] in water (25 ml.). After a stirring period of 1 hr., the mixture was centrifuged, then filtered. The filtrate was concentrated below 40° to about 15 ml., diluted with water (65 ml.), and extracted with two 200-ml. portions of ether. Ether then was placed in contact with the aqueous phase and a cold solution of potassium hydroxide (1.0 g.) in water (25 ml.) was added slowly with shaking. Concentration of the aqueous phase below 40° left an oil which crystallized upon standing for 6 weeks at *ca.* 25°. Trituration of the mass under cold water gave solid (2.2 g., 55%), m.p. 180–185° dec. Recrystallizations from vigorously boiling water gave **14**, m.p. 200–202° dec.

Anal. Calcd. for $C_9H_{11}NO_2S_2$: C, 47.15; H, 4.84; N, 6.11; S, 27.98. Found: C, 47.06; H, 4.83; N, 6.15; S, 27.95.

Dissolution of the acid **14** in 0.1 *N* hydrochloric acid followed by freeze drying gave the hydrochloride salt (**17**), m.p. 260°; the salt **17** also rapidly precipitated as needles after the acid **14** had been dissolved in 10% hydrochloric acid.

o-(**2-***n*-**Decylaminoethyldithio**)**benzoic Acid** (**20**).—One equivalent (46.0 ml.) of a standard solution (1.0 *N*) prepared by mixing concentrated hydrochloric acid and ethanol was added to a solution of 2-*n*-decylaminoethanethiol (9.90 g.) in ethanol (22 ml.). The resulting mixture immediately was added to a solution of crude *o*-carboxyphenyl *o*-carboxybenzenethiolsulfonate (15.50 g.) in ethanol (135 ml.).

After 20 min. at *ca.* 25°, the solution was evaporated (below 40°) to remove solvent. The residue, in ether (180 ml.) and water (135 ml.), was shaken vigorously while a cold solution of sodium hydroxide (3.68 g.) in water (120 ml.) was added.

An emulsion containing **20** resulted. Additional ether (*ca.* 600 ml.) was added slowly with scratching to initiate crystallization. At about 0°, the zwitterion **20** was obtained by filtration as white crystalline solid (15.40 g., 92%, m.p. 157–161°). Recrystallization from 1-butanol gave **20** identical (mixture melting point and infrared spectrum) with an analytical sample prepared on a smaller scale and recrystallized from 1-butanol and chloroform–ether to constant m.p. 161–162°. The product was soluble in alcoholic acid or base, but not in aqueous ethanol alone, and hence was amphoteric.

Anal. Calcd. for $C_{19}H_{31}NO_2S_2$: C, 61.75; H, 8.46; N, 3.79; S, 17.35. Found: C, 61.54; H, 8.41; N, 3.64; S, 17.60.

Disproportionation of Unsymmetrical Disulfides.—Approximately 1 mmole of disulfide was made to exactly 0.1 *M* in water (ethanol for disulfides **5** and **18**) and was heated in a sealed ampoule at 100° for 3 or for 22 hr. by suspension in vapors of refluxing water. The products from the hydrochloride salts gave precipitates directly; the products from the zwitterions gave precipitates only after acidification. After being heated, the samples were kept overnight at *ca.* 4°. Solid then was removed by filtration either directly (amine hydrochlorides), or after acidification (zwitterions) with 1 equiv. of hydrochloric acid. For the two water-insoluble disulfides (**5** and **18**) the water-soluble N,N′-diacetylcystamine was determined after evaporation of the ethanol, partitioning of the residue between water and ether, and evaporation of the separated water layer (in which the aromatic disulfide was virtually insoluble). After isolation, all solid symmetrical disulfides were dried to constant weight and were identified by their infrared spectra. When the "per cent disproportionated" was below 10, the initial unsymmetrical disulfides were recovered and shown to be essentially unchanged (mixture melting point and infrared spectra).

(24) Prepared by reducing the disulfide mentioned above with zinc dust in glacial acetic acid under nitrogen according to a recent procedure for the *para* analog[15]: yield 97%, m.p. 140–143° (lit.[15] m.p. 146–147°).

(25) Crude reaction product prepared according to the method of Campaigne and Meyer[15]; the content of the thiol could not be easily increased.

Synthesis of Laurolenic Acid

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The structure of laurolenic acid (**2**), one of the products which results from treatment of α-bromocamphoric anhydride with sodium carbonate, has been confirmed by synthesis of its racemic form. The synthesis proceeds by methylation of 2-carbomethoxycyclopentanone (**5**), methanolysis of the product **6** to dimethyl α-methyladipate (**7**), Dieckmann cyclization to 5-methyl-2-carbomethoxycyclopentanone (**8**), and methylation to the 2,5-dimethyl derivative **9**. These steps could be carried out starting with dimethyl adipate (**4**) without isolation of intermediates **5**, **6**, **7**, or **8**, 80% of the dimethyl keto ester **9** being obtained. Addition of the methyl Grignard reagent to **9**, dehydration, and hydrolysis completes the synthesis.

Laurolenic acid (1,2,3-trimethylcyclopent-2-ene carboxylic acid, **2**, described in the older literature as lauronolic acid) is a molecular rearrangement product derivable from camphoric acid by treatment of the corresponding bromo anhydride **1** with sodium carbonate[2] or by distillation of camphanic acid (**3**).[3] These reactions, particularly the former, played a complicating role in the classic structure determination of camphor,

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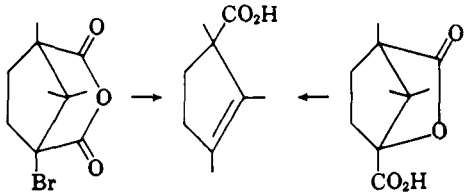
(2) O. Aschan, *Ber.*, **27**, 2112, 3504 (1894).

(3) R. Fittig and L. Woringer, *Ann.*, **227**, 1 (1885).

for it was not initially apparent that formation of laurolenic acid involved skeletal rearrangement. It was thus presumed that the debrominative decarboxylation was that characteristic of a β-bromo acid, which led to deduction of 1,2-dicarboxy structures for camphoric acid.[2,4] These conclusions were subsequently corrected,[4] and various pieces of degradative and physical evidence eventually allowed formulation of laurolenic acid as 2.[4-9] The nature of the molecular rearrangement involved in conversion of the bromo anhydride 1 to laurolenic acid received no further attention, however, although it remains as an almost unique example of such structural changes, *i.e.*, loss of carbon dioxide and bromide from an α- or γ-bromo acid accompanied by a 1,2-alkyl migration.[10]

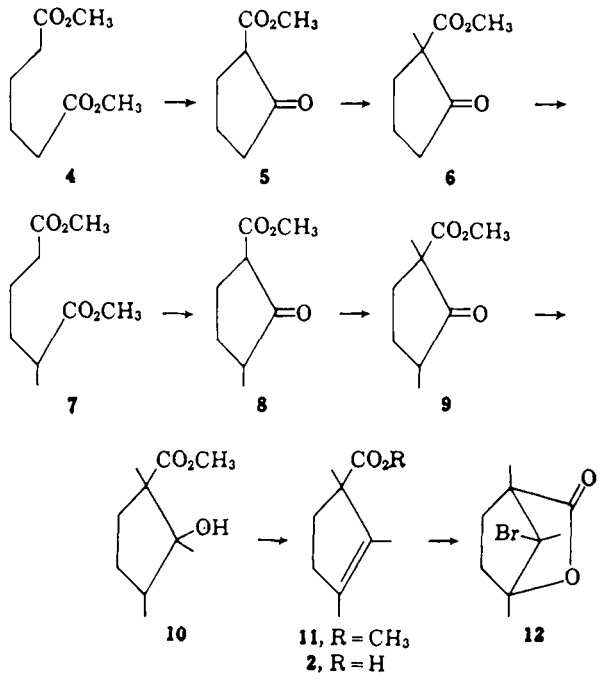


1 2 3

With a view to examining the mechanism and particularly the stereochemistry of this unusual rearrangement, as well as of other reactions which produce laurolenic acid or its decarboxylation product laurolene, we had need of samples of laurolenic acid which were selectively deuterated in the β-methyl and in the γ-methyl groups. This paper reports a synthesis of laurolenic acid which will be suitable for preparation of these derivatives, and which also serves to confirm the structure 2 for the acid.

The reaction sequence of choice, which involved introduction of each methyl group at a unique stage as methyl iodide and which thus is potentially applicable to synthesis of the α-, β-, or γ-trideuteriomethyl analog by use of deuteriomethyl iodide, proceeded from dimethyl adipate (4) *via* 2,5-dimethyl-2-carbomethoxycyclopentanone (9). Although the dimethyl keto ester 9 has not been reported, the corresponding ethyl ester has been prepared by a similar sequence,[11] and the intermediates 5-8 in the methyl[12] as well as the ethyl ester[13] series are well known. 2-Carbomethoxycyclopentanone (5), prepared by sodium[14] or sodium hydride catalyzed Dieckmann cyclization of dimethyl adipate, was methylated[15] to the 2-methyl derivative 6,[12] and methoxide-catalyzed reverse Dieckmann cleavage of this produced dimethyl α-methyladipate (7).[12] The

SCHEME I



Dieckmann equilibria 4 ⇄ 5 and 7 ⇄ 8 are known to be shifted away from β-keto ester by α-substitution on the adipic ester,[16] and thus in an effort to drive the latter to completion the substituted adipic ester 7 was treated with sodium methoxide in xylene, and methanol was distilled as it formed. Early experiments provided the 5-methyl keto ester 8 in yields of 65% by this technique, and much better results can be obtained. Methylation then afforded the key intermediate, 2,5-dimethyl-2-carbomethoxycyclopentanone (9), as a mixture of two stereoisomers in nearly equal quantities. (See Scheme I.)

For synthetic purposes it proved to be most convenient to carry out the entire sequence from dimethyl adipate directly to the dimethyl keto ester 9 without isolation of the intermediates. Treatment of the diester 4 with 1 equiv. of sodium hydride in xylene followed by distillation to remove methanol as it is formed drives the initial Dieckmann cyclization to completion, forming the sodium enolate of the keto ester 5. When this conversion is complete (conveniently ascertained by g.l.c.), addition of methyl iodide forms the 2-methyl keto ester 6. Introduction of 1 equiv. of methoxide produces the methyladipic ester 7 and again distillation of methanol leads to complete formation of the enolate of the 5-methyl keto ester 8. Addition of methyl iodide completes the sequence, and 80% yields of the 2,5-dimethyl keto ester 9 which is 95% pure as estimated by g.l.c. can be isolated. Obviously by interrupting the sequence of operations at suitable intermediate stages, comparable or superior yields of any of the intermediates can be obtained.[17]

(4) *Cf.* A. Lapworth and W. H. Lenton, *J. Chem. Soc.*, **79**, 1284 (1904).
(5) J. F. Eykman, *Chem. Weekblad*, **4**, 41 (1906).
(6) W. A. Noyes and C. G. Derick, *J. Am. Chem. Soc.*, **31**, 669 (1909).
(7) W. A. Noyes and L. P. Kyriakides, *ibid.*, **32**, 1064 (1910).
(8) J. Bredt, *J. prakt. Chem.*, [2] **83**, 395 (1911).
(9) W. A. Noyes and C. E. Burke, *J. Am. Chem. Soc.*, **34**, 174 (1912).
(10) A related example may be provided by rearrangement of bromonorcedrene dicarboxylic acid: *cf.* G. Stork and R. Breslow, *J. Am. Chem. Soc.*, **75**, 3292 (1953).
(11) A. Haller and R. Cornubert, *Bull. soc. chim. France*, [4] **39**, 1621 (1926).
(12) L. Bouveault and R. Locquin, *Compt. rend.*, **146**, 138 (1908); *Bull. soc. chim. France*, [4] **3**, 432 (1908).
(13) W. Dieckmann, *Ber.*, **27**, 102 (1894); L. Bouveault, *Bull. soc. chim. France*, **21**, 1019 (1899); L. Bouveault and R. Locquin, *ibid.*, [4] **3**, 441 (1908); M. E. Dobson, J. Ferns, and W. H. Perkin, Jr., *J. Chem. Soc.*, **95**, 2015 (1909); M. van Rysselberge, *Bull. soc. chim. Belges*, **35**, 310 (1926); F. H. Case and E. E. Reid, *J. Am. Chem. Soc.*, **50**, 3062 (1928); R. Cornubert and C. Borrel, *Bull. soc. chim. France*, [4] **47**, 301 (1930).
(14) R. P. Linstead and E. M. Meade, *J. Chem. Soc.*, 935 (1934).
(15) F. J. Marshall and W. N. Cannon, *J. Org. Chem.*, **21**, 245 (1956).
(16) R. I. Reed and M. B. Thornley, *J. Chem. Soc.*, 2148 (1954).
(17) Many cases of direct alkylation of an enolate formed by Dieckmann cyclization exist: for example, W. E. Bachmann, S. Kushner, and A. C. Stevenson, *J. Am. Chem. Soc.*, **64**, 974 (1942); and W. S. Johnson, R. G. Christiansen, and R. E. Ireland, *ibid.*, **79**, 1995 (1957). Likewise rearrangement of α-alkyl cyclic β-keto esters to γ-alkyl-β-keto esters without isolation of the intermediate diesters has been carried out, although yields have often been inferior to those obtained by the present technique: *cf.* N. S. Vul'fson and V. I. Zaretskii, *Zh. Obshch. Khim.*, **29**, 2737 (1959). Recently L. Nicole and L. Berlinquet, *Can. J. Chem.*, **40**, 353 (1962), reported conversion of diethyl adipate to diethyl α-methyladipate, corresponding to 4 → 7, without isolation of the β-keto esters.

Reaction of the dimethyl β-keto ester **9** with the methyl Grignard reagent proceeded in only moderate yield, no doubt for steric reasons, to give a mixture of stereoisomeric 1,2,3-trimethyl-2-hydroxycyclopentane carboxylic esters (**10**), which was dehydrated using 50% sulfuric acid.[18] A single unsaturated ester resulted, and that it corresponded to structure **11** was evident from its infrared (5.82 μ, ester carbonyl) and n.m.r. spectra (methoxyl singlet at τ 6.40, two broad C-methyl peaks at 8.36 and 8.45, and a quaternary C-methyl singlet at 8.80, no vinyl proton resonance). Spectra of this substance and a sample prepared by esterification of naturally derived *d*-laurolenic acid (from bromocamphoric anhydride[2]) were superimposable, and the two samples were unseparable by g.l.c.

Synthetic *dl*-methyl laurolenate was converted to the racemic acid **2** by Eschenmoser's lithium iodide–collidine technique.[19] Infrared and n.m.r. spectra of the synthetic racemate and the naturally derived *d*-acid were superimposable, as were those of the corresponding amides[2] and bromo lactones **12**.[2] Thus the identity of laurolenic acid as **2** is confirmed.

Experimental[20]

2,5-Dimethyl-2-carbomethoxycyclopentanone (9). A. From 5-Methyl-2-carbomethoxycyclopentanone (8).—To an ice-cold stirred mixture of 250 ml. of benzene, 250 ml. of dimethylformamide, and 4.8 g. (0.20 mole) of sodium hydride under a nitrogen atmosphere was added dropwise 31.2 g. (0.20 mole) of 5-methyl-2-carbomethoxycyclopentanone, b.p. 103–105° (15 mm.).[12] The cold mixture was stirred for 2 hr., 25 g. (0.24 mole) of methyl iodide was added dropwise, and the cold bath was removed. After 1 hr. at room temperature another 8.5-g. (0.06-mole) portion of methyl iodide was added and the mixture was heated at 50° for 1 hr. The mixture was cooled to room temperature, another 8.5 g. of methyl iodide was added, and heating was resumed for 2 hr. After being cooled, the neutral mixture was treated with 4 ml. of methanol and then 100 ml. of water. The benzene layer was separated, washed with water, and dried with sodium sulfate. Distillation afforded 26.2 g. (77%) of the dimethyl keto ester **9**, b.p. 101–106° (15 mm.), which gave no color with alcoholic ferric chloride and slowly formed a 2,4-dinitrophenylhydrazone. This sample was identical (gas chromatogram and infrared spectrum) with the sample prepared by method B below.

B. From Dimethyl Adipate.—A 5-l. three-necked flask fitted with an efficient Hershberg stirrer, a Vigreux column carrying a partial take-off head for distillation, and a dropping funnel was charged with 2000 ml. of dry xylene and 24.0 g. (1.0 mole) of sodium hydride as a 53% dispersion in mineral oil. Under a nitrogen atmosphere (which was maintained throughout the reaction) 174 g. (1.0 mole) of dimethyl adipate[21] was added and the mixture was stirred and slowly distilled over a 3–4-hr. period until the boiling point reached 120° and the gas chromatogram of an acidified aliquot showed less than 1% of residual starting material. The mixture was cooled to room temperature, 213 g. (1.5 moles) of methyl iodide was slowly added, and stirring was continued for 6 hr. An additional 71.0 g. (0.5 mole) of methyl iodide was added, stirring was continued for 10 hr., and the mixture was then slowly distilled until the boiling point reached 120° to remove all excess methyl iodide. The gas chromatogram showed only one product, with retention time identical with authentic 2-methyl-2-carbomethoxycyclopentanone, to be present at this point. The mixture was cooled to room temperature and a slurry of 1.0 mole of freshly prepared alcohol-free sodium methoxide (prepared from 23 g. of sodium) in 500 ml. of xylene was added. The mixture was heated at reflux for 9 hr. and then slowly distilled over a 2–5-hr. period until the boiling point reached 120–126° and the gas chromatogram showed the presence of only one product, with retention time identical with that of authentic 5-methyl-2-carbomethoxycyclopentanone. The mixture was again cooled to room temperature, 284 g. (2.0 moles) of methyl iodide was slowly added, and the mixture was stirred for 12 hr. The mixture was poured onto 1000 g. of ice and 300 ml. of 6 *N* hydrochloric acid with vigorous stirring. The layers separated, the aqueous layer was extracted twice with 50:50 ether–benzene, and the combined organic layers were washed with saturated sodium bisulfite solution and dried with sodium sulfate. Distillation afforded, after removal of solvent, 129–132 g. (76–78%) of dimethyl keto ester, b.p. 108–114° (23–25 mm.). The gas chromatogram of this product showed two major components in nearly equal proportions, neither of which corresponded in retention time to any other intermediate in the sequence, and 3–5% of dimethyl α,α′-dimethyladipate. Redistillation afforded material of analytical purity (two isomers): b.p. 110–111° (25 mm.); $n^{27}D$ 1.4452; $\lambda_{max}^{CHCl_3}$ 5.72, 5.82 μ; n.m.r. (CCl_4) τ 6.63 (s), 8.73 (s), 8.85 (d, J = 6 c.p.s.), and 8.90 (d, J = 6 c.p.s.). This product was identical with that from procedure A, and gave no color with ferric chloride.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found (B): C, 63.62; H, 8.36.

A 2,4-dinitrophenylhydrazone was prepared and recrystallized from 95% ethanol to m.p. 173–175°.

Anal. Calcd. for $C_{15}H_{18}N_4O_6$: C, 51.42; H, 5.18; N, 15.99. Found (B): C, 51.52; H, 5.54; N, 16.00.

Methyl 1,2,3-Trimethyl-2-hydroxycyclopentane-1-carboxylate (10).—A solution of methyl Grignard reagent prepared from 1.3 g. (0.054 mole) of magnesium and 7.24 g. (0.051 mole) of methyl iodide in 20 ml. of ether was added slowly with stirring and intermittent warming to 8.6 g. (0.051 mole) of 2,5-dimethyl-2-carbomethoxycyclopentanone [**9**, b.p. 110° (23 mm.)] in 250 ml. of anhydrous ether. After 3 hr. at reflux hydrolysis was accomplished with 250 ml. of saturated ammonium chloride. The organic layer was washed with 25% sodium bisulfite and dried over sodium sulfate. Removal of ether left 9.1 g. (96%) of a light yellow liquid, g.l.c. of which showed it to contain 47% of the hydroxy ester **10** (at least two stereoisomers) together with starting keto ester. Repeated distillation afforded nearly pure hydroxy ester, b.p. 124–125° (27 mm.), in relatively small amounts. An analytical sample (isomer mixture) was collected from this fraction by gas chromatography (Z, 125°). It had $n^{27}D$ 1.4627; $\lambda_{max}^{CHCl_3}$ 2.8 (broad), 5.82 μ; n.m.r. (CCl_4) τ 6.34 (s), 6.42 (s), 8.78 (s), 8.82 (s), 8.97 (s), 9.08 (s), and peaks at 58 and 52 c.p.s. at 60 Mc.p.s. downfield from internal tetramethylsilane.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found (B): C, 64.87; H, 9.76.

It proved to be practical not to purify the hydroxy ester, but to carry out the dehydration on the mixture of hydroxy esters **10** and keto ester **9**.

***dl*-Methyl Laurolenate (11).**—Following the procedure of Church, *et al.*,[18] a mixture of 0.8265 g. (0.0044 mole) of hydroxy ester **10** (95% purity according to g.l.c., contaminated only with keto ester **9**) and 0.0296 g. of 50% sulfuric acid was heated at 95–100° for 2 hr. By diluting with ether, washing with water and 5% sodium bicarbonate, drying over sodium sulfate, and evaporating, there was obtained 0.5261 g. (70%) of crude laurolenic ester. Chromatography over activity grade III alumina followed by distillation afforded 0.3533 g. (47%) of pure methyl laurolenate as a colorless liquid: b.p. 69–70° (22 mm.), 41–43° (1.5 mm.); $n^{24.5}D$ 1.4623; $\lambda_{max}^{CHCl_3}$ 5.82 μ; n.m.r. (CCl_4) τ 6.40 (s), 8.36 and 8.45 (broad "singlets," long-range coupled to other allylic protons), and 8.80 (s).

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found (B): C, 71.47; H, 9.38.

(18) J. M. Church, F. C. Whitmore, and R. V. McGrew, *J. Am. Chem Soc.*, **56**, 176 (1934).

(19) A. Eschenmoser, F. Elsinger, and J. Schreiber, *Helv. Chim. Acta*, **43**, 113 (1960).

(20) Infrared spectra were obtained on Perkin-Elmer Models 21 and 137 spectrophotometers and n.m.r. spectra were obtained from dilute solutions with tetramethylsilane as internal standard using a Varian A-60 spectrometer or a Varian DP-60 spectrometer operating at 60 Mc. and equipped with a Model 3506 flux stabilizer. Band positions in DP-60 spectra were determined by the audio side-band technique. N.m.r. spectra are described by the use of abbreviations, (s) for singlet and (d) for doublet. Gas–liquid chromatograms (g.l.c.) were run on a Perkin-Elmer Model 154D vapor fractometer with helium as carrier gas and a thermal conductivity detector, a 2-m. 20% Apiezon L grease column, designated Q, or a 2-m. 9% silicone gum (SE 30) on Chromosorb W column, designated Z, being employed. Compositions of mixtures were estimated as the ratios of peak areas. Microanalyses were by Alfred Bernhardt, Mülheim (Ruhr), Germany, indicated B, and by Midwest Microanalytical Laboratory, Indianapolis, indicated M. Melting points (open capillary tubes) and boiling points are uncorrected.

(21) R. O. Clinton and S. C. Laskowski, *J. Am. Chem. Soc.*, **70**, 3135 (1948).

dl-**Laurolenic Acid (2).**—Following the procedure of Eschenmoser, *et al.*,[19] 0.3469 g. (0.002 mole) of methyl laurolenate (95–97% pure) was boiled under reflux with 2.4739 g. (0.013 mole) of lithium iodide trihydrate[22] in 40 ml. of 2,4,6-collidine. After 8 hr. the mixture was cooled and poured into a mixture of ether–chloroform (2:1) and ice-cold 0.5 *N* hydrochloric acid; the acid phase was washed thoroughly with 2:1 ether–chloroform. The combined organic solutions were washed with 2 *N* hydrochloric acid until collidine was completely removed, dried over sodium sulfate, and evaporated to leave 0.3350 g. (100%) of crude laurolenic acid as a dark liquid. Distillation afforded the pure *dl*-acid: b.p. 75° (0.7 mm.); $n^{27}D$ 1.4717; $\lambda_{max}^{CHCl_3}$ 2.8 (broad), 5.9 μ; n.m.r. (CCl_4) τ 8.38 (broad peak, 6 protons) and 8.77 (s).

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found (M): C, 70.34; H, 8.70.

Infrared and n.m.r. spectra of this sample were identical with those of material derived from *d*-α-bromocamphoric anhydride by the procedure of Aschan.[2] Spectra of the naturally derived methyl ester, prepared from the acid with diazomethane, were identical with the synthetic ester described above.

Bromo Lactone of *dl*-Laurolenic Acid (12).—To 0.2156 g. (0.0014 mole) of *dl*-laurolenic acid, b.p. 75° (0.7 mm.), in 2 ml. of chloroform was added 0.2156 g. (0.0014 mole) of bromine in 0.5 ml. of chloroform. After 1 hr. the solvent was evaporated under nitrogen to leave 0.3642 g. (89%) of a semisolid. This was taken up in 25 ml. of ether and washed with 35 ml. of 15% sodium carbonate solution, the ether solution was dried over sodium sulfate, and ether was evaporated to afford 0.2759 g. (69%) of colorless pointed needles which tended to turn black on standing. Sublimation gave a pure *dl*-bromo lactone (12) as white rosettes: m.p. 193–194°; $\lambda_{max}^{CHCl_3}$ 5.58 μ; n.m.r. τ ($CDCl_3$) 8.38 (s), 8.50 (s), and 8.77 (s).

Anal. Calcd. for $C_9H_{13}BrO_2$: C, 46.36; H, 5.62; Br, 34.28. Found (B): C, 46.70; H, 5.65; Br, 34.10.

Infrared and n.m.r. spectra of this sample were identical with those of authentic *d*-bromo lactone, m.p. 193–194° (lit. m.p. 187°,[2,9] 194°[23]), prepared in the same manner from *d*-laurolenic acid.

Amide of *dl*-Laurolenic Acid.—The procedure is a modification of that of Noyes and Burke.[9] To 0.0776 g. (0.00050 mole) of ice-cold *dl*-laurolenic acid, b.p. 75° (0.7 mm.), was added 0.105 g. (0.00050 mole) of phosphorous pentachloride. After the vigorous reaction had subsided, 2–3 ml. of 30–60° petroleum ether followed by 3–4 ml. of ammonium hydroxide were added and the mixture was allowed to stand at room temperature for 1.5–2 hr. The mixture was extracted with ether and the ether solution was dried over sodium sulfate. Removal of ether afforded 0.0451 g. (58%) of a white solid which was sublimed to yield white needles of the amide: m.p. 71–72°; $\lambda_{max}^{CHCl_3}$ 2.83, 2.92, 5.98, 6.01, 6.36 μ; n.m.r. ($CDCl_3$) τ 8.33 (broad), 8.42 (broad), and 8.77 (s).

Anal. Calcd. for $C_9H_{15}NO$: C, 70.55; H, 9.87; N, 9.14. Found (B): C, 70.27; H, 9.65; N, 9.35.

Infrared and n.m.r. spectra of this sample were identical with those of an authentic sample of *d*-laurolenamide, m.p. 71–72° (lit.[2,9] m.p. 71–72°), prepared in the same manner.

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(22) Anhydrous lithium iodide served equally well.

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The Synthesis of N-Benzylthieno[2,3-*b*]pyrrole[1,2]

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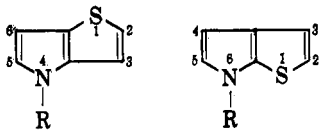
The synthesis of N-benzylthieno[2,3-*b*]pyrrole has been accomplished. Thiocyanation of diethyl 1-benzylpyrrole-3,4-dicarboxylate with thiocyanogen chloride gave diethyl 1-benzyl-2-thiocyanopyrrole-3,4-dicarboxylate. The thiocyanopyrrole was converted by reduction with sodium borohydride and alkylation with ethyl bromoacetate to ethyl (1-benzyl-3,4-dicarbethoxy-2-pyrrolylthio)acetate. Dieckmann ring closure of the pyrrolylthioacetate furnished diethyl 6-benzylthieno[2,3-*b*]pyrrole-2,4-dicarboxylate. The thienopyrrole diester was converted by hydrolysis, decarboxylation, and reduction to 6-benzylthieno[2,3-*b*]pyrrole-4-carboxylic acid. The thienopyrrole acid underwent decarboxylation at 200–220° in an evacuated, sealed tube to give N-benzylthieno[2,3-*b*]pyrrole.

Interest in the synthesis of isoteres of indole has led to the preparation of thieno[3,2-*b*]pyrrole (I)[4] and its N-benzyl derivative II.[5] The isomeric thieno[2,3-*b*]-pyrrole (III) is not known. The synthesis of the N-benzyl analog of III, 6-benzylthieno[2,3-*b*]pyrrole (IV), has now been accomplished and is described herein.

Diethyl 1-benzylpyrrole-3,4-dicarboxylate (V) was prepared by the condensation of diethyl 1-formyl-2-diethoxymethylsuccinate[6] with benzylamine according to the procedure of Kornfeld and Jones.[6] Hydrolysis of the pyrrole diester V gave the known diacid.[7] The pyrrole diester V was converted by thiocyanation with thiocyanogen chloride[8] in acetic acid to the thiocyanopyrrole VI. The infrared spectrum of VI had a band at 2160 cm.$^{-1}$ due to the thiocyano group, while the n.m.r. spectrum showed the ethyl ester groups to be nonequivalent, establishing that substitution had occurred in the pyrrole ring.



I, R = H; II, R = $CH_2C_6H_5$ III, R = H; IV, R = $CH_2C_6H_5$

Lithium aluminum hydride is known to reduce thiocyanates to mercaptans.[9] It was found that sodium borohydride also effects this reaction. The thiocyanopyrrole VI was converted to the pyrrolylthioacetate VII by reduction of the thiocyano group with sodium borohydride followed by alkylation of the resulting thiol anion with ethyl bromoacetate. The n.m.r. spectrum was in accord with the proposed structure; in

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(3) National Science Foundation Fellow, 1962-1963. U. S. Public Health Service Fellow, 1963-1964.

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