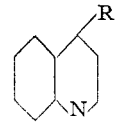
TABLE I

ALIPHATIC AMINO COMPOUNDS FROM CINCHONINALDEHYDE



R	M. p., °C.	Cryst. solvent	Yield, %	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
—CH_2—N(—CH_2CH_3)(—$CH_2CH_2COOCH_3$)·2HCl	223–225	MeOH–acetone	50	55.62	55.25	6.43	6.34
—CH_2—N(—CH_2CH_3)(—$CONH_2$)	143–144	EtOAc–hexane	45	68.12	68.28	6.60	6.75
—CH_2—NH—$CH_2CH_2CH_3$·HCl	162–163	EtOH–Et_2O	60	65.93	65.89	7.24	7.57
—CH_2—N(—$CH_2CH_2CH_3$)(—$CONH_2$)	169–170	EtOAc–hexane	55	69.14	69.13	7.05	7.46
—CH_2—NH—$CH_2CH_2CH_2CH_3$·HCl	147–148	EtOH–Et_2O	54	67.01	66.86	7.64	7.56
—CH_2—NH—$CH_2C_6H_5$·2HCl·$2H_2O$	205–210	EtOH–Et_2O	70	57.11	57.40	6.22	6.01
—CH_2—N(—$CH_2C_6H_5$)(—$CONH_2$)	209–210	EtOAc–hexane	75	74.19	73.96	5.89	5.71
—CH_2—N(—$CH_2C_6H_5$)(—$CONHC_6H_5$)	153–154	Benzene–hexane	100	78.44	78.20	5.77	5.77
—CH=N—$CH_2CH_2C_6H_3$—3,4—$(OCH_3)_2$	84–85	Hexane	85	74.96	74.72	6.30	5.93
—CH_2—NH—$CH_2CH_2C_6H_3$—3,4—$(OCH_3)_2$·HCl	175–176	EtOH–acetone	50–60	66.91	66.92	6.46	6.61
—CH_2—N(—$CONH_2$)—CH_2CH_2—N(—$CONH_2$)–CH_2–	250–251	EtOH	70–75	67.26	67.10	5.65	5.73

C. Preparation of the Ureas.—The secondary amine in the presence of at least 2 equivalents of dilute hydrochloric acid was treated with 1.5–2.0 equivalents of potassium cyanate and the mixture was heated for two hours on the steam-bath. The product ordinarily precipitated from the aqueous solution either as a solid or viscous oil which solidified on cooling and scratching. The solution was brought to *p*H 5–6, and after cooling the urea was collected by filtration.

D. Preparation of the Phenyl Urea.—The secondary amine base in benzene solution was treated with a slight excess of phenyl isocyanate, and was heated one hour on the steam-bath. The product was precipitated by the addition of hexane and cooling.

E. Preparation of N-Ethyl-N-(β-carbomethoxyethyl)-ω-lepidylamine.—The secondary amine base (ethyllepidylamine) was combined with 4 equivalents of methyl acrylate in an equal volume of benzene and the mixture was refluxed for ten hours. After cooling an excess of methanolic hydrogen chloride was added and the dihydrochloride was precipitated with ether.

Acknowledgment.—Thanks are due to Mr. Samuel W. Blackman for the microanalytical results reported here.

Summary

A series of lepidylamine derivatives has been obtained by catalytic hydrogenation of the Schiff base-like products formed from cinchoninaldehyde and some primary aliphatic amines.

TUCKAHOE 7, NEW YORK RECEIVED JANUARY 10, 1947

[CONTRIBUTION FROM THE DIVISION OF MEDICINAL CHEMISTRY, THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH]

Barbituric Acids and Related Compounds Containing Alicyclicalkyl Groups[1]

BY WILLIAM BRAKER, EDWARD J. PRIBYL AND W. A. LOTT

The observation that cyclopropylcarbinol and cyclobutylcarbinol had anesthetic activity when administered rectally suggested that these alicyclicalkyl residues might confer desirable pharmacological properties if introduced into compounds containing an auxapharm group, such as ureides, carbamates, barbituric acids or thiobarbituric acids.

The literature records only a very few barbituric acids containing alicyclicalkyl groups attached to the 5-carbon atom.[2,3,4] Apparently no such compounds containing cyclopropyl or cyclobutylalkyl groups are recorded.

A number of compounds containing the alicyclic-alkyl radical have been prepared in which the size of the alicyclicalkyl group was varied to determine any differences in pharmacological properties.

The alicyclic carbinols utilized in this investigation were prepared by known literature methods. Thus, cyclopentylcarbinol and cyclohexylcarbinol were prepared by the action of gaseous formaldehyde on the Grignard compound of the corresponding cycloalkyl halide according to the method described for cyclohexylcarbinol.[5] Cyclopropylcarbinol and cyclobutylcarbinol were prepared by the method of Demjanow.[6] β-(Δ²-Cyclopentenyl)-ethanol was obtained from cyclopentadiene by the method of Noller and Adams.[7] Ethylcyclopropylcarbinol was prepared according to the method of Bruylants[8] in a 60% yield by reduction

(1) Presented before the Division of Medicinal Chemistry, 109th Meeting of the American Chemical Society, Atlantic City, New Jersey, April, 1946.

(2) Keach, THIS JOURNAL, **55**, 2977 (1933).

(3) Katsnelson and Brodski, *Compt. rend. acad. sci., U. R. S. S.*, **17**, 477 (1937); *C. A.*, **32**, 2912 (1938); Merkulov, *Bull. med. exptl., U. R. S. S.*, **6**, 64 (1938); *C. A.*, **33**, 2922 (1939).

(4) Blicke and Zienty, THIS JOURNAL, **63**, 2991 (1941).

(5) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 182.

(6) Demjanow, *Ber.*, **40**, 4960 (1907).

(7) Noller and Adams, THIS JOURNAL, **48**, 2446 (1926).

(8) Bruylants, *Rec. trav. chim.*, **28**, 187 (1909).

TABLE I

Barbituric acid	Yield, %[a]	M. p., °C.[b]	Formula	Nitrogen, % Calcd.	Found
5-Cyclopropylmethyl-5-ethyl	63.2[c]	159–160	$C_{10}H_{14}N_2O_3$	13.33	13.04
5-Ethyl-cyclopropylmethyl-5-ethyl	60.0	100–101	$C_{12}H_{18}N_2O_3$	11.76	11.33
5-Cyclobutylmethyl-5-allyl	66.9	151–152	$C_{12}H_{16}N_2O_3$	11.86	11.98
5-Cyclobutylmethyl-5-allyl-1-methyl	48.0	[d]	$C_{13}H_{18}N_2O_3$	11.19	11.38
5-Cyclobutylmethyl-5-ethyl	57.0	158–159	$C_{11}H_{16}N_2O_3$	12.50	12.52
5-Cyclobutylmethyl-1-methyl	71.7[c]	77–81	$C_{10}H_{14}N_2O_3$	13.33	13.04
5-Cyclobutylmethyl-5-methyl-1-methyl	30.3	125–126	$C_{11}H_{16}N_2O_3$	12.50	12.20
5-Cyclopentylmethyl-5-ethyl	57.0	190–191	$C_{12}H_{18}N_2O_3$	11.76	11.55
5-(Δ^2-Cyclopentenylethyl)-5-methyl	37.5[c]	110.5–11.5	$C_{12}H_{16}N_2O_3$	11.86	11.62
5-(Δ^2-Cyclopentenylethyl)-1,5-dimethyl	25.1	113–114	$C_{13}H_{18}N_2O_3$	11.19	10.84
5-(Δ^2-Cyclopentenylethyl)-5-ethyl	72.8	136–137	$C_{13}H_{18}N_2O_3$	11.19	11.36
5-Cyclohexylmethyl-5-methyl	45.3[e]	223–224	$C_{12}H_{18}N_2O_3$	11.76	11.64
5-Cyclohexylmethyl-1,5-dimethyl	34.0	148.5–149.5	$C_{13}H_{20}N_2O_3$	11.06	10.58
5-Methyl-cyclopropylmethyl-5-ethyl	30.0	139.0	$C_{11}H_{16}N_2O_3$	12.50	12.48
5-Methyl-cyclopropylmethyl-5-ethyl-1-methyl	15.4	67–68	$C_{12}H_{18}N_2O_3$	11.75	11.75
Thiobarbituric acids				**Sulfur, % Calcd.**	**Found**
5-Cyclobutylmethyl-5-ethyl-2-thio	9.5	134–135	$C_{11}H_{16}N_2O_2S$	13.33	13.48
5-Cyclobutylmethyl-5-allyl-2-thio	38.7	164–165	$C_{12}H_{16}N_2O_2S$	12.70	12.81
5-Cyclopentylmethyl-5-ethyl-2-thio	56.8	189–190	$C_{12}H_{18}N_2O_2S$	12.59	12.52
5-Cyclohexylmethyl-5-methyl-2-thio	Low	169	$C_{12}H_{18}N_2O_2S$	12.59	12.58
5-Methyl-cyclopropylmethyl-5-ethyl-2-thio	15.3	100–101	$C_{11}H_{16}N_2O_2S$	13.33	13.27

Diethyl malonic esters Substituents R—	—R^1	B. p., °C.	Mm.	Yield, %	Formula	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
Cyclopropylmethyl	Ethyl	96–98	1	76.2	$C_{13}H_{22}O_4$	64.42	64.70	9.16	9.28
Ethyl-cyclopropylmethyl	Ethyl	106–107	1	61.7	$C_{15}H_{26}O_4$	66.62	66.17	9.69	9.57
Cyclobutylmethyl	H	97–99	2.5	50.4	$C_{12}H_{20}O_4$	60.87	60.61	8.48	8.62
Cyclobutylmethyl	Methyl	112–114	3	18	$C_{13}H_{22}O_4$	64.41	63.52[f]	9.16	8.93
Cyclobutylmethyl	Ethyl	113–115	4	65	$C_{14}H_{24}O_4$	65.57	65.70	9.44	9.11
Cyclobutylmethyl	Allyl	117–122	2	86.3	$C_{15}H_{24}O_4$	67.11	66.52[f]	9.02	8.87
Cyclopentylmethyl	Ethyl	110–112	1	60	$C_{15}H_{26}O_4$	66.62	66.38	9.69	9.56
Δ^2-Cyclopentenylethyl	Methyl	121–122	1	56.4	$C_{15}H_{24}O_4$	67.11	67.08	9.02	8.96
Δ^2-Cyclopentenylethyl	Ethyl	130–133	1.5	46.1	$C_{16}H_{26}O_4$	68.04	67.03[f]	9.28	9.17
Cyclohexylmethyl	Methyl	130–132	5	64.5	$C_{15}H_{26}O_4$	66.62	65.79[f]	9.69	9.43
Methyl-cyclopropylmethyl	Ethyl	100–106	2	59.0	$C_{14}H_{24}O_4$	65.59	64.57[f]	9.45	9.13

[a] Yield of purified compound unless otherwise stated. [b] All melting points are uncorrected. [c] Crude product. [d] Not obtained in crystalline form, an oil. [e] *Cf.* ref. 3. [f] No further effort was made to obtain these intermediate esters analytically pure.

of the corresponding ketone with sodium and ethanol. The latter was obtained in 67% yield by the action of ethylmagnesium bromide on cyclopropyl cyanide in dry ether. Methylcyclopropylcarbinol[9] was prepared in a similar manner.

Malonic esters containing, in addition to a lower alkyl group, the cyclobutylmethyl or cyclopentylmethyl radical, were best prepared from the corresponding *p*-toluenesulfonates since the corresponding carbinols were convertible to the bromides in low yields. Cyclopropylmethyl bromide and ethylcyclopropylmethyl bromide, however, reacted satisfactorily with diethyl ethylmalonate and cyclohexylmethyl iodide with diethyl methylmalonate to give the corresponding disubstituted malonic esters; in the latter case use of butyl alcohol as a solvent gave better yields than ethyl alcohol. Diethyl Δ^2-cyclopentenylethylmethylmalonate was obtained through either the corresponding *p*-toluenesulfonate or through the halide in practically the same yields.

The disubstituted malonic esters were converted to the corresponding barbiturates by reaction with urea in the usual manner. However, condensation of methylurea with diethyl cyclobutylmethylmethylmalonate failed to give the desired barbituric acid, while reaction of methylurea with diethyl allylcyclobutylmethylmalonate or the corresponding acid chloride gave uncrystallizable oils. These barbituric acids were subsequently prepared by reaction of the appropriate alkyl halide with 1-methyl-5-cyclobutylmethylbarbituric acid; the 5-allyl derivative, however, was even then not crystallizable.

Properties and yields of barbituric acids and thiobarbituric acids and of the intermediate substituted malonic esters are recorded in Table I.

With the exception of 5-cyclohexylmethly-5-methyl-barbituric acid,[3] the barbituric acids are

(9) Demjanow and Pinegin, *Chem. Zentr.*, **85**, I, 1998 (1914).

described for the first time. The *p*-toluenesulfonates of three of the alcohols were prepared according to the method of Tabern.[10]

Experimental

5-Allyl-5-cyclobutylmethyl-barbituric Acid.—To a solution of 23 g. (1 mole) of sodium in 400 cc. of absolute ethanol, 200 g. (1 mole) of diethyl allylmalonate was added and 250 cc. of alcohol was then distilled off *in vacuo*. A solution of 240 g. of cyclobutylmethyl *p*-toluenesulfonate (1 mole) dissolved in 400 cc. of benzene was added to the residue with vigorous stirring, and the reaction mixture stirred for four hours and then allowed to stand at 30–35° for fifteen hours. The mixture was then refluxed and stirred for ten hours after which 500 cc. of water was added and the benzene layer was separated. The aqueous layer was extracted several times with ether and the ether extracts combined with the benzene layer; the whole was then washed with salt solution and dried over sodium sulfate. After distillation of the solvents, the residual oil was fractionated *in vacuo*, yielding diethyl allylcyclobutylmethylmalonate as a colorless oil, b. p. 116–119° at 2 mm.

Twenty and three-tenths grams (0.075 mole) of the above malonic ester and 10 g. (0.166 mole) of urea were added to a solution of 3.75 g. (0.169 mole) of sodium in 65 cc. of absolute ethanol and the mixture refluxed for fifty hours and the alcohol distilled off. The residue was dissolved in water and the solution filtered and acidified with concentrated hydrochloric acid. The precipitated material was filtered, washed with water, and vacuum dried. When crystallized from dilute alcohol, 5-allyl-5-cyclobutylmethyl-barbituric acid was obtained as a white crystalline substance, m. p. 151–152°.

To prepare the sodium salt, 5.13 g. of the barbituric acid was dissolved in 41.9 cc. of a 0.5189 *N* solution of sodium in absolute ethanol. The sodium salt separated from the solution and was filtered off, washed with alcohol and dried in a vacuum desiccator over phosphorus pentoxide. It was obtained as a white powder which dissolved easily in water, forming a clear solution, stable in the absence of carbon dioxide.

Carbamates. Ethyl-cyclopropylmethyl Carbamate.—A solution of 10 g. (0.10 mole) of ethyl-cyclopropylcarbinol in 30 cc. of benzene was maintained at 10° while adding dropwise 23 cc. (0.10 mole) of a 44% solution of phosgene in benzene with stirring. On completion of the reaction and while stirring, a solution of 12.1 g. (0.10 mole) of dimethylaniline in 62 cc. of benzene was added at 10–20°; the mixture was stirred for half an hour, washed with ice water and dried over sodium sulfate. The benzene solution was then agitated with 15 cc. of 28% aqueous ammonia and the mixture maintained at a temperature of 6° for fifteen hours; it was then washed successively with water, dilute hydrochloric acid, dilute sodium carbonate solution and finally with water, and then dried over sodium sulfate. The benzene was removed by distillation *in vacuo* and the crude product crystallized from dilute ethanol. The desired carbamate was then obtained as white needle-like crystals, m. p. 95–96°. The compound is slightly soluble in water. The yield was poor.

Anal. Calcd. for $C_7H_{13}NO_2$: N, 9.80. Found: N, 10.00.

The following compounds were prepared in a similar manner:

Cyclopropylmethyl carbamate, m. p. 80°, obtained in low yield.

Anal. Calcd. for $C_5H_9NO_2$: N, 12.17. Found: N, 11.89.

Cyclobutylmethyl carbamate, m. p. 60°, yield, 82.8%.

Anal. Calcd. for $C_6H_{11}NO_2$: N, 10.85. Found: N, 10.93.

Δ^2-Cyclopentenylethyl carbamate, m. p. 71–72°, yield, 94%.

Anal. Calcd. for $C_8H_{13}NO_2$: N, 9.03. Found: N, 9.30.

p-Toluenesulfonates. Cyclopentylmethyl *p*-Toluenesulfonate.—One hundred and sixty-five grams (0.865 mole) of *p*-toluenesulfonyl chloride was dissolved in 450 cc. of benzene, and 88 g. (0.88 mole) of cyclopentylmethanol and 88 g. of pyridine were then added. The mixture was allowed to stand at 10° overnight and then at room temperature for four days, after which it was filtered. The solid was washed several times with benzene and the washings added to the filtrate. The combined filtrate and washings were washed with 10% hydrochloric acid to remove excess pyridine, then with cold water, and then dried over sodium sulfate. The benzene was distilled off *in vacuo* at a temperature below 60°. The residue, after being heated at 50° at 2 mm. for two hours, was an oil and weighed 206 g., representing a yield of 93.2%.

Anal. Calcd. for $C_{13}H_{18}O_3S$: S, 12.59. Found: S, 12.45.

In a similar manner were prepared:

Cyclobutylmethyl *p*-toluenesulfonate, yield, 94.4%.

Anal. Calcd. for $C_{12}H_{16}O_3S$: S, 13.32. Found: S, 13.34.

Δ^2-Cyclopentenylethyl *p*-toluenesulfonate, yield, 90%.

Anal. Calcd. for $C_{14}H_{18}O_3S$: S, 12.60. Found: S, 12.15.

α-Bromopropylcyclopropane.—Twenty grams of ethyl-cyclopropylcarbinol and 40 cc. of 48% hydrobromic acid solution were refluxed in an oil-bath at 150–155° for five hours. After the reaction mixture had cooled, 50 cc. of water was added and the bromide extracted with ether. The ether extract was washed with water and dried over sodium sulfate. After removal of the ether by distillation the desired bromide was obtained as a colorless oily residue having a b. p. of 151–153°; yield, 70%. This compound was not obtained analytically pure.

α,β-Diethylcyclopropanepropionamide.—Diethyl ethyl-cyclopropylmethylethylmalonate (57.6 g.) was hydrolyzed by refluxing for ten hours with potassium hydroxide (90 g.) in 1.2 liters of alcohol; the alcohol was then distilled off and the residue acidified and extracted with ether. The ethereal solution was dried over sodium sulfate and was then distilled leaving a yellowish residual liquid which was the crude dicarboxylic acid, weighing 50–60 g. Without further purification this acid was decarboxylated by heating in an oil-bath at 180–185° until evolution of carbon dioxide had ceased. The residue was then fractionated *in vacuo*, the larger fraction of 27.5 g. distilled at 130–131° at 6 mm. and represented a 75.8% yield of α,β-diethylcyclopropanepropionic acid.

Fourteen grams of the acid and 8 g. of phosphorus trichloride were heated together on a steam-bath for one hour, when the evolution of hydrogen chloride had ceased. The liquid phase was then decanted from the reaction mixture, leaving a sirup which was rinsed with two 10-cc. portions of petroleum ether. The combined rinsings and liquid phase were then fractionated giving 9.3 g. of the desired α,β-diethylcyclopropanepropionyl chloride, b. p. 84–86° at 5.5 mm., yield, 61%.

Anal. Calcd. for $C_{10}H_{17}ClO$: Cl, 24.91. Found: Cl, 25.01.

α,β-Diethylcyclopropanepropionyl chloride (9.1 g.) was dissolved in 150 cc. of absolute ether and the solution cooled to −5°. Dry ammonia gas was then passed in with stirring over a period of one hour and forty-five minutes, after which the precipitate was filtered off and washed with ether. After crystallization from benzene and petroleum ether mixture, the product had a melting point of 113°.

Anal. Calcd. for $C_{10}H_{19}NO$: N, 8.28. Found: N, 8.28.

α-Allylcyclobutanepropionic Acid, Ureide and Thioureide.—Diethyl allylcyclobutylmethylmalonate (200 g.) was hydrolyzed with potassium hydroxide (150 g.) in 600 cc. of absolute ethanol as in the preceding preparation.

(10) Tabern and Volwiler, THIS JOURNAL, **56**, 1141 (1934).

After ten hours of refluxing 250 cc. of water was added, the alcohol distilled off, and the residual solution treated with 275 cc. of concentrated hydrochloric acid with stirring and external cooling. The reaction mixture, now acid to congo red, was extracted with five 200-cc. portions of ether. The combined ethereal extracts were washed with saturated salt solution, dried over sodium sulfate and the ether distilled. The resulting crude dicarboxylic acid weighed 157 g. which was recrystallized from benzene–petroleum ether, giving 136 g. of a white crystalline product melting at 105–106.5° in a yield of 85%. This was decarboxylated by heating at 190–200° for five hours and then fractionated *in vacuo*, giving 61.2 g. of α-allylcyclobutanepropionic acid, b. p. 142–150° at 17 mm., in a yield of 85.8%.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.58. Found: C, 71.09; H, 9.33.

This acid was converted to the acid chloride by means of phosphorus trichloride, as above, and fractionated *in vacuo*, giving a 70.5% yield of α-allylcyclobutanepropionyl chloride, b. p. 90–95° at 13 mm. Subsequently, improved yields were obtained by chlorinating with thionyl chloride: 31 g. of the acid and 33 g. of thionyl chloride were mixed and heated on a water-bath maintained at 40–50° for thirty minutes and then refluxed for three hours. The thionyl chloride was removed and the residue fractionated yielding 28.7 g. of the desired acid chloride, b. p. 95–99° at 14 mm. in a yield of 83.5%.

Anal. Calcd. for $C_{10}H_{15}ClO$: Cl, 19.03. Found: Cl, 18.59.

To prepare the ureide, the acid chloride and urea in molar proportions of 1:4 were mixed in the absence of water and allowed to stand in a Petri dish in an oven maintained at 110–130° for five hours. The mixture was then heated on a steam-bath for five hours, after which it was cooled, triturated with 5% sodium carbonate solution and the insoluble material extracted with ether. The combined ether extracts were washed with 5% sodium carbonate solution and then dried over sodium sulfate. On distilling the ether there was obtained an 81.2% yield of crude product which was recrystallized from benzene–petroleum ether giving a product, m. p. 124.5–125.5°, in a yield of 58%.

Anal. Calcd. for $C_{11}H_{18}N_2O_2$: N, 13.33. Found: N, 13.52.

The thioureide was similarly prepared, m. p. 108–109°, in a yield of 29%.

Anal. Calcd. for $C_{11}H_{18}N_2OS$: S, 14.15. Found: S, 14.41.

Summary

A number of alicyclicalkyl alkyl malonic esters have been prepared and their properties described.

The corresponding barbituric acids as well as some thiobarbituric acids and 1-methyl derivatives have been prepared.

Several carbamates and ureides containing the alicyclicalkyl group have been prepared and their properties described.

NEW BRUNSWICK, N. J. RECEIVED AUGUST 14, 1946

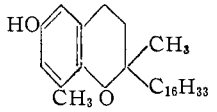
[COMMUNICATION 93 FROM THE LABORATORIES OF DISTILLATION PRODUCTS, INC.]

δ-Tocopherol. I. Isolation from Soybean Oil and Properties[1]

BY MAX H. STERN, CHARLES D. ROBESON, LEONARD WEISLER AND JAMES G. BAXTER

During the assay of tocopherol concentrates prepared from soybean oil by molecular distillation, evidence was obtained of the presence of a previously unidentified member of the vitamin E complex. α-, β- and γ-tocopherols give substantially complete color formation in a modified Emmerie and Engel assay method,[2] using a reaction time of two minutes; and there is only a small percentage increase in color intensity or "rise" as the time is increased to ten minutes. The mixture of tocopherols in the distillate from soybean oil, however, exhibited a rise of about 10%. The substance responsible for this has been separated in pure form and found to be a tocopherol, which we have named δ-tocopherol following the nomenclature introduced by H. M. Evans.

The evidence to be described indicates that δ-tocopherol is 8-methyltocol with the formula



δ-Tocopherol

It differs from α-, β- and γ-tocopherols in having only one methyl group in the aromatic ring of the chroman nucleus and is the first monomethyl tocol isolated from natural sources.

This paper is concerned with the occurrence of δ-tocopherol, with the method used for its isolation, with certain of its physical, chemical, and biological properties and with the methods used to investigate its structure.

Occurrence.—δ-Tocopherol appears to be one of the more common members of the vitamin E complex. It was found to constitute approximately 30% of the mixed tocopherols in soybean oil,[3] 5% of those in wheat germ oil,[4] and there is evidence of its occurrence in cottonseed and peanut oils.[3]

Isolation.—The mixture of δ-, γ- and α-tocopherols in soybean oil was concentrated by molecular distillation, separated from glycerides by saponification and freed of α-tocopherol by selective adsorption. The resulting concentrate was then esterified with palmitoyl chloride to give an ester concentrate which was crystallized from acetone at 5°.

γ-Tocopherol palmitate was found to crystallize readily while δ-tocopherol palmitate stayed in solution. After saponification of the soluble fraction, a concentrate was obtained which was separated from the last traces of γ-tocopherol by

(1) Presented before the Division of Biological Chemistry of the American Chemical Society, Chicago Meeting, September 1946.

(2) Baxter and Stern, *Analytical Chemistry*, in press.

(3) Weisler, Robeson and Baxter, *Analytical Chemistry*, in press.

(4) Unpublished work by H. M. Kascher of this Laboratory.