eral times with ether. The combined ether extracts were washed twice with 25-ml. portions of water, and were dried over sodium sulfate. The dried ether solution was combined with the dried ether that had been used to wash the zinc, and the solvent was evaporated at room temperature. The residual solids, crystallized three times from ethyl acetate, furnished 0.15 g. (48%) of 9,10-dihydroxystearic acid, m.p. 94.5–95°. A fourth crystallization did not affect the melting point.

Anal. Calcd. for $C_{18}H_{36}O_4$: C, 68.3; H, 11.5; neut. equiv., 316.5. Found: C, 68.5; H, 11.4; neut. equiv., 318.

The melting point of this material admixed with authentic 9,10-dihydroxystearic acid (m.p. 94.5–95°) was 94.5–95°. Repetition of this preparation afforded the same product (m.p. 94–95°) in 65% yield from the tosyl compound.

When authentic *erythro*-9,10-dihydroxystearic acid, m.p. 131.5–132°, was carried through the entire procedure, unchanged starting material was obtained in over 90% recovery. *threo*-9,10-Dihydroxystearic acid, m.p. 94.5–95°, was likewise unchanged under the conditions of the experiment.

BOSTON, MASSACHUSETTS

[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT LABORATORIES OF THE COLGATE–PALMOLIVE CO.]

The Preparation of Long Chain N-Acylamino Acids

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A series of long chain acylamino acids were prepared by treating an acid chloride with the appropriate amino acids in an aqueous system. When the dicarboxylic amino acids were used and the acylation effected in an organic solvent, the N-acylamino acid anhydrides were obtained. Some of the physical properties of the long chain N-acylamino acids and their salts are reported.

The reported activity[1,2] of sodium N-lauroylsarcosine[3] as an effective anti-caries agent has prompted us to investigate a series of long chain acylamino acids. It is the purpose of this publication to present the syntheses and physical properties of the compounds prepared.

Most of the available literature on long-chain acylamino acids is concerned with the commercial grade of "Medialan" detergents[4,5] and only in a few instances are individual compounds described. Bondi[6] and Abderhalden[7] have reported the preparation of lauroyl and palmitoyl derivatives of glycine and alanine. Karrer, *et al.*,[8] and Miyamichi[9] studied the formation of ethoxyoxazoles from the ethyl esters of long-chain acylamino acids. Staudinger[10] was first to report the preparation and analysis of palmitoyl and stearoyl derivatives of sarcosine (N-methylglycine). Koebner[11] prepared palmitoyl and stearoyl derivatives of glycine, glycylglycine and diglycylglycine to investigate the surface films of the corresponding amides. Naudet[12,13] evaluated the detergent properties of some of the higher fatty acid derivatives of some polyfunctional amino acids. In a series of papers on microörganisms capable of hydrolyzing acylated amino acids, Kameda, *et al.*,[14–16] investigated a number of long chain acylamino acids. Neuberg, *et al.*,[17,18] reported the preparation of D- and L-amino acids by the enzymatic hydrolysis of DL-acylamino acids.

We synthesized the following two series of acylated amino acids: (I) the sarcosine derivatives, varying the length and nature of the acyl chain. (II) The lauroyl and/or palmitoyl derivatives of other amino acids.

In the preparation of all of the derivatives of monoaminomonocarboxylic acids, an acid chloride was treated with an excess of the sodium salt of the amino acid in aqueous medium while maintaining the *p*H in the range of 9–12.5. The amino acids containing an N-alkyl substituent were prepared by the reaction between the appropriate α-chloro acid and primary amine.

Kester[19] reported the acylation of glutamic acid in the presence of potassium hydroxide in sufficient proportion to maintain the *p*H at 7 or above, but we were unable to acylate aminopolycarboxylic acids such as glutamic and aspartic acids by this method or by the method employed by us for acylating the monoaminomonocarboxylic acids. We were able to accomplish this in low yield by refluxing a suspension of the amino acid with acid chloride in anhydrous ethyl acetate.[20] The intermediate acylated anhydrides were first isolated and then converted to the acylated dicarboxylic acids.

The melting points of the homologous series of acylated sarcosines show an alternation similar to that observed in other series of long chain compounds. When the alkyl group of the N-lauroyl-N-alkylglycines is increased from C_1 to C_4, a maximum is found for the N-ethyl derivative. The N-acyl-N-alkyl compounds in general melt at much lower temperatures than the corresponding derivatives of primary amino acids.

The sodium salts are usually white, crystalline, water-soluble materials, often with good foaming

(1) W. J. King, U. S. Patent 2,689,170.
(2) L. S. Fosdick, J. C. Calandra, R. O. Blackwell and J. H. Burrill, *J. Dental Research*, **32**, 486 (1953).
(3) Colgate–Palmolive Co. Trade name: Gardol.
(4) W. Hentrich, H. Keppler and K. Hintzmann, German Patent 635,522.
(5) W. Hentrich, H. Keppler and K. Hintzmann, British Patents 459,039, 461,328.
(6) S. Bondi, *Z. Biochem.*, **17**, 543 (1909).
(7) E. Abderhalden and C. Funk, *Z. physiol. Chem.*, **65**, 61 (1910).
(8) P. Karrer, E. Miyamichi, H. C. Storm and R. Widmer, *Helv. Chim. Acta*, **8**, 205 (1925).
(9) E. Miyamichi, *J. Pharm. Soc. Japan*, **548**, 863 (1927).
(10) H. Staudinger and H. V. Becker, *Ber.*, **70B**, 889 (1937).
(11) A. Koebner, *J. Chem. Soc.*, 564 (1941).
(12) M. Naudet and P. Desnuelle, *Bull. soc. chim. France*, 1143 (1948).
(13) M. Naudet, *ibid.*, 358 (1950).
(14) Y. Kameda and E. Toyoura, *J. Pharm. Soc. Japan*, **67**, 1 (1947).
(15) Y. Kameda and E. Toyoura, *ibid.*, **68**, 143 (1948).
(16) Y. Kameda and E. Toyoura, *ibid.*, **72**, 402 (1952).
(17) C. Neuberg, U. S. Patent 2,511,867.
(18) C. Neuberg and I. Mandl, *Enzymologia*, **14**, 128 (1950).
(19) E. B. Kester, U. S. Patent 2,463,779.
(20) E. Ronwin, *J. Org. Chem.*, **18**, 127 (1953).

characteristics. The sodium N-acylsarcosines can be crystallized as monohydrates from 90% ethanol. No extended investigation was undertaken of the crystallization behavior of the simple acylated α-amino acids, but it was noted that several crystallized from 90% ethanol with one to four molecules of water of crystallization.

TABLE I

N-ACYLSARCOSINES[a]

N-Acyl-	M.p., °C.[b]	Nitrogen, % Calcd.	Nitrogen, % Found	Neut. equiv. Calcd.	Neut. equiv. Found
Decanoyl	37.5–38.5	5.76	5.62	243	243
Hendecanoyl	49.4–50.2	5.45	5.40	257	258
Lauroyl	45.2–45.8	5.17	5.14	271	271
Tridecanoyl	59.8–60.0	4.91	4.90	285	287
Myristoyl	51.0–52.0	4.68	4.68	299	298
Pentadecanoyl	66.3–67.0	4.47	4.44	313	311
Palmitoyl	65.5–66.5	4.28	4.26	327	327
Heptadecanoyl	71.4–71.9	4.11	4.07	341	343
Stearoyl	71.8–72.0	3.94	3.95	355	354
Elaidoyl	43.0–44.6	3.97	3.96	353	353
Oleoyl	16.1–17.0	3.97	3.94	353	353

[a] The yields of crystallized N-acylsarcosines ranged from 55–75%. [b] All melting points are corrected.

rides by the action of phosphorus trichloride or oxalyl chloride and distilled.[23]

II. **Amino Acids.**—a. All the common amino acids were obtained from commercial suppliers and further purified when necessary. Sarcosine was used as an aqueous solution as supplied by the General Aniline & Film Co. b. The remaining N-alkyl substituted amino acids were prepared by the following general method in which N-propylglycine is given as an example. The amino acids were not isolated but used directly in the acylation step as the concentrated aqueous solution; the presence of N-alkyliminodicarboxylic acid is not harmful since it is a tertiary amino acid and therefore inert in the acid chloride condensation.

c. **Preparation of N-Propylglycine.**—Chloroacetic acid, 28.4 g. (0.3 mole) was dissolved in 100 ml. of water and neutralized with sodium carbonate. This solution was added dropwise at room temperature to an aqueous solution containing 270 g. (4.5 moles) of *n*-propylamine. After one hour the solution was heated on the steam-bath and allowed to reflux for 30 minutes. Fifty ml. of 30% aqueous sodium hydroxide solution was added and the excess amine was taken off under reduced pressure. The solution was concentrated to a volume of 300 ml. and analyzed by a non-aqueous titration with perchloric acid.[24]

III. **N-Acylsarcosines.**—The preparation of N-decanoylsarcosine and its sodium salt will be given to illustrate these preparations.

The acylated sarcosines and their properties are listed in Table II.

TABLE II

N-ACYLAMINOACIDS[a]

Name	M.p., °C.[e]	Nitrogen, % Calcd.	Nitrogen, % Found	Neut. equiv. Calcd.	Neut. equiv. Found	Sodium salt nH_2O,[d]
N-Lauroylglycine	118–119	5.43	5.31	258	255	0
N-Palmitoylglycine	121–122	4.48	4.51	313	317	0
N-Lauroylalanine	104–105	5.17	5.16	271	273	3
N-Ethyl-N-lauroylglycine	56–57.5	4.91	4.87	285	284	v.d.
N-Ethyl-N-palmitoylglycine	67–69	4.11	4.05	341	343	0
N-Methyl-N-lauroylalanine	65–65.5	4.91	4.87	285	287	1
N-Methyl-N-palmitoylalanine	76–77	4.11	4.13	341	338	1
N-Propyl-N-lauroylglycine	47–47.5	4.68	4.67	299	299	0
N-Butyl-N-lauroylglycine	38.5–39	4.47	4.43	313	314	0
N-Lauroyl-β-alanine	93–95	5.17	5.12	271	272	0
N-Lauroyl-α-aminobutyric acid	102–103	4.91	4.88	285	285	4
N-Decanoylleucine	109–109.5	4.91	4.95	285	283	1
N-Lauroyl-ε-aminocaproic acid	85–86	4.47	4.56	313	309	0
N-Lauroyl-α-aminocaproic acid	79–80	4.47	4.52	313	310	0
N-Lauroylmethionine	74.5–75.5	4.23	4.21	331	330	...
N-Lauroylserine	103–103.5	4.88	4.95	287	292	0
N-Lauroylphenylalanine	100–100.5	4.03	4.00	347	344	v.d.
N-Palmitoylphenylalanine	98–99	3.47	3.52	403	403	0
N-Lauroyl-*p*-aminobenzoic[c] acid	230–231	4.39	4.43	319	319	0
N-Lauroyl-*p*-aminophenylacetic acid	155–156.5	4.20	4.22	333	335	0
N-Lauroyl-α-aminophenylacetic acid	113–114	4.20	4.27	333	335	v.d.
N,N′-Dilauroyllysine	119.5–121	5.61	5.56	499	496	0
N-Lauroylaspartic acid[b]		4.44	4.40	158	160	v.d.
N-Lauroylglutamic acid[b]	95–96	4.26	4.31	164.5	162	v.d.
N-Lauroylaspartic anhydride[b]	112.5–114	4.71	4.78	..	98[f]	...
N-Lauroylglutamic anhydride[b]	123–125	4.50	4.38	..	97[f]	...

[a] Unless otherwise noted the N-acylamino acids listed were prepared by the general method IIa. Prepared by method IVb. [c] Prepared by method of Ford.[24] [d] Crystallized from 90% ethanol, v.d. very deliquescent. [e] All melting points are corrected. [f] Determined as % anhydride by method described by Smith, *et al.*[27]

Experimental

I. **Acid Chlorides.**—The fatty acids, except tri-, penta- and heptadecanoic acids which were purchased[21] and purified by crystallization, were first fractionated as the methyl esters and hydrolyzed to the acids. The methyl oleate and elaidate were additionally purified by low temperature crystallization.[22] All the acids were converted to the acid chlo-

a. **Preparation of N-Decanoylsarcosine.**—To 200 ml. of a well-stirred aqueous solution containing 23 g. (0.24 mole) of the sodium salt of sarcosine in an 800-ml. beaker equipped with thermometer and *p*H electrodes, 38.1 g. (0.20 mole) of decanoyl chloride was added dropwise. The solution was kept in the range of *p*H 9–12.5 by the simultaneous addition of a 10% aqueous sodium hydroxide solution and the tem-

(21) From Sapon Laboratories, N. Y.

(22) D. Swern, H. B. Knight and T. W. Findley, *Oil and Soap*, **21**, 133 (1944).

(23) S. T. Bauer, *ibid.*, **23**, 1 (1946).

(24) The analytical method has been kindly supplied by L. S. Luskin of the Rohm and Haas Co.

perature was maintained below 35°. After the addition was completed the solution was acidified with 30% sulfuric acid to a *p*H below 4.5 and extracted with ethyl ether.[25] The ether extracts were washed with water to neutrality and then dried over anhydrous sodium sulfate. The solvent was distilled *in vacuo*. The residue was recrystallized from hexane (petroleum grade); m.p. 37.5–38.5°. The sodium salt was prepared by dissolving the acid in ethanol and neutralizing the solution with alcoholic sodium hydroxide. On cooling, the sodium salt crystallized and was filtered off and dried.

IV. Other N-Acylamino Acids.—a. The other monoaminomonocarboxylic acids (Table II) were acylated by the same method as the sarcosine derivatives except that *p*-aminobenzoic acid was acylated by the method of Ford.[26] b. The dicarboxylic amino acids (Table II) were acylated by the procedure described for the preparation of N-lauroylaspartic acid.

Preparation of N-Lauroylaspartic Acid.—Aspartic acid, 26 g. (0.2 mole) was suspended in 100 ml. of dry ethyl acetate. Lauroyl chloride, 21.8 g. (0.1 mole) was added and the mixture refluxed for 18 hours. Unreacted amino acid was filtered off and the solvent removed by distillation *in vacuo*. The residue was dissolved in hot hexane and allowed to crystallize; yield 10 g., m.p. 112.5–114.0°; anhydride analysis[27] agreed with that for N-lauroylaspartic anhydride. The anhydride was converted to the acid by dissolving in pyridine and adding 5% aqueous NaOH to a *p*H of 9. The solution was acidified with aqueous hydrochloric acid and extracted with ethyl acetate. This solution was washed with water until the washings were neutral, dried over anhydrous sodium sulfate and the solvent stripped *in vacuo*. Sodium salts were prepared as in IIIa.

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(25) Colgate–Palmolive, British Patent 704,585.

(26) G. M. Ford, *Iowa State College, J. Sci.*, **12**, 121 (1937).

(27) D. M. Smith and W. M. D. Bryant, THIS JOURNAL, **58**, 2452 (1936).

JERSEY CITY, N. J.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Formation of Carene [Bicyclo(4.1.0)heptene] Derivatives from Eucarvone[1,2]

BY E. J. COREY AND H. J. BURKE

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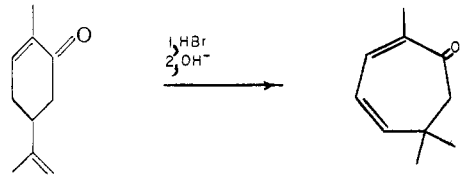
A number of substitution reactions of eucarvone (1) have been shown to yield bicyclic products in the bicyclo[4.1.0]heptene series. These reactions are described together with chemical and physical data which prove the assigned structures.

The terpenoid eucarvone (I), which was first prepared by Baeyer[3] in 1894 from the naturally occur-



II I

ring carvone (II), has been the subject of only desultory chemical study, despite its ready availability. As a consequence, the chemistry of eucarvone, apart from the degradative studies leading to the establishment of structure, has remained ambiguous and in certain areas completely unknown. This fact, together with the interesting possibilities inherent in this unusual seven-membered cyclic dienone system, has prompted the investigation which is reported in part in the present article.

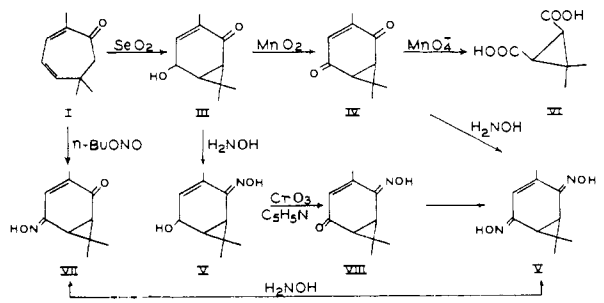


FIG. 1.

We first turned our attention to a study of certain substitution reactions of eucarvone aimed at replacement of the hydrogens of the α-methylene group.

Oxidation of eucarvone, $C_{10}H_{14}O$, by excess selenium dioxide in absolute ethanol at reflux produced a colorless solid, $C_{10}H_{14}O_2$, m.p. 85–86°, (38% yield) whose properties indicated it to be a hydroxy ketone rather than the expected 1,2-diketone. Eventually, the hydroxy ketone was shown to be a bicyclo[4.1.0]heptene derivative of structure III (Fig. 1) and, as will become apparent later, this oxidation became a point of more than passing interest both on its own account and in connection with other transformations of eucarvone.

The presence of a hydroxyl group in the oxidation product is indicated by absorption peaks at 3610 and 3408 cm.$^{-1}$ in the infrared and the formation of *p*-nitrobenzoate and phenylurethan derivatives. The ultraviolet spectrum provides evidence for a structure containing an α,β-monounsaturated ketone function (λ_{max} 239 mμ, log ε 4.05) and rules out a dienone system as in eucarvone (λ_{max} 302 mμ, log ε 3.82) as well as non-conjugated systems. In agreement, the hydroxy ketone manifests conjugated carbonyl absorption in the infrared at 1659, 1641 cm.$^{-1}$ and forms an α,β-unsaturated oxime (λ_{max} 237 mμ, log ε 4.15). Catalytic reduction of the unsaturated hydroxy ketone with palladium–Darco catalyst resulted in the uptake of only one equivalent of hydrogen with the production of a saturated ketone (carbonyl absorption at 1700

(1) Previous communication on this subject, THIS JOURNAL, **76**, 5257 (1954).

(2) Taken from the Ph.D. dissertation of H. J. Burke.

(3) A. Baeyer, *Ber.*, **27**, 810 (1894).