loss of weight upon heating 41.8 mg. at 100° *in vacuo* for 12 hours (calcd. loss, 2.04 mg.; found, 2.1 mg.).

The free α-longinecic acid was isolated by dissolving an exactly known quantity of the barium salt in water in a 10-ml. beaker, and then adding carefully, dropwise, with stirring 90% of the theoretical quantity of dilute sulfuric acid, the concentration of which had been accurately determined. After heating the resulting suspension gently for several minutes, the barium sulfate was removed by filtration. The filtrate was then extracted exhaustively with dry ether, and the combined ether extracts dried over anhydrous sodium sulfate. Upon solvent removal, the colorless residual oil obtained crystallized rapidly after standing briefly in a vacuum desiccator over phosphorus pentoxide. The yield of α-longinecic acid was 70 mg., m. p. 111-113° (cor.).

Hydrolysis of 521 mg. of seneciphylline by 494 mg. of barium hydroxide octahydrate was carried out in an identical manner, except that a reflux period of 40 minutes was employed, and no further addition of water was made. The yield of the barium salt was 122 mg. Liberation of the free acid gave 46 mg. of crude, crystalline residue, melting at 98-105°. Washing with a considerable volume of benzene at room temperature raised the melting range to 102-110°. This material was suspended in benzene, sufficient dry ether added to effect complete solution, and the resulting mixture permitted to evaporate slowly overnight. Scratching with a glass rod initiated a rapid crystallization of material melting at 100-108°; slow concentration of the benzene filtrate gave a slow crystallization leading to the purest isoseneciphyllic acid obtained; m.p. 110-111° (cor.); with softening at 108°. Upon admixture with α-longinecic acid melting at 111-113° (cor.), a melting point of 110-112° (cor.) was observed.

Summary

1. Evidence is presented which demonstrates conclusively the identity of the *Senecio* alkaloids seneciphylline and α-longilobine.

2. Isoseneciphyllic acid and α-longinecic acid have been shown to be identical.

URBANA, ILLINOIS RECEIVED JULY 12, 1950

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

The Effect of α-Methyl Substituents on the Anhydridization of Aliphatic Dibasic Acids

BY ROGER ADAMS AND JOHN L. ANDERSON[1,2]

Succinic and glutaric acids form cyclic anhydrides upon loss of water. The α-methylated succinic and glutaric acids are converted into cyclic anhydrides more readily than the unsubstituted acids, and the anhydrides are more stable. The ease of formation and stability of the anhydrides are proportional to the number of α-methyl groups present in the acids.[3] When adipic acid is dehydrated[4,5] it forms exclusively a polymeric anhydride. On the other hand, $\alpha,\alpha,\alpha',\alpha'$-tetramethyladipic acid is converted exclusively under similar conditions to a cyclic monomer.[6]

This investigation was undertaken to determine the ease of dehydration of the $\alpha,\alpha,\alpha',\alpha'$-tetramethyl substituted dibasic acids from pimelic to tetradecanedioic acids and to compare the products with those obtained from the corresponding unsubstituted acids.

Since the procedures described by Hill and Carothers[7] on the anhydridization of the unsubstituted high molecular weight acids with acetic anhydride or acetyl chloride were adopted, in this research their results are reviewed briefly. They observed that polymeric anhydrides (I) were obtained and that the molecular weights of the products were of the order of 3000–5000.

$$\text{—(CO—(CH}_2)_n\text{—COO)}_x\text{—} \qquad \text{I}$$

They further investigated the behavior of these polymeric anhydrides under molecular distillation. To differentiate the various anhydrides, they proposed the following terminology which will be used in this Communication.

α-Anhydrides are the products prepared by the action of acetic anhydride or acetyl chloride on dicarboxylic acids.

β-Anhydrides (distillates) are the products of disproportionation of α-anhydrides upon heating in a molecular still. They are cyclic monomers or dimers.

γ-Anhydrides are the products formed from β-anhydrides on heating or on standing at room temperature. They are very similar to the α-modifications.

ω-Anhydrides are the residues of very high molecular weights remaining after the distillation of the β-anhydrides. They may be converted into β-anhydrides by continued molecular distillation.

The β-anhydrides obtained by molecular distillation of the α-anhydrides of adipic, pimelic, azelaic, undecanedioic, tridecanedioic, tetradecanedioic and octadecanedioic acids were unstable monomeric cyclic compounds (II) possessing the odors characteristic of the various ring sizes.[8]

$$\underline{\ulcorner\text{(CO-(CH}_2)_n\text{—COO)}_x\urcorner}$$

II, $x = 1$; IIa, $x = 2$

The β-anhydrides derived from suberic, sebacic and dodecanedioic acids proved to be entirely dimeric (IIa) in nature.

The reaction of the anhydrides with aniline was used by these authors to determine the structures. Each anhydride group reacts very rapidly with aniline to form one anilide and one acid group. A linear or cyclic homopolymeric anhydride thus reacts with aniline to form three products (neglecting the effect of end groups): the dianilide, the monoanilide (anilic acid), and the dibasic acid in the fixed molar ratio 1:2:1 as determined

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[1] An abstract of a thesis submitted by Mr. John L. Anderson to the Graduate College of the University of Illinois, 1950, in partial fulfillment of the requirements for the Degree of Doctor of Philosophy.

[2] University of Illinois Predoctoral Fellow, 1948-1949; Allied Chemical and Dye Fellow, 1949-1950.

[3] Auwers and Meyer, *Ber.*, **22**, 2011 (1889); **23**, 101, 293 (1890).

[4] Voerman, *Rec. trav. chim.*, **23**, 265 (1904).

[5] Hill, THIS JOURNAL, **52**, 4110 (1930).

[6] Farmer and Kracovski, *J. Chem. Soc.*, 2318 (1926); 680 (1927).

[7] Hill and Carothers, THIS JOURNAL, **54**, 1569 (1932); **55**, 5023 (1933).

[8] Hill and Carothers, *ibid.*, **55**, 5039 (1933).

statistically. Monomeric cyclic anhydrides, however, yield only the anilic acid. From quantitative measurements of the amounts of dianilides and anilic acids formed from the α- and β-anhydrides, the structures were deduced.

The synthesis of the tetramethyldicarboxylic acids was accomplished by the method of Haller and Bauer.[9,10] The application of the method to the preparation of the previously unknown tetramethylsuberic, azelaic, undecanedioic, dodecanedioic, tridecanedioic and tetradecanedioic acids indicates the generality of the reaction.

The melting points of the α,α,α',α'-tetramethyldicarboxylic acids and those of the unsubstituted dibasic acids containing the same number of carbon atoms in the normal chain are plotted in Fig. 1.

It is apparent that the melting points of the unsubstituted acids approach each other as the carbon chains become longer. This phenomenon is not found in the series of substituted acids. The alternating melting points for molecules with odd and even numbers of carbon atoms are analogous in both series. The acids with an odd number of carbon atoms melt appreciably lower than the next lower homologs. The higher molecular weight tetramethyl dibasic acids have unexpectedly low melting points as compared with the analogous unsubstituted acids.

The tetramethyl derivatives of pimelic acid and its higher homologs distil or sublime *in vacuo* unchanged, whereas the analogous derivatives of succinic, glutaric and adipic acids are converted by heat into cyclic monomeric anhydrides. The tetramethyl dibasic acids from pimelic to tetradecanedioic upon treatment with acetic anhydride dehydrate following a pattern somewhat similar to that found for the analogous unsubstituted acids.

The structures of the α- and β-anhydrides of the tetramethylated acids were deduced from the results of a study of the elementary analyses, molecular weights as determined cryoscopically in benzene, formation of amides and odor.

Hill and Carothers[7,8] employed the reaction with aniline to characterize their products. In this investigation, aniline could not be used, since it reacted only slowly with the tetramethylated dibasic acid anhydrides even at reflux temperature. Farmer and Kracovski[6] have reported a similar observation in attempting to convert the anhydride of α,α,α',α'-tetramethyladipic acid to the anilic acid. β-Anhydrides rearrange to γ-forms on standing and especially on heating. Any ring opening reaction for valid structure proof must therefore be rapid and must take place in the cold.

The reaction of polymeric anhydrides of unsubstituted dibasic acids with ammonia in boiling benzene has been reported to give the diamide, amic acid and dibasic acid.[11] It was observed, however, that liquid ammonia did not react rapidly and quantitatively with the β-anhydrides of the tetramethylated dibasic acids. In this investigation, sodium in liquid ammonia catalyzed by traces of ferric nitrate was used as a reagent upon the anhydrides suspended in liquid ammonia and was found to give quantitative scission.

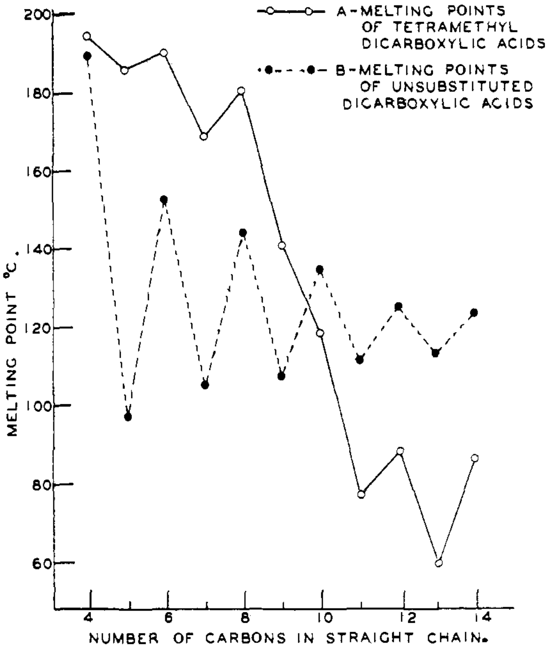

Fig. 1.—Melting points °C.: C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}; A, 195, 186, 192, 169, 181, 141, 118, 77, 88, 59, 86; B, 190, 98, 153, 105, 144, 107, 135, 111, 125, 113, 123.

The α-anhydrides were prepared by heating the various acids with an eight- to ten-fold excess of acetic anhydride followed by removal of the solvent under diminished pressure until all but minute traces of the latter remained. No purification was attempted. The products were viscous, sticky oils with the exception of the α-anhydride of tetramethylpimelic acid which was a solid. The liquid α-anhydrides are soluble in anhydrous ether. From such solutions of the tetramethylsuberic to the tetramethyldodecanoic anhydrides inclusive on standing at low temperatures, solid α-anhydrides separated. Whether the liquid α-anhydrides are mixtures from which the solid α-anhydrides separate, or whether a partial transformation of liquid to solid occurs in the ether solution, was not determined.

The properties of the liquid and solid α-anhydrides of the various acids are summarized in Table I.

It is noteworthy that all of the solid α-anhydrides are essentially dimeric in molecular weight except that derived from tetramethylazelaic acid which is polymeric. Analyses indicate they are cyclic dimers since linear dimers with acetyl or hydroxyl end groups would have caused wide variations from the values actually found. The liquid α-anhydrides, however, probably have some hydroxyl or acetyl end groups since the carbon analyses are in general lower than those expected for pure homopolymeric anhydrides. The solid α-anhydrides are colorless.

The β-anhydrides were produced by molecular distillation of the liquid or solid α-anhydrides at temperatures ranging in different experiments

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(9) Haller and Bauer, *Compt. rend.*, **152**, 1638 (1911).

(10) Buu-Hoi and Cagniant, *Z. physiol. Chem.*, **279**, 76 (1943).

(11) Etaix, *Ann. chim.*, [7] **9**, 356 (1896).

TABLE I

α-ANHYDRIDES

Di-acids[a]	Analyses, % Calcd.	Analyses, % Found Liq. α	Analyses, % Found Solid α	M. p., °C. Solid α	Mol. wt. Liquid α Found	Mol. wt. Dimer Calcd.	Mol. wt. Solid α Found
C_7	C, 66.64		66.51	139-142		396	352
	H, 9.15		9.24				
C_8	C, 67.89	67.15	67.82	100-104	1110	424	445
	H, 9.50	9.55	9.69				
C_9	C, 68.99	68.17	68.71	107-111	1580	452	1150
	H, 9.80	9.78	9.88				1050
C_{10}	C, 69.96	69.32	70.04	99-103	2140	480	446
	H, 10.07	10.28	10.20		1460		
					1840		
C_{11}	C, 70.82	70.09	70.70	100-104	1470	508	455
	H, 10.30	10.21	10.28				
C_{12}	C, 71.60	69.79	71.73	83-87	1040	536	560
	H, 10.51	10.41	10.69				
C_{13}	C, 72.29	72.45			1700		
	H, 10.71	10.46					
C_{14}	C, 72.93	72.06			1720		
	H, 10.88	10.79					

[a] The numbers used in the column refer to the carbon atoms in the dibasic acid without inclusion of the substituent methyl groups.

from 100–160°. When a temperature of 160–200° was used in the case of tetramethyldodecanedioic acid anhydride, the character of the β-anhydride was different and more complex than that obtained at lower temperatures. The β-anhydrides of the tetramethylpimelic to the tetramethylundecanoic acid inclusive were solids. The products were removed from the cold finger receiver and subjected immediately to molecular weight determinations. After drying *in vacuo* at room temperature or at 65°, they were analyzed. By this procedure, the effect of spontaneous γ-anhydride formation was minimized. The residual material in the still consisted of ω-anhydrides which were insoluble in all cold or hot common solvents and consequently were obviously high molecular weight polymers. The physical properties of the β-anhydrides are summarized in Table II.

TABLE II

β-ANHYDRIDES

Diacids[a]	Analyses, % Calcd.	Analyses, % Found		M. p., °C.	Mol. wt. for monomer Calcd.	Mol. wt. for monomer Found
C_7	C, 66.64	66.52	Solid	134-135	198	412
	H, 9.15	9.46				
C_8	C, 67.89	68.15	Solid	96-100	212	335
	H, 9.50	9.50				
C_9	C, 68.99	68.88	Solid	82-87	226	402
	H, 9.80	10.02				
C_{10}	C, 69.96	70.15	Solid	103-108	240	334
	H, 10.07	10.05				430
						430
C_{11}	C, 70.82	70.91	Solid	55-59	254	305
	H, 10.30	10.25				
C_{12}	C, 71.60	71.62	Liquid		268	300
	H, 10.51	10.66				290
C_{13}	C, 72.29	72.96	Liquid		282	312
	H, 10.71	10.69				
C_{14}	C, 72.93	73.00	Liquid		296	298
	H, 10.88	10.95				

[a] The numbers used in the column refer to the carbon atoms in the dibasic acids without inclusion of the substituent methyl groups.

The β-anhydrides are pure as shown by their analyses. The molecular weights of the β-anhydrides of tetramethylundecanedioic, dodecanedioic, tridecanedioic and tetradecanedioic acids support their formulation as cyclic monomers. The molecular weights of the β-anhydrides of tetramethyl-pimelic, suberic, azelaic and sebacic acids, however, agree more nearly with those expected of dimeric structures. Apparently the determinations of molecular weights of the anhydrides of the lower acids are somewhat unreliable, since the β-anhydride of tetramethylazelaic acid was found to be chiefly monomeric as shown by the amidation reaction.

The β-anhydrides, with the exception of that from the tetramethyltetradecanedioic acid, are hygroscopic. Consequently, in the amidation reaction anhydrous ammonia was circulated around the cold finger during the period of warming to room temperature and subsequent transfer of the distillate to the liquid ammonia. Isolation in good yields of pure monoamides from the β-anhydrides of tetramethyl-azelaic, undecanedioic, dodecanedioic, tridecanedioic and tetradecanedioic acids proved the monomeric cyclic anhydride structure of these products. The amidation of the β-anhydrides of tetramethylpimelic, suberic and sebacic acids resulted in mixtures which were not successfully separated into pure components.

Characteristic of cyclic monomers, all the β-anhydrides possess odors, which, however, disappear after standing overnight in air at room temperature. Loss of the odor is prevented by storage at liquid nitrogen temperature. In a vacuum desiccator at room temperature, the odor persists for two or three days. The lower molecular weight β-anhydrides have camphoraceous to minty odors while the fifteen-membered ring from the tetradecanedioic acid has a pronounced musk-like odor. Loss of odor on standing is ascribed to gradual conversion to γ-type anhydrides.

The presence of α-methyl groups in the dibasic acids studied appears to lower the molecular weight of the α-anhydrides into which they are converted by means of acetic anhydride. The β-anhydrides of these acids are in all cases partially or completely cyclic monomers. They are more stable to moisture or aniline than the analogous β-anhydrides of unsubstituted acids. Although the methyl groups appear to promote anhydride ring formation, the tendency for rings of eight to fourteen atoms to be produced is not appreciable.

The reduction of $\alpha,\alpha,\alpha',\alpha'$-tetramethylsebacic acid to the glycol using lithium aluminum hydride[12] gave an 82% yield of 2,2,9,9-tetramethyldecane-1,10-diol.

The authors are indebted to Mr. L. F. Goodyear for the construction of the molecular still and vacuum apparatus used in this work, to Miss Emily Davis, Miss Rachel Kopel and Mr. Maurice Dare for the microanalyses.

Experimental

The melting points of all the compounds reported have been corrected.

$\alpha,\alpha,\alpha',\alpha'$-Tetramethyl Dibasic Acids.—All of the eight dibasic acids from tetramethylpimelic to tetramethyltetra-

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[12] Nystrom and Brown, THIS JOURNAL, **69**, 2548 (1947).

decanedioic acid inclusive were synthesized by the general method of Haller and Bauer.[9]

Sodium amide[13] was prepared from 12.0 g. (0.52 mole) of sodium in 400 ml. of dry liquid ammonia using 0.15 g. of ferric nitrate hexahydrate as catalyst. After the disappearance of the blue color and the formation of the solid sodium amide, the residual ammonia was removed by permitting the mixture to warm gradually. During this period of evaporation, 400 ml. of anhydrous toluene was added. The same 2-l. three-necked flask used for the synthesis of the sodium amide was used as the reaction vessel for the condensation reaction.

After evaporation of the ammonia, 74.0 g. (0.5 mole) of isobutyrophenone was added all at once to the toluene-sodium amide suspension. The resulting mixture was heated under reflux with vigorous stirring for 1 to 1.5 hours. Then 0.25 mole of the alkylene bromide was added over a period of one to two hours. Refluxing was continued for eight to ten hours.

The following procedure was used for obtaining $\alpha,\alpha,\alpha',\alpha'$-tetramethyl-pimelic, suberic, azelaic and sebacic acids. After cooling, the toluene solution was washed with water, dilute sulfuric acid, water, sodium bicarbonate, and finally with water. The toluene was removed *in vacuo* and the diketones distilled. The diketones were then added to a twofold excess (4 moles) of fresh sodium amide suspended in toluene (prepared as described above). The mixture was heated under reflux with vigorous stirring from two to six hours (the shorter period when the contents gelled in the flask and on the stirrer). After cooling, 500 ml. of water was gradually added with stirring and the mixture filtered as rapidly as possible. The diamides thus formed were washed with water and the wash waters added to the filtrate. The toluene was separated from the filtrate and the aqueous solution evaporated to small volume. Upon acidification, a small additional amount of crude diamide was obtained which was combined with the main portion.

The crude diamide was hydrolyzed by dissolving in a thirty- to forty-fold excess by weight of concd. sulfuric acid, followed by gradual addition at 0-5° of a twofold excess of sodium nitrite in a minimal amount of water. After heating to 50°, water was added gradually with stirring. The acid separated as a solid during the heating and the addition of water. The solid acid was separated by filtration, washed with water and purified initially by dissolving in aqueous sodium carbonate (Darco) and by precipitating with mineral acid.

The procedure for preparing the $\alpha,\alpha,\alpha',\alpha'$-tetramethyl-undecanedioic, dodecanedioic, tridecanedioic and tetradecanedioic acids differed only slightly. The diketones, from which these acids were derived, were not distilled prior to treatment with sodium amide. The toluene condensation mixture was not washed with water but merely cooled and filtered from the sodium bromide. This solution was then added to the sodium amide. With these higher molecular weight acids, essentially no diamide was retained in the aqueous layer upon decomposition of the reaction mixture. Upon treatment with nitrous acid the free dibasic acids separated as oils.

$\alpha,\alpha,\alpha',\alpha'$-**Tetramethylpimelic Acid.**—The 2,6-dimethyl-2,6-dibenzoylheptane which distilled at 200-210° (2 mm.) weighed 56 g. (67%). Treatment with sodium amide of this diketone yielded 24.2 g. (68%) of crude diamide. Hydrolysis of 21 g. of crude diamide gave 12 g. (57%) of crude acid.

$\alpha,\alpha,\alpha',\alpha'$-**Tetramethylsuberic Acid.**—The 2,7-dimethyl-2,7-dibenzoyloctane which distilled at 225-242° (2-3 mm.) weighed 62 g. (71%). Treatment with sodium amide yielded 31.5 g. (78%) of crude diamide. Hydrolysis of 29.5 g. of crude diamide gave 24.8 g. (84%) of crude acid.

$\alpha,\alpha,\alpha',\alpha'$-**Tetramethylazelaic Acid.**—The 2,8-dimethyl-2,8-dibenzoylnonane which distilled (with partial decomposition) at 200-260° (4-8 mm.) weighed 66.4 g. (73%). Treatment with sodium amide yielded 38.0 g. (87%) of crude diamide. Hydrolysis of 36.0 g. of crude diamide gave 28.5 g. (79%) of crude acid.

$\alpha,\alpha,\alpha',\alpha'$-**Tetramethylsebacic Acid.**—The 2,9-dimethyl-2,9-dibenzoyldecane which distilled (with partial decomposition) at 200-265° (4-8 mm.) weighed 70.9 g. (75%). Treatment with sodium amide yielded 42.0 g. (87.5%) of crude diamide. Hydrolysis of 40 g. of diamide gave 28 g. (70%) of crude acid.

$\alpha,\alpha,\alpha',\alpha'$-**Tetramethylundecanedioic Acid.**—The diketone was not isolated. Treatment with sodium amide yielded 26.5 g. (39%) of crude diamide. Hydrolysis of 20 g. of diamide gave 14.6 g. (73%) of crude acid.

$\alpha,\alpha,\alpha',\alpha'$-**Tetramethyldodecanedioic Acid.**—The diketone was not isolated. Treatment with sodium amide yielded 39 g. (55%) of crude diamide. Hydrolysis of 30.0 g. of crude diamide gave 12.0 g. (40%) of crude acid.

$\alpha,\alpha,\alpha',\alpha'$-**Tetramethyltridecanedioic Acid.**—The diketone was not isolated. Treatment with sodium amide yielded 43.5 g. (58.5%) of crude diamide. Hydrolysis of 14.5 g. of crude diamide gave an oil which solidified only with great difficulty. After recrystallization of the solid from petroleum ether (Darco), 2.66 g. (18%) of pure acid resulted.

In another preparation using a 25% larger proportion of isobutyrophenone a high yield of crude diamide resulted from which, however, hydrolysis gave only a 16% yield of crude acid.

TABLE III

$\alpha,\alpha,\alpha',\alpha'$-TETRAMETHYLATED DIBASIC ACID DIAMIDES

	M. p., °C.	Solvent	Analyses, % Calcd.	Found
Pimelic[a]	191-193	Ethyl acetate		
$C_{11}H_{22}O_2N_2$				
Suberic	196-197.5	Ethyl acetate	C, 63.12	63.14
$C_{12}H_{24}O_2N_2$			H, 10.59	10.76
			N, 12.27	12.00
Azelaic	156-159	Ethyl acetate	C, 64.42	64.39
$C_{13}H_{26}O_2N_2$			H, 10.81	11.00
			N, 11.56	11.15
Sebacic[b]	210-213	Ethanol	C, 65.58	65.63
$C_{14}H_{28}O_2N_2$			H, 11.01	10.96
			N, 10.93	10.78
Undecanedioic	152-157	Ethyl acetate	C, 66.62	66.52
$C_{15}H_{30}O_2N_2$			H, 11.18	11.39
			N, 10.34	10.41
Dodecanedioic	170-176	Ethyl acetate	C, 67.56	67.70
$C_{16}H_{32}O_2N_2$			H, 11.34	11.30
			N, 9.85	9.62
Tridecanedioic	156-162	Ethyl acetate	C, 68.41	68.53
$C_{17}H_{34}O_2N_2$			H, 11.48	11.61
			N, 9.39	9.41
Tetradecanedioic	172-178	Ethyl acetate	C, 69.18	69.27
$C_{18}H_{36}O_2N_2$			H, 11.61	11.85
			N, 8.97	8.77

[a] Haller and Bauer report m. p. 191-192°. [b] Buu-Hoi and Cagniant report m. p. 185-186°.

TABLE IV

$\alpha,\alpha,\alpha',\alpha'$-TETRAMETHYLATED DIBASIC ACIDS

	M. p., °C.	Solvent	Analyses, % Calcd.	Found
Pimelic[a]	168-169	Pet. ether		
$C_{11}H_{20}O_4$		(b. p. 80-110°)		
Suberic	179-181	Ethyl acetate	C, 62.58	62.56
$C_{12}H_{22}O_4$			H, 9.63	9.77
Azelaic	139.5-141	Ethyl acetate	C, 63.90	64.09
$C_{13}H_{24}O_4$			H, 9.90	9.98
Sebacic[b,c]	117-118	Ethyl acetate	C, 65.08	65.10
$C_{14}H_{26}O_4$			H, 10.15	10.10
Undecanedioic	75-77	Pet. ether	C, 66.14	66.24
$C_{15}H_{28}O_4$		(b. p. 80-110°)	H, 10.36	10.47
Dodecanedioic	86-88	Pet. ether	C, 67.09	67.29
$C_{16}H_{30}O_4$		(b. p. 80-110°)	H, 10.56	10.86
Tridecanedioic	57-59	Pet. ether	C, 67.96	67.87
$C_{17}H_{32}O_4$		(b. p. 30-60°)	H, 10.74	10.80
Tetradecanedioic	84-86	Pet. ether	C, 68.76	68.77
$C_{18}H_{34}O_4$		(b. p. 30-60°)	H, 10.90	11.02

[a] Haller and Bauer report m. p. 168-169°. [b] Buu-Hoi and Cagniant report this product as melting at 102-103°. [c] Alberti, unpublished results, m. p. 119-120°.

$\alpha,\alpha,\alpha',\alpha'$-**Tetramethyltetradecanedioic Acid.**—The diketone was not isolated. Treatment with sodium amide yielded 67 g. (86%). Hydrolysis of 30.0 g. of crude diamide gave 16.5 g. (54.5%) of crude acid.

Short Path Distillation of the Dicarboxylic Acids.—Distillation of the various $\alpha,\alpha,\alpha',\alpha'$-tetramethyldicarboxylic

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[13] *Organic Syntheses*, **25**, 25 (1945).

acids was carried out on 0.5-g. samples using a sublimation apparatus with a total path of less than 1.5 cm. Recovery of distilled acid was always greater than 95%. The melting points of the acids were unchanged by this treatment; in no case was any dehydration to an anhydride observed. The bath temperature used was 190-200° and the time of distillation varied from five to forty-five minutes. The pressure was 1 mm.

α-Anhydrides (Polymers).—A solution of 1.0 g. of tetramethyldicarboxylic acid in an eight- to ten-fold weight excess of pure, redistilled acetic anhydride was heated under reflux for from two to forty-eight hours. Usually two hours of heating was adequate to bring the reaction to the point where further heating caused no observable differences in properties of the anhydrides. The acetic anhydride and acetic acid were removed at steam-bath temperature under water-pump vacuum; the final traces at oil-pump pressure (1-2 mm.) for another hour or two.

The α-anhydrides were colorless to dark brown, viscous, sticky liquids. The only exception was the α-anhydride of tetramethylpimelic acid. It was a crystalline solid and was never obtained as an oil. The α-anhydrides were extremely soluble in benzene and ether. White, crystalline modifications (see Table I) were obtained from most of the initial oily anhydrides by crystallization from anhydrous ether. The α-anhydrides of tetramethyltridecanedioic and tetramethyltetradecanedioic acid, however, could not be obtained crystalline. Solid α-anhydrides could also be obtained by dissolving the liquid α-anhydrides in benzene and precipitating with petroleum ether. This method is not as satisfactory as crystallization from ether and was applied only to a few α-anhydrides. The solid α-anhydrides prepared in both ways were highly crystalline and possessed similar melting points.

Experiments using 0.5-4.0 g. of α-anhydrides gave similar results. The yields of liquid α-anhydrides were quantitative. The yields of solid α-anhydrides varied from quantitative for the tetramethylpimelic acid to about 20% for the tetramethyldodecanedioic acid.

β-Anhydrides (Molecular Distillates).—The molecular distillation apparatus consisted of a still which had an evaporation area of approximately three sq. cm. for 0.25 g. of liquid anhydride and a flat condensing surface of 30-35 sq. cm. area placed 40 mm. above the evaporation surface. The total available area of condensing surface was very much greater due to the cold finger design which enabled distillate also to collect on the sides of the condenser. The still was heated with a Glas-col mantle whose temperature could be accurately determined and controlled. The vacuum system consisted of a mercury diffusion pump backed by a Welch Duo Seal oil-pump. Vacuums of less than 0.1 micron were obtained consistently.

The liquid α-anhydrides in quantities of 0.1 to 0.5 g. were dissolved in absolute ether and aliquot portions transferred by pipet to the still. The ether was removed with water-pump vacuum prior to distillation. No differences in the properties of the β-anhydrides were observed when liquid or solid α-forms were used. Distillations were made at temperatures usually from 100-220° at less than 10^{-4} mm. pressure. Durations of distillations varied from three hours to twelve hours depending on the quantities distilled, the temperature used, and the particular anhydride.

The cold finger of the still was cooled with liquid nitrogen during the actual distillations. When the distillation was complete, dry air was passed into the still, the apparatus was allowed to come to room temperature and the β-anhydrides were removed for analysis and molecular weight determinations as rapidly as possible to prevent change to the γ-anhydrides and to prevent absorption of moisture. For analytical samples the products were merely vacuum dried.

The properties of the β-anhydrides are shown in Table II. The β-anhydrides were hygroscopic, particularly those of dodecanedioic and tridecanedioic acids, and became cloudy on exposure to air of moderate humidity for short periods of time. They all had odors which indicated they were in part monomeric. The yields of β-anhydrides were virtually quantitative.

Molecular Weight Determinations.—A solution of 0.05-0.25 g. of the α- or β-anhydride in 10 ml. of dry, thiophene-free benzene was cooled intermittently with a Dry Ice-methanol-bath with vigorous stirring. Too rapid cooling caused the formation of very large crystals. The cooling was continued until the benzene solution had become a thick paste at which time the coolant was removed and the mixture was allowed to warm slowly with constant stirring. The temperatures were recorded every thirty seconds during the melting process. It was observed that the plot of temperatures showed a sharp rise during the first few minutes, then a leveling off and finally a very sudden rise when the solution became free of crystals. The melting point recorded was that intersection of the slope during the gradual rise and the ordinate representing a completely liquid phase.

ω-Anhydrides (Very High Polymers).—If the molecular distillations were not continued for a length of time necessary to distil all the anhydride, the residues which remained in the still were ω-anhydrides. They were always extremely insoluble in the common organic solvents such as ether, benzene, ethanol, acetone and acetic acid even when hot.

γ-Anhydrides (from β-Anhydrides).—Conversion of the β-anhydrides to the γ-forms took place spontaneously on standing in air at room temperature (twelve hours), on standing in a vacuum desiccator for several days, and on heating. This conversion was deduced on the basis of disappearance of odor.

The Reaction of β-Anhydrides with Ammonia.—To a suspension of 0.05-0.2 g. of β-anhydride in 30-50 ml. of anhydrous liquid ammonia, 0.2-0.5 g. of clean sodium was added. A deep blue solution resulted. After introduction of a small crystal of ferric nitrate hexahydrate the suspension was stirred intermittently for thirty to sixty minutes. The excess ammonia was evaporated and a few drops of methanol were added to the whitish solid to decompose any unchanged sodium. Addition of water caused the formation of a light brown, very soapy solution. No solids, aside from very small amounts of ferric hydroxide, could be separated by filtration from these solutions. Acidification with dilute hydrochloric acid caused the separation of white solids. These were then further purified.

When the monoamides of the tetramethyl-azelaic, undecanedioic, dodecanedioic and tridecanedioic acids were prepared, it was found advisable to pass anhydrous ammonia over the cold finger containing the distillate before removal to the liquid ammonia. The yields which were based on the original weight of dibasic acid less the weight of residue removed from the still were 70-75%.

$\alpha,\alpha,\alpha',\alpha'$-Tetramethylpimelic Acid Anhydrides and Monoamide.—The α-anhydride was always obtained as a solid, usually melting at 139-145°. The β-anhydride was obtained in virtually quantitative yield by distillation at 240° (0.05 mm.), m. p. 137-143°, and at 150° (0.002 mm.), m. p. 134-135°. Both samples of β-anhydrides possessed very strong, pungent, irritating, minty to camphoraceous odors. In one preparation of the β-anhydride a very small amount of crystals, m. p. *ca.* 60°, was obtained from the cold finger, above the main distillate. These crystals seemed to possess more odor than the main distillate. The reaction of the distillate with ammonia and sodium gave only very impure solid on acidification of the soapy solution. The melting point of this solid was 108-142°.

$\alpha,\alpha,\alpha',\alpha'$-Tetramethylsuberic Acid Anhydrides and Monoamide.—A yield of approximately 85% of solid α-anhydride was obtained by crystallization from ether. Molecular distillation at 150-160° ($<10^{-4}$) mm. gave a β-anhydride which had the typical irritating, minty and camphoraceous odor of the pimelic anhydride. A second similar molecular distillation for ten hours gave a distillate which was treated with anhydrous ammonia before isolation. The monoamide thus obtained was a white solid, m. p. 160-180°. This was probably a mixture of diamide, monoamide and dibasic acid. No pure monoamide was obtained by fractional crystallization from benzene and ethyl acetate.

$\alpha,\alpha,\alpha',\alpha'$-Tetramethylazelaic Acid Anhydrides and Monoamide.—The yield of solid α-anhydride was *ca.* 75%. Molecular distillation at 120-140° ($<10^{-4}$ mm.) for ten hours of 0.2 g. of solid α-anhydride gave a distillate with an irritating, penetrating, spicy and cedarlike odor. The odor completely disappeared on standing in air overnight. A second molecular distillation at 120-130° ($<10^{-4}$ mm.) of liquid α-anhydride gave a product which was covered with ammonia vapors prior to removal. Reaction with ammonia and sodium gave a solid, m. p. 140-146°. Four recrystallizations from ethyl acetate raised the melting point to 152-153.5°.

Anal. Calcd. for $C_{13}H_{25}O_3N$: C, 64.16; H, 10.36; N, 5.76. Found: C, 64.37; H, 10.59; N, 5.98.

α,α,α′,α′-Tetramethylsebacic Acid Anhydrides and Monoamide.—The solid α-anhydride was obtained in approximately 80% yield. Molecular distillation at 140° ($<10^{-4}$ mm.) for ten hours of either solid or liquid α-forms gave a white solid distillate which had a penetrating, cedarlike, spicy odor. Attempted formation of the monoamide, both by weighing the β-anhydride in air before ammonia treatment and passage of ammonia over the cold finger receiver, gave a solid, m. p. 110-140°. No pure monoamide was isolated.

α,α,α′,α′-Tetramethylundecanedioic Acid Anhydrides and Monoamide.—The yield of crystalline α-anhydride was approximately 40%. The β-anhydride, obtained on molecular distillation at 200° (10^{-4} mm.), melted at 55-59° and possessed a spicy and somewhat aromatic odor, more pleasant and less irritating than those of the lower-molecular weight β-anhydrides. Formation of the monoamide from 0.2 g. of anhydride gave an 85% yield of product, m. p. 88-95°. The β-anhydride obtained by distillation at 210-220° and treatment with ammonia before isolation melted at 99-103° without recrystallization. In a second similar distillation at 130° the monoamide had an m. p. 98-102°. These samples of monoamides were recrystallized from acetone and water, petroleum ether (b. p. 80-110°), and finally from water. The melting points of the analytical samples were 104-104.5° in each case.

Anal. Calcd. for $C_{15}H_{29}O_3N$: C, 66.38; H, 10.77; N, 5.16. Found: C, 66.27; H, 10.89; N, 5.17.

α,α,α′,α′-Tetramethyldodecanedioic Acid Anhydrides and Monoamide.—The solid α-form was obtained in about 20% yield. Molecular distillations were carried out at 100°, 150-160° and 160-200°, all at 10^{-4} mm. The β-anhydrides possessed rather sweetish, cedarlike odors with very little of the irritating properties common to the lower members. Formation of monoamide from the 100° distillate gave pure monoamide, m. p. 122-123.5°, without the necessity of passing ammonia vapors over the cold condenser. Monoamide from the 160-200° distillate always gave impure product, m. p. <100°; from the 150-160° distillate by passage of ammonia vapors over the cold condenser prior to addition to sodium in liquid ammonia gave a 71% yield of monoamide, m. p. 120-122.5°. The yield was based on the use of 0.25 g. of dibasic acid and recovery of 0.042 g. of residue from the still. Three recrystallizations from petroleum ether (b. p. 80-110°) gave a maximum melting point of 123-123.5°.

Anal. Calcd. for $C_{16}H_{31}O_3N$: C, 67.33; H, 10.95; N, 4.91. Found: C, 67.12; H, 10.83; N, 4.98.

α,α,α′,α′-Tetramethyltridecanedioic Acid Anhydrides and Monoamide.—The α-anhydride was always obtained as an oil which yielded no solid from anhydrous ether or petroleum ether solutions. Molecular distillation of the α-anhydride from 0.250 g. of acid at 130-140° (10^{-4} mm.) followed by passage of ammonia vapors over the cold finger gave 0.120 g. (78% based on reacted material), m.p. 107.5-109.5°. Two recrystallizations from petroleum ether (b. p. 80-110°) gave pure monoamide, m. p. 109.5-110°. Molecular distillation at 150° ($<10^{-4}$ mm.) gave the β-anhydride that was used for molecular weight determinations and analysis. The odor of the β-anhydride was a rather pleasant, sweetish odor similar to musk.

Anal. Calcd. for $C_{17}H_{33}O_3N$: N, 4.68. Found: N, 4.76.

α,α,α′,α′-Tetramethyltetradecanedioic Acid Anhydrides and Monoamide.—No solid form of the α-anhydride was ever isolated. Molecular distillation at 120-130° (10^{-3} mm.) gave β-anhydride, a mobile, colorless liquid much less hygroscopic than the homologs containing one and two less carbon atoms. It had a musk-like odor which it retained for a period of one to two days at room temperature in air. From 0.052 g. in 30 ml. of ammonia, 0.15 g. of sodium and a trace of ferric nitrate, 0.043 g. (78%) of monoamide, m. p. 122-125.5°, resulted. Two recrystallizations from petroleum ether (b. p. 80-110°) gave the pure monoamide, m. p. 126-127°.

Anal. Calcd. for $C_{18}H_{35}O_3N$: N, 4.47. Found: N, 4.48.

β,β,β′,β′-Tetramethyldecamethylene Glycol.[12]—A solution of 5.16 g. of α,α,α′,α′-tetramethylsebacic acid in 150 ml. of anhydrous ether was added dropwise with stirring to a refluxing suspension of 1.90 g. of lithium aluminum hydride in 150 ml. of dry ether. After permitting to react for fifteen minutes, water was added, followed by dilute sulfuric acid. After drying over sodium sulfate, the ether was removed *in vacuo*. The residue was taken up in benzene and crystallized by the addition to the boiling solution of an equal amount of petroleum ether (b. p. 80-110°) and subsequent cooling. The yield was 3.75 g. (82%) of white crystals. Heating the product with aqueous sodium carbonate and subsequent recrystallization from 1:1 benzene-petroleum ether (b. p. 80-110°) gave 2.46 g. of solid. Two recrystallizations from petroleum ether (b. p. 30-60°) gave a pure product, m. p. 60-61.5°.

Anal. Calcd. for $C_{14}H_{30}O_2$: C, 72.98; H, 13.13. Found: C, 73.18; H, 13.15.

Summary

The diamides of α,α,α′,α′-tetramethyl-pimelic, suberic, azelaic, sebacic, undecanedioic, dodecanedioic, tridecanedioic and tetradecanedioic acids have been synthesized and from them the corresponding dibasic acids.

The anhydridization of the α,α,α′,α′-tetramethyl dibasic acids from pimelic to tetradecanedioic inclusive has been effected by heating with acetic anhydride. The anhydrides are liquids and polymeric. By dissolving the liquid anhydrides in dry ether, solid dimers separate in many cases. Molecular distillation of the liquid or solid anhydrides of tetramethyl-azelaic, undecanedioic, dodecanedioic, tridecanedioic and tetradecanedioic acids give monomeric cyclic compounds as proved by analyses, molecular weights, odor characteristics and essentially quantitative conversion to the monoamides of the dibasic acids by treatment with sodium in liquid ammonia. Molecular distillation of the anhydrides of tetramethyl-pimelic, suberic and sebacic acids resulted in mixtures of cyclic monomers and dimers.

The anhydrides obtained by molecular distillation appear to be more stable than the corresponding anhydrides obtained in a similar manner and derived from the unsubstituted dibasic acids.

URBANA, ILLINOIS

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