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A SYNTHESIS OF 2-CARBOMETHOXY-5-PENTADECYLCYCLOPENTANONE FROM BHILAWANOL

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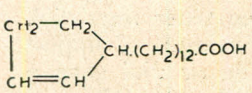
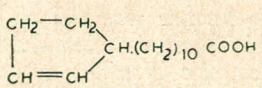
Syntheses of 2-carbomethoxy-5-pentadecylcyclopentanone and of 2-pentadecylcyclopentanone from 3-pentadecylcatechol (tetrahydrobhilawanol) is described.

The active constituent of *Semecarpus anacardium* Linn. (bhilawan), isolated and named by Pillay and Siddiqui[1] as 'bhilawanol,' was established as a derivative of catechol containing a straight unsaturated $C_{15}H_{27}$- side chain at position 3. This substance which is extremely vessicant in character, is soluble in oils but insoluble in water and dilute alkalies. The vessicating property of bhilawanol was found to depend on the two phenolic hydroxyls and the presence of two double bonds in the side chain. It was thus possible to mitigate its vessicant character by hydrogenation of the side chain or by methylation or acetylation of the two phenolic groups, while the toxicity completely disappears by a combination of the two processes yielding dimethyl or diacetyltetrahydro derivative. In view of the enormous importance ascribed to bhilawan in the indigenous systems of medicine as a cure for rheumatism, epilepsy, nervous debility, leprosy, eczema, and skin diseases in general, it was considered of interest to carry out a systematic chemotherapeutic study on its active principle, bhilawanol. Theoretical considerations based on the presence of a long side chain attached to the benzene nucleus in bhilawanol made such a study particularly significant with reference to the therapeutic properties and the structures of products like chaulmoogric and hydnocarpic acids, the cyclic acids of chaulmoogra oil.

Chaulmoogra oil and its cyclic acids have long been a subject of medical and scientific interest, due to their therapeutic value in the treatment of leprosy. It has been conclusively proved by Muir,[2] Walker and Sweeney[3] and Schobl[4] that the cyclic acids present in chaulmoogra and allied oils are responsible for their curative properties. Investigations of Dean and co-workers[5] have shown that these curative properties are likewise possessed by the ethyl esters of chaulmoogra oil fatty acids. Their investigations on the isolation and chemical constitution of the naturally occurring cyclic acids were extended by these workers to the synthesis of other closely related acids in an endeavour to correlate bactericidal activity with chemical structure. Chaulmoogric and hydnocarpic acids contain a terminal cyclopentene group and have the following structures:—



Chaulmoogric acid



Hydnocarpic acid

Since Dean, Wrenshall and Fujimoto[6] and also Schobl[7] have shown that ethyl dihydrochaulmoograte is nearly as effective as ethyl chaulmoograte in the treatment of leprosy, it is evident

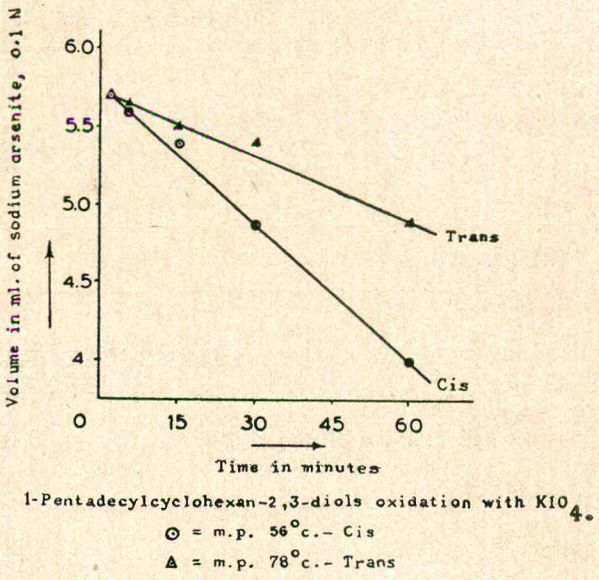
*Part of the work was carried out at the West Regional Laboratories, P.C.S.I.R., Lahore.

that the presence of an ethylenic bond in the cyclopentene ring does not play a decisive role in their curative action. Moreover, Adam et al.[8] have shown that the position of carboxyl group in the cyclic acids is of secondary importance to their bactericidal activity towards *B. leprae*, and they expressed the view that the activity is a function of the molecular weight of the acids rather than their structure.

With reference to the work and observations briefly described above, the present authors considered it of interest to synthesise 2-carbomethoxy-5-pentadecylcyclopentanone and allied derivatives from bhilawanol with a view to evaluating their activity against *B. leprae*. It was visualised that the bhilawanol molecule with two phenolic hydroxyls in *ortho* position offered the possibility of leading to this compound, which forms an interesting variant to chaulmoogric acid in so far as it would carry the COOH group directly attached to the ring bearing the long aliphatic side chain of 15 carbons, in contrast to chaulmoogric acid containing a terminal COOH group in its C_{12} side chain.

With this end in view, hydrogenation of bhilawanol was carried out under pressure, with 5% palladium charcoal catalyst, whereby the reduction of the side chain and the benzene ring was achieved in one step, yielding a mixture of 1-pentadecylcyclohexan-*cis*- and *trans*-2,3-diols. Separation of these two isomers was carried out through fractional crystallisation from acetone and they were finally obtained in pure form showing m.p. 56°C. and 80°C., respectively.

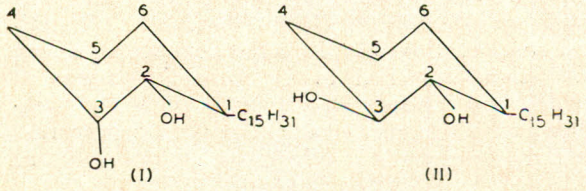
In so far as the *cis* isomers have a lower melting point than the corresponding *trans* isomers, the product melting at 56°C. could be taken as *cis* diol. However, to establish *cis* or *trans* configuration of the two OH groups, the potassium periodate oxidation rates of the two diols were compared, as it is known that the rate of oxidation of *cis* diols is faster than that of the corresponding *trans* diols.[9] The rate of oxidation of the isomer melting at 56°C. was found to be faster than that of the higher melting (80°C.) isomer, showing that the former was the *cis* and the latter *trans* diol. This conclusion found a further measure of support from the N.M.R. spectra. The *cis* diol gave a strong band at τ 6.75 with peaks at τ 6.83 and τ 6.45 representing superimposed absorption of OH and CH groups α to the OH group; the latter is normally absorbed at about τ 6.3. The *trans* diol gave bands at τ 8.77 (most of the saturated CH), τ 7.70 (OH), τ 6.15 (CHs α to OHs). It was expected that the two CH.(OH) groups would show a sufficiently resolved fine structure to



1-Pentadecylcyclohexan-2,3-diols oxidation with KIO_4.
⊙ = m.p. 56°c.– Cis
▲ = m.p. 78°c.– Trans

indicate whether they have an axial-equatorial (i.e. *cis* 2:3 diol) or axial-axial (i.e. CHs equatorial-equatorial as in *trans* 2:3-diol) conformation. Such a fine resolution, however, could not be obtained; but on the basis of another criterion, namely, that the axial CHs usually have higher values than equatorial, the CHs of the isomer m.p. 80°C. (τ 6.45) seemed to be more axial than those of the isomer m.p. 56°C., suggesting that the diol with m.p. 80°C. represents the *trans* diol system with equatorial-equatorial OH groups and consequently have axial-axial CHs.

The conformation of the two OH groups having been established, the remaining conformational structure of 1-pentadecyl-2,3-diol isomers can be worked out. It has been established that groups like the methyl and the isopropyl will prefer an equatorial to the axial conformation in cyclohexane.[10] On this basis, the pentadecyl group would prefer the equatorial conformation, and since in the 1,2-substitutions in cyclohexane diequatorial conformation is preferred, the OH



Cis: m.p., 56°C.
1. $C_{15}H_{31}$- equatorial
2. OH- ,,
3. OH- axial

Trans: m.p. 80°C.
1. $C_{15}H_{31}$- equatorial
2. OH- ,,
3. OH- ,,

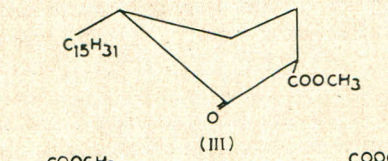
next to the pentadecyl group must also be equatorial. This means that the pentadecyl and the OH groups are *trans* to each other and consequently the second OH in the third position will be axial to the first OH in the *cis* diol (I) and equatorial in the *trans* diol (II).

The diols were characterised through their urethane derivatives. Whereas the *trans* diol gave monophenylurethane, the *cis* diol yielded the diphenylurethane under the same conditions. Methylation of the two OH groups in the *trans* diol was also attempted by preparing the Na salt in dry benzene and then reacting it with methyl iodide, but only the monomethyl derivative could be obtained. No attempt was made to separate the optical antipodes consequent upon the presence of the three asymmetric carbons.

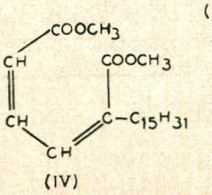
Oxidation of the two isomeric diols with lead tetraacetate gave the α-pentadecyladipic aldehyde (m.p. 87°C.), which was oxidized to the pentadecyladipic acid (m.p. 91°C.) with silver oxide. With diazomethane, the acid thus obtained gave methyl α-pentadecyladipate which, on intramolecular cyclisation with sodium methoxide in dry ether and heating the residue after removal of ether at 140°C. (5 hrs.), following the method of Kompa and Talvitie,[11] gave 2-carbomethoxy-5-pentadecylcyclopentanone (III) and not 2-carbomethoxy-2-pentadecylcyclopentanone. This was to be expected, because similar cyclisation of ethyl α-methyladipate takes place on the unsubstituted methylene group adjacent to carboethoxyl group, yielding 2-carboethoxy-5-methylcyclopentanone[12] and not on the -CH- on which both CH_3 and the carboethoxyl groups are located.

Alkaline hydrolysis of the ester resulted in the opening of the cyclopentanone ring giving α-pentadecyladipic acid. This was in accordance with the alkaline hydrolysis of 2-carbomethoxy-5-methylcyclopentanone, which lead to the opening of the ring, yielding α-methyladipic acid.[13] Demethylation with HI in acetic anhydride[14] also resulted in the formation of α-pentadecyladipic acid. Further attempt at hydrolysis with 40% BF_3 in glacial acetic acid[14] gave back unchanged material on carrying out the reaction in the cold, while α-pentadecyladipic acid was obtained when the contents were heated on water bath.

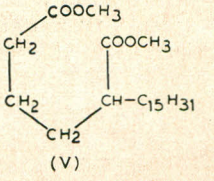
Preparation of the cyclic ketone, 2-pentadecylcyclopentanone was carried out through the destructive distillation of the barium salt of α-pentadecyladipic acid. The pale yellow 2-pentadecylcyclopentanone, which distilled over, was odourless and solidified on standing (m.p. 29°C.).



(III)



(IV)



(V)

To obtain methyl α-pentadecyladipate (V) by a shorter route, ozonisation of dimethyltetrahydrobhilawanol,[15] prepared through stepwise methylation of tetrahydrobhilawanol, was carried out. This reaction, however, gave palmitic acid instead of dimethyl α-pentadecylmuconate (IV) for further hydrogenation to the desired key intermediate (V).

Further studies in this field and work on the pharmacological activity of the cyclic ketonic ester are under way and will form the subject of a separate communication.

Experimental

All melting points are corrected. I.R. absorption spectra were determined with Beckman I.R. 5A and ultraviolet absorption spectra with a Beckman spectrophotometer Model D.U. in 95% ethanol. N.M.R. spectra were determined with Varian 60 Mc. N.M.R.

1-*Pentadecylcyclohexan*-2 : 3-*diol*.—Freshly distilled bhilawanol (19.2 g., 0.06 mole) or hydrobhilawanol (19.2 g., 0.06 mole) was dissolved in ethyl alcohol (500 ml.) containing freshly prepared Raney nickel catalyst[16] (2 teaspoonfuls) and set for hydrogenation at a pressure of 60 atmospheres and 70°C., with continuous stirring (12 hrs.). Filtration and removal of solvent gave a mixture of *cis* and *trans* isomers of 1-pentadecylcyclohexan-2,3-diol, (17.3 g., 88.4%) as a white solid. The isomers were separated through fractional crystallization from acetone, giving from the top fractions the *trans* isomer m.p. 80°C. (7.75 g., 39.5%). The residue from the mother liquor was dissolved in ether and chromatographed over Brockman's alumina, (30 cms. × 1 cm. dia. column; wt. 23 g.). The column was eluted repeatedly with ether when the *cis* isomer was obtained in pure form (8.9 g., 45.5%), m.p. 56°C.

Periodate Oxidation of the Cis and Trans Diols.—The two 1-pentadecyl-2,3-diols (m.p. 80°C. and 56°C.) (100 mg.) were each dissolved in methyl

alcohol (165 ml.) separately and aqueous potassium periodate solution (1.0%, 35 ml.) added to the solutions. At intervals of 2, 5, 15, 30 and 60 minutes, 10 ml. of each were pipetted out into iodine flasks kept in ice, and potassium iodide (100 mg.) added to each. The flasks were allowed to stand in the dark for 10 minutes and excess of iodine titrated against standard (0.1 N) sodium arsenite solution, using starch as an indicator. Following observations were recorded:—

Time in minutes	Sodium arsenite in ml.	
	Isomer m.p. 80°C.	Isomer m.p. 56°C.
2	5.70	5.70
5	5.65	5.60
15	5.50	5.40
30	5.40	4.00
60	4.90	4.00

The rate of consumption of 0.1 N sodium arsenite solution by the lower melting isomer (m.p. 56°C.) was, therefore, distinctly slower than that of the higher melting isomer showing that the isomer (m.p. 56°C.) consumed potassium periodate at a greater rate than the higher melting (m.p. 80°C.) isomer. The isomer (m.p. 56°C.) was, therefore, the *cis* and the isomer (m.p. 80°C.) the *trans* diol.

1-*Pentadecylcyclohexan-cis*-2,3-*diol*.—The *cis* diol was recrystallized from ether-light-petroleum (60-80°C.), microscopic needles, (8.2 g., 45.0%), m.p. 56°C. 1-Pentadecylcyclohexan-*cis*-2,3-diol is easily soluble in acetone, benzene, chloroform, ethyl and methyl alcohols, ethyl acetate, and sparingly in light petroleum (60-80°C.). Ultraviolet absorption bands at $\lambda_{max.}$ 275 mμ ($\log\varepsilon$ 3.2); $\lambda_{min.}$ 295 mμ ($\log\varepsilon$ 3.02). N.M.R. absorption bands at τ 8.75 with peaks at τ 6.83 and τ 6.45 representing superimposed absorption of OH and CH groups α to the OH groups; (the latter is normally absorbed at about τ 6.3). Found: C, 77.44; H, 12.76; O, 9.87. $C_{21}H_{42}O_2$ requires: C, 77.23; H, 12.96; O, 9.80.

Diphenylurethane of 1-*Pentadecylcyclohexan-cis*-2,3-*diol*.—1-Pentadecylcyclohexan-*cis*-2,3-diol (0.978 g., 0.003 mole) was refluxed (4 hrs). in light petroleum (60-80°C., 10 ml.) containing phenyl isocyanate (1.0 ml.). The diphenylurethane was collected through suction and crystallized from acetone, microscopic colourless needles, 1.7 g. (quantitative), m.p. 138°C. Diphenylurethane of 1-pentadecylcyclohexan-*cis*-2,3-diol is easily soluble in benzene, chloroform, ethyl and methyl alcohols, ethyl acetate, and sparingly in acetone. Ultraviolet absorption bands at $\lambda_{max.}$ 300 mμ ($\log\varepsilon$ 3.05); 235 mμ ($\log\varepsilon$ 3.85); $\lambda_{min.}$ 305 mμ. ($\log\varepsilon$ 2.90); 290 mμ ($\log\varepsilon$ 2.83); 265 mμ ($\log\varepsilon$ 3.39). Found: C, 74.08; H, 9.00; O, 11.91; N, 5.33. $C_{35}H_{52}O_4N_2$ requires: C, 74.43; H, 9.28; O, 11.33; N, 4.96.

1-*Pentadecylcyclohexan-trans*-2,3-*diol*.— The *trans* diol obtained above was crystallized from acetone, white shining plates, 7.24 g., (37%), m.p. 80°C. 1-Pentadecylcyclohexan-*trans*-2,3-diol is readily soluble in benzene, chloroform, carbon tetrachloride, ethyl acetate, ethyl and methyl aclohols, and sparingly in acetone. Ultraviolet absorption bands at $\lambda_{max.}$ 275 mμ ($\log\varepsilon$ 2.68); $\lambda_{min.}$ 300 mμ ($\log\varepsilon$ 2.54); 260 mμ ($\log\varepsilon$ 2.65). N.M.R. absorption bands at τ 8.77, (most of the saturated CH); τ 7.70 (OH); τ 6.15 (CHs α to OHs). Found: C, 76.93; H, 13.30; O, 9.87. $C_{12}H_{42}O_2$ requires: C, 77.23; H, 12.96; O, 9.80.

1-*Pentadecylcyclohexan - trans - 3 - methoxy -2 - ol*. — 1-Pentadecylcyclohexan-*trans*-2,3-diol (3.26 g., 0.01 mole) was refluxed (1/2 hr.) with finely divided sodium (0.5 g.) in dry benzene (50 ml.). Methyl iodide (5 ml.) was added in 1 ml. portions after every two hours and the contents refluxed (10 hrs.). Removal of solvent and addition of water (25 ml.) followed by acidification and extraction with ether, gave a reddish liquid (3.01 g., 88%), b.p. 196-200°C./0.2 mm. 1-Pentadecylcyclohexan-*trans*-3-methoxy-2-ol is soluble in practically all the bench solvents. Ultraviolet absorption bands at $\lambda_{max.}$ 275 mμ ($\log\varepsilon$ 4.01); $\lambda_{min.}$ 250 mμ ($\log\varepsilon$ 3.7). Found: C, 77.90; H, 12.41; O, 9.62 and $-OCH_3$, 8.6. $C_{22}H_{44}O_2$ requires: C, 77.58; H, 13.02; O, 9.40; $-OCH_3$, 7.98.

Monophenylurethane of 1-*Pentadecylcyclohexan-trans*-2:3-*diol*—To 1-pentadecylcyclohexan-*trans*-2:3-diol (0.978 g., 0.003 mole) dissolved in light petroleum (60-80°C., 10 ml.), phenyl isocyanate (10 ml.) was added and the contents refluxed on water bath (4 hrs.). The resulting solid was filtered through suction and crystallized from acetone, white broom-shaped crystals (1.3 g., quantitative), m.p. 116°C. Monophenylurethane of 1-pentadecylcyclohexan-*trans*-2,3-diol is readily soluble in benzene, chloroform, carbon tetrachloride, ethyl and methyl alcohols, ethyl acetate, and sparingly in acetone. Ultraviolet absorption bands at $\lambda_{max.}$ 300 mμ ($\log\varepsilon$ 3.24); 265 mμ ($\log\varepsilon$ 3.44); $\lambda_{min.}$ 2.80 mμ ($\log\varepsilon$ 3.08); 250 mμ ($\log\varepsilon$ 3.04). Found: C, 76.09; H, 10.58; O, 10.42; N, 3.00. $C_{28}H_{47}O_3N$ requires: C, 75.46; H, 10.63; O, 10.77; N, 3.14.

α-Pentadecyladipaldehyde.–To 1-pentadecylcyclohexan-*cis*-or *trans*-2,3-diol (0.98 g., 0.003 mole), in dry benzene (400 ml.), freshly prepared lead tetraacetate (1.5 g.; 0.004 mole) was added, the mixture shaken for 72 hrs. and diluted with water (150 ml.). The benzene layer was separated, washed a few times with water and dried. Removal of the solvent gave a pale yellow oil (0.93 g.), which crystallized on standing. On recrystallization from ether-light-petroleum (60-80°C.), microscopic needles were obtained (0.91 g., 93%), m.p. 78°C. α-Pentadecyladipaldehyde is easily soluble in acetone, benzene, chloroform, ethyl and methyl alcohols and light petroleum (60-80°C.). Ultraviolet absorption bands at λmax. 315 mμ (log ε 2.26); 280 mμ (log ε 2.74); 245 mμ (log ε 2.98); λmin. 305 mμ (log ε 2.25); 270 mμ (log ε 2.72), and I.R. absorption band at 1738 cm.$^{-1}$ (-CHO) (Nujol mull). Found: C, 78.00; H, 12.10; O, 9.8. $C_{21}H_{40}O_2$ requires: C, 77.72; H, 12.42.O, 9.86.

α-Pentadecyladipic Acid.— α-Pentadecyladipaldehyde (9.69 g., 0.03 mole) was refluxed with freshly prepared silver oxide (7 g., 0.03 mole), diluted with 2 volumes of hot water, filtered and the filtrate acidified with hydrochloric acid and extracted with ether. On drying the extract and removal of the solvent, a solid mass was left (7.79 g., 75%) which gave α-pentadecyladipic acid in the form of microscopic needles when crystallized from light petroleum (60-80°C.) (7.47 g., 72%), m.p. 91°C. It is easily soluble in acetone, benzene, chloroform, ether, ethyl acetate, ethyl and methyl alcohols, and sparingly in light petroleum (60-80°C.). Ultraviolet absorption bands at λmax. 270 mμ (log ε 3.25); λmin. 295 mμ (log ε 3.07) and I.R. absorption band at 1709 cm.$^{-1}$ (CO of COOH) (Nujol mull). Found: C, 71.19; H, 11.00; O, 17.85. $C_{21}H_{40}O_4$ requires: C, 70.74; H, 11.31; O, 17.95.

Methyl α-Pentadecyladipate.—α- Pentadecyladipic acid (10.74 g., 0.03 mole) was dissolved in ice-cold ether (100 ml.) and treated with a slight excess of ethereal solution of diazomethane (prepared from 10 g. of N-nitrosomethylurea) and left overnight in the refrigerator. Excess of diazomethane was decomposed with HCl. Drying and removal of ether gave methyl α-pentadecyladipate as a golden yellow liquid (9.2 g., 79%), b.p. 158-172°C./0.4 mm. It is easily soluble practically in all the bench solvents. Ultraviolet absorption bands at λmax. 305 mμ (log ε 2.29); 295 mμ (log ε 2.48); 270 mμ (log ε 3.31); λmin. 300 mμ. (log ε 2.21); 290 mμ (log ε 2.57); 250 mμ (log ε 3.13) and I.R. absorption bands at 2960 cm.$^{-1}$; 2880 cm.$^{-1}$ (-CH_2-, CH_3-) and at 1750 cm.$^{-1}$ (CO of -$COOH_3$) (in Nujol mull) .Found: C, 71.79; H, 11.41, O, 16.62. $C_{23}H_{44}O_4$ requires: C, 71.83; H, 11.53; O,16.64.

Cyclisation of Methyl α-Pentadecyladipate

2-Carbomethoxy-5-pentadecylcyclopentanone.— Methyl α-pentadecyladipate (1.92 g., 0.005 mole) was taken up in dry ether (50 ml.) containing sodium methylate (0.54 g., 0.01 mole), allowed to stand (0.5 hr.) until homogeneous, and freed of the solvent. The residue was heated at 140°C. for 5 hrs., acidified with dilute sulphuric acid (10%) and extracted with ether. On drying the ethereal extract and removal of the solvent 2-carbomethoxy-5-pentadecylcyclopentanone was obtained as a colourless mass which crystallized from dilute methyl alcohol (1.55 g., 88%), m.p. 40°C. (1.64 g., 99%). Ultraviolet absorption bands at λmax. 305 mμ (log ε 2.62); 290 mμ (log ε 2.91); 265 mμ (log ε 3.52) λ min. 300 mμ (log ε 2.49); 2.82 mμ (log ε 2.19); 250 mμ (log ε 3.25) and infra-red absorption bands at 1740 cm.$^{-1}$ (CO in cyclopentanone)[16]; 1670 cm.$^{-1}$ (>CO of the ester) and 1630 cm.$^{-1}$ (>C=C.OH). Found: C, 74.32; H, 11.44; O, 13.73 and -OCH_3, 9.06. $C_{22}H_{40}O_3$, requires: C, 74.95; H, 11.94; O, 13.62 and -OCH_3, 8.8.

2 - Carbomethoxy-5-pentadecylcyclopentanone is not hydrolysed with 40% BF_3 in acetic acid in the cold. On warming on water bath for 6 hrs. the ring opens up to yield 2-pentadecyladipic acid. Alkaline hydrolysis with 10% alcoholic KOH similarly results in the opening up of the ring. Demethylation with HI in acetic anhydride similarly gives the 2-pentadecyladipic acid. This acid was identified by its undepressed mixed melting point with an authentic sample of the material and its identical U.V. and I.R. absorption bands.

2 - *Pentadecylcyclopentanone.*— α-Pentadecyladipic acid (1.07 g., 0.003 mole) was dissolved in alcohol (25 ml.), and neutralised with 10% alcoholic potassium hydroxide, using phenolphthalein as an indicator. The residue left on removal of the solvent was taken up in water and a saturated solution of barium hydroxide added to it. The barium salt of the acid which precipitated out, was sucked, dried (1.25 g.) and subjected to destructive distillation with a smoky flame under vacuum (0.8 mm.). 2-Pentadecylcyclopentanone was obtained as an odourless pale yellow distillate which congealed on cooling to a semi-crystalline mass. Purified through distillation, b.p. 215-220°C. /0.8 mm. It crystallized from dilute methyl alcohol, (0.8 g., 90.8%), m.p. 29°C. The cyclic ketone is soluble in all the bench solvents. It gives infra-

red absorption band at 1740 cm.$^{-1}$ (CO in cyclopentanone),[17] (in chloroform). Found: C, 81.89; H, 12.93; O, 5.35. $C_{20}H_{38}O$ requires: C, 81.56; H, 13.01; O, 5.43.

Monomethyltetrahydrobhilawanol.— Tetrahydrobhilawanol[1] (1.6 g., 0.005 mole) dissolved in alcoholic potassium hydroxide (50%, 5 ml.) was treated dropwise with dimethyl sulphate (2 ml.) with shaking and cooling (1/2 hr.) and the mixture refluxed on sand bath (1 hr.). On working up the reaction mixture in the usual way the monomethyl derivative was obtained as a brownish oil (0.70 g., 44%), b.p. 190-200°C./1.5 mm., m.p. 52 °C. It is readily soluble in the usual organic solvents. Found: C, 78.51; H, 11.44; O, 9.46 and $-OCH_3$, 9.50. Monomethyltetrahydrobhilawanol, $C_{22}H_{38}O_2$, requires: C, 78.98; H, 11.45; O, 9.57; and $-OCH_3$, 9.28.

Dimethyltetrahydrobhilawanol

(*a*) *From Tetrahydrobhilawanol.*—Tetrahydrobhilawanol (1.6 g., 0.005 mole) was dissolved in dry acetone (25 ml.) containing anhydrous potassium carbonate (2.5 g.) and methyl iodide (1 ml.) and refluxed. Methyl iodide (10 ml.) was added in 1 ml. portions after every two hours and the contents refluxed (10 hrs.). Removal of solvent, gave an oily mass which crystallized from toluene in microscopic colourless needles (1.0 g., 62.5%), m.p. 36°C.[15]

(*b*) *From Monomethyltetrahydrobhilawanol.*— To monomethyltetrahydrobhilawanol (3.34 g., 0.01 mole) in pure dry acetone (50 ml.), containing anhydrous potassium carbonate (5 g.), methyl iodide (5 ml.) was added and the contents refluxed. Methyl iodide (20 ml.) was added in 1 ml. portions after every 1 hr. and a drop was tested with ferric chloride. Methylation was complete after about 24 hrs. Removal of solvent gave dimethyltetrahydrobhilawanol as an oily mass which crystallized from toluene (3.4 g., m.p. 36°C.[15]). Dimethyltetrahydrobhilawanol is soluble practically in all bench solvents. Found: C 79.5; H, 11.44; O, 9.46. $C_{23}H_{40}O_2$ requires: C, 79.25; H, 11.57; O, 9.18.

Ozonolysis of Dimethyltetrahydrobhilawanol.—Dimethyltetrahydrobhilawanol (1.4 g., 0.003 mole) in dry chloroform (60 ml.) was cooled to – 20°C. and ozonized oxygen was passed (1/2 hr.). Removal of chloroform gave an oily residue which was treated with 10% aqueous sodium carbonate (5 ml.) and 20% hydrogen peroxide (5 ml.). After the vigorous effervescence had subsided, 5% alcoholic solution of potassium hydroxide (10 ml.) was added and the contents heated on water bath (3 hrs.). Ethyl alcohol was removed *in vacuo*, water was added and the contents repeatedly extracted with ether. Drying and removal of ether gave the unreacted dimethyltetrahydrobhilawanol (0.35 g.). The aqueous phase was acidified with dilute hydrochloric acid and extracted with ether. The colourless waxy residue left on removal of the solvent was crystallized from ether-light-petroleum (60-80°C.), 0.63 g., m.p. 62 °C., undepressed on admixture with an authentic sample of palmitic acid. Found: C, 74.77; H, 12.44 ; O, 12.54; M.W. (Rast), 246. Palmitic acid, $C_{16}H_{32}O_2$, (M.W. 256) requires: C, 74.94; H, 12.58; O, 12.48.

Anilide (m.p. 90 °C.) and amide (m.p. 106°C.) were also identical with the corresponding palmitic acid derivatives.

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