Tetrahedron, 1966, Vol. 22, pp. 1495 to 1498. Pergamon Press Ltd. Printed in Northern Ireland

ISOLATION AND CONSTITUTION OF PEDICELLIC ACID

A NEW DICARBOXYLIC ACID FROM THE LEAVES OF *DIDYMOCARPUS PEDICELLATA**

K. V. RAO,† T. R. SESHADRI and M. S. SOOD
Department of Chemistry, University of Delhi, India

(*Received* 4 *November* 1965; *in revised form* 25 *November* 1965)

Abstract—Pedicellic acid ($C_{18}H_{34}O_4$) obtained from the leaves of *Didymocarpus pedicellata* is a dicarboxylic acid. Its UV and IR spectra indicate that it is a long chain aliphatic acid without unsaturation. The NMR spectrum of its dimethyl ester confirms the molecular formula and shows the presence of two different C-methyl groups and two identical carboxylic groups.

Pedicellic acid has been converted into the corresponding hydrocarbon called pedicellane. The constitution of the acid as α-methyl-α′-tridecylsuccinic acid has been established.

A CHEMICAL investigation of the leaves of *Didymocarpus pedicellata* (Gesneriaceae), well known for their medicinal properties,[1] was first carried out by Siddiqui *et al.*,[2] who reported the presence of chalkones,[3] flavanones[4] and fatty material[5] which gave on saponification saturated long chain fatty acids. During re-investigation of these medicinal leaves, a new dicarboxylic acid has been isolated and named *pedicellic acid.*

Pedicellic acid is a crystalline solid, m.p. 92–93°; corresponding to $C_{18}H_{34}O_4$ with carboxyl as the only functional group. The UV spectrum has no characteristic absorption and the IR spectrum has strong absorption at 1709 cm^{-1} ($>C{=}O$), a band at 2941 cm^{-1} ($-CH_2$) and another at 720 cm^{-1} attributable to a chain of four or more methylene groups. Pedicellic acid should, therefore, be a long chain aliphatic acid. Conductometric titration with sodium methoxide indicated the presence of two carboxylic groups of similar nature. Further, pedicellic acid gives a positive fluorescein reaction indicating the presence of a succinic or glutaric acid skeleton. Volumetric titration using a non-aqueous medium (pyridine; sodium methoxide) showed that its equivalent weight is 157 and therefore, its mol. wt. should be 314 which is in accordance with the proposed molecular formula.

The NMR spectrum of the dimethyl ester of pedicellic acid gives a total proton count of 34. The singlet at 6·38 τ integrating to 6 protons, is due to the methyl groups of the diester, and this confirms the results of conductometric titration that the

---

* This paper was presented at IUPAC symposium on Natural Products held in Kyoto, Japan (1964).

† Present address: Chemistry Division, Cancer Chemotherapy Unit, Chaz Pfizer, Maywood, New Jersey.

[1] R. N. Chopra, I. C. Chopra, K. L. Handa and L. D. Kapoor, *Indigenous drugs of India* (2nd Edition) p. 33 U.N. Dhur & Sons, Calcutta-12 (1958).

[2] S. Siddiqui, *J. Indian Chem. Soc.* **14**, 703 (1937).

[3] V. Sharma and S. Siddiqui, *J. Indian Chem. Soc.* **16**, 1 (1939).

[4] G. S. Krishana Rao, K. V. Rao and T. R. Seshadri, *Proc. Indian Acad. Sci.* **28A**, 198 (1949); T. R. Seshadri, *Rev. Pure & Applied Chem.* **1**, 186 (1951).

[5] S. Warsi and S. Siddiqui, *J. Indian Chem. Soc.* **16**, 423 (1939).

two carboxylic groups are of identical nature. The signal at 8·65 τ is indicative of methylene groups and the integrated intensity shows that it contains 24 protons as 12 methylene groups. The signals at 9·15 τ and 9·25 τ correspond to the C-methyl groups of non-identical nature.

When pedicellic acid was treated with dicyclohexyl carbodiimide a quantitative yield of dicyclohexylurea was obtained indicating the ready elimination of a molecule of water. The product analysed for $C_{18}H_{32}O_3$ and proved to be an anhydride which was also obtained by the acetic anhydride–pyridine method.

Reduction of the dimethyl ester of pedicellic acid with LAH employing the conditions of Downing *et al.*,[6] afforded the corresponding diol, $C_{18}H_{38}O_2$, with an IR spectrum showing a band at 3400 cm^{-1}, characteristic of an alcoholic hydroxyl group. The diol on treatment with iodine and red phosphorus gave a diiodide which on reduction with LAH afforded a hydrocarbon, $C_{18}H_{38}$, with an IR spectrum characteristic of an aliphatic hydrocarbon. It has been named *pedicellane*.

The structure of pedicellic acid as an α,α′-disubstituted succinic acid was established by further chemical evidence. It was subjected to Schmid's reaction when the corresponding diamine was obtained. This on treatment with nitrous acid yielded a C_{16} glycol (1,2-diol) which on periodic acid cleavage gave rise to two aldehydic fragments. One was identified as acetaldehyde; and the other characterized as myristic aldehyde by its oxidation to myristic acid. Hence pedicellic acid is α-methyl-α′-tridecylsuccinic acid. The diol should therefore be 2-methyl-3-tridecylbutane-1,4-diol and pedicellane, 2-methyl-3-tridecylbutane. Though the acid is apparently optically inactive, its derivatives e.g. anhydride and 2-methyl-3-tridecylbutane-1,4-diol show dextro-rotation.

EXPERIMENTAL

All m.ps are uncorrected. Rotations were taken in $CHCl_3$ solution. The pet. ether had b.p 60–80°. The IR spectra were recorded on Perkin–Elmer spectrophotometer.

Isolation. The dried leaves of *Didymocarpus pedicellata* were obtained from Dehra Dun in October, 1960. The coarse powder (2 kg) was extracted 4 times with ether (1 l. each time) in a Soxhlet, each extraction being carried out for 4 days. The solvent was removed from the combined extracts and the concentrate shaken with 5% $NaHCO_3$aq (20 × 100 ml). The clear alkaline solution was acidified with cold HCl and the mixture kept in a refrigerator for 2 days. The solid thus deposited was filtered off and dried in a vacuum desiccator. The dried mass was extracted with hot benzene (500 ml) and the benzene extract filtered from insoluble impurities and concentrated under red. press. when it yielded pedicinin (25 g). The red pigment was filtered off and crystallized from $CHCl_3$ when pure pedicinin (20 g) was obtained as red needles, m.p. 202–203° (Lit.,[3] 202–203°).

Pet. ether (200 ml) was added to the mother liquor obtained after filtering off pedicinin when resinous impurities precipitated. These were filtered off and the filtrate kept in the ice chest for 2 days when pedicellic acid separated as a pale yellow crystalline solid, m.p. 90–93°. It was finally crystallized from aqueous alcohol and obtained (20 g) as colourless silky needles, m.p. 92–93°. (Found: C, 68·2; H, 11·0. $C_{18}H_{34}O_4$ requires: C, 68·7; H, 10·9%.) It gives a positive fluorescein reaction. The UV spectrum did not show any characteristic absorption. The IR spectrum (KBr) included the following peaks: 2941, 2740, 1709, 1471, 1439, 1408, 1351, 1316, 1250, 1255, 1205, 1190, 1163, 1020, 971, 720 and 676 cm^{-1}.

Anhydride of pedicellic acid

(a) *Reaction with dicyclohexyl carbodiimide.* Pedicellic acid (0·31 g) was dissolved in dry ether (50 ml) and dicyclohexyl carbodiimide (0·2 g) added. The reaction mixture was stirred for 4 hr and

---

[6] D. T. Downing, Z. H. Kranz and K. E. Murray, *Austral. J. Chem.* **13**, 80 (1960).

the colourless crystalline solid that separated filtered off and dried (0·22 g), m.p. 225–226°; mixed m.p. with an authentic sample of dicyclohexylurea was undepressed.

The filtrate was evaporated; and the residue crystallized from $CHCl_3$ as colourless plates (0·2 g), m.p. 63°. (Found: C, 73·7; H, 11·5. $C_{18}H_{32}O_3$ requires: C, 73·0; H, 11·0%), $[\alpha]_D^{29}$ + 9·9 (*c*, 0·605).

(b) *Reaction with acetic anhydride pyridine*. A solution of pedicellic acid (0·1 g) in acetic anhydride (10 ml) and pyridine (2 ml) was heated on a boiling water bath for 10 min and then allowed to stand overnight at room temp. The mixture was poured over crushed ice to decompose the excess acetic anhydride. The colourless solid which separated out was filtered off, washed with water and dried. Crystallization from $CHCl_3$ yielded colourless plates (0·05 g), m.p. 63° either alone or on admixture with a sample obtained by method (a).

Conversion into hydrocarbon

(a) *Pedicellic acid dimethyl ester*. A mixture of pedicellic acid (0·2 g), absolute MeOH (10 ml), dry benzene (5 ml) and conc. H_2SO_4 (2 ml) was refluxed for 6 hr. The solvent was removed under red. press. and the residue poured over crushed ice. The solution was extracted with ether and the ether washed with 5% Na_2CO_3aq to remove unreacted acid. The ether extract was washed with water and dried over Na_2SO_4. On removal of the solvent, the dimethyl ester was obtained as a viscous oil (0·2 g). The IR spectrum (in CCl_4) includes the following peaks: 3030, 2857, 1754, 1724, 1562, 1460, 1430, 1342, 1250, 1140, 1099 and 1053 cm^{-1}. The NMR spectrum of the dimethyl ester (in $CDCl_3$) was taken using TMS as the internal standard. It contains the following signals: Singlet at $\tau = 6{\cdot}38$ (6H; 2-$COOCH_3$) singlet at $\tau = 8{\cdot}65$ (24H; 12-CH_2), singlet at $\tau = 9{\cdot}15$ (3H; C-CH_3) and singlet at $\tau = 9{\cdot}25$ (3H; C-CH_3).

(b) *The* (C_{18}) 1,4-*diol*. A suspension of LAH (0·4 g) in dry ether (100 ml) was refluxed on a water bath, and a solution of the dimethyl ester (0·2 g) in dry ether was added dropwise during the course of 2 hr, the mixture was then refluxed for a further 6 hr. It was cooled in ice and cold dil. HCl added dropwise to decompose the complex. The reaction mixture was extracted with ether, the ether layer washed with dil. HCl, and then with water and dried over Na_2SO_4. On removal of the solvent, the dried ether extract afforded a colourless solid which on crystallization from pet. ether was obtained as colourless plates (0·12 g), m.p. 73–75°. (Found: C, 75·4; H, 13·1. $C_{18}H_{38}O_2$ requires: C, 75·5; H, 13·4%), $[\alpha]_D^{29}$ + 6·3 (*c*, 1·57). The IR spectrum (nujol) includes the following characteristic peaks: 3400, 2985 and 720 cm^{-1}.

(c) *Conversion of diol into* Pedicellane. (i) A mixture of above diol (0·1 g), I_2 (0·3 g), and red phosphorus (0·05 g) was heated on a oil bath between 110–130° for 2 hr. The mixture was cooled, filtered and the filtrate poured over crushed ice. It was extracted with ether, the ether layer washed with 5% $Na_2S_2O_3$aq to remove the excess of I_2 and then with water and dried over Na_2SO_4. On removal of solvent the diiodide was obtained as a pale yellow viscous oil.

(ii) A suspension of LAH (0·2 g) in dry ether (100 ml.) was refluxed on a water bath, and a solution of the above diiodide in dry ether was added dropwise during the course of 2 hr. The mixture was then worked up as in the case of the reduction of pedicellic dimethyl ester. The hydrocarbon was obtained as a viscous oil and was purified by passing through an alumina column in pet. ether. (Found: C, 85·0; H, 14·5. $C_{18}H_{38}$ requires: C, 85·0; H, 14·9%.) The IR spectrum (thin film) includes the following characteristic peaks: 3030, 2985, 2935, 1475, 1385, and 1370 cm^{-1}.

Conversion of pedicellic acid into the corresponding 1:2 *diol*

(a) *Conversion into the diamine*. A mixture of pedicellic acid (0·5 g), dry $CHCl_3$ (25 ml), conc. H_2SO_4 (2 ml) and sodium azide (0·2 g) was stirred with a magnetic stirrer for 2 hr, the mixture being kept at 40–50°. It was cooled and the $CHCl_3$ layer was decanted off. The aqueous layer was diluted with water (100 ml) when the diamine separated out as its disulphate. It was decomposed with 5% NaOHaq (200 ml) and the free diamine extracted with ether. The ether layer was washed with water and dried over Na_2SO_4; removal of the solvent afforded the diamine (0·05 g) as a low melting solid. It gave a positive test for N_2 and was soluble in HCl.

(b) *Conversion into diol*. A solution of diamine (0·05 g) in conc. HCl (10 ml) was cooled to 0° and 10% $NaNO_2$aq (20 ml.) added. The mixture was kept for 2 hr at room temp, then extracted with ether, the ether layer washed with water and dried over Na_2SO_4. On removal of the solvent, the C_{16} glycol) (1,2-diol was obtained as a colourless solid.

Fission of the skeleton by periodic acid oxidation

The 1,2-diol was dissolved in alcohol (20 ml) and the solution treated with periodic acid (1·5 ml; 5% w/w). The mixture was then warmed to 40° and kept at that temp for 4 hr. It was diluted with water (100 ml) and steam distilled. The steam distillate was treated with 2,4-dinitrophenylhydrazine, yeilding an orange precipitate. This crystallized from alcohol, m.p. 144–146° alone or when mixed with an authentic sample of 2,4-dinitrophenylhydrazone of acetaldehyde. R_f values of both the samples on an ascending paper chromatogram (solvent system, pet. ether saturated with alcohol) were 0·92.

A saturated solution of $KMnO_4$ (10 ml) and Na_2CO_3aq was added to the non-volatile fraction. The mixture was kept at room temp for 2 hr, acidified with dil. HCl and decolourized with SO_2. The solution was extracted with ether, the ether layer washed with water and dried over Na_2SO_4. On concentration a colourless solid was obtained which was identified as myristic acid by a chromatographic comparison with an authentic sample. The chromatogram was run on paper coated with paraffin using acetic acid as solvent system and developed with copper acetate. Further confirmation was done by the conversion of the acid into its amide, which was found to be identical with that of myristic acid by direct comparison.