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PREPARATION AND CONSTITUTION OF *ISO*PINASTRIC ACID

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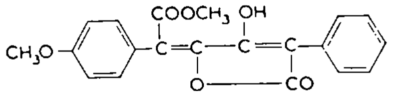
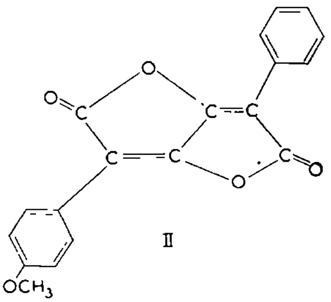
Abstract—In the synthesis of pinastric acid by Volhard's method the alcoholysis of 4-methoxypulvinic dilactone yields pinastric acid and an equal amount of an isomeric compound having the same chemical properties as pinastric acid and giving the same degradation products, but differing in physical properties and in the properties of the derivatives. The new compound is therefore a stereoisomer and is named *iso*pinastric acid. It seems to be the *trans-trans* form with reference to the 1 : 4-diphenylbutadiene system, pinastric acid being *cis-trans*. This interpretation is supported by the study of absorption spectra.

IN a recent publication (Mittal and Seshadri[1]) the isolation of pinastric acid from *Lepraria flava* was reported and a revised constitution (I) was suggested based on its reaction with *o*-phenylenediamine. With a view to studying this question more thoroughly, its synthesis was carried out by the method of Volhard.[2] 4-Methoxypulvinic dilactone (II) was obtained as an intermediate and it had all the properties recorded by Asano and Kamada.[3] When subjected to treatment with absolute methanolic potash or methanolic hydrochloric acid, a mixture of two products (in almost equal amounts) was obtained and not pinastric acid as reported by earlier workers. The mixture could be separated by fractionation from methanol. The sparingly soluble first fraction, when crystallised from benzene, agreed in all its properties with naturally occurring pinastric acid (I), m.p. 202-204°. The more soluble second fraction had a much lower melting point, 120-121°, but had the same composition, two methoxyl groups and similar properties. Parallel study has been made of the derivatives of the two compounds; the carboxylic acids obtained by ester hydrolysis, the methyl ethers and acetates formed two different series. As compared with pinastric acid derivatives, the new series was characterised by lower melting points and higher solubility. But both the isomers, when hydrolysed and



I



II

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[1] O. P. Mittal and T. R. Seshadri, *J. Chem. Soc.* 1734 (1956).
[2] J. Volhard, *Liebigs Ann.* **282**, 1 (1894).
[3] M. Asano and Y. Kamada, *Ber. Dtsch. Chem. Ges.* **67B**, 1522 (1934).

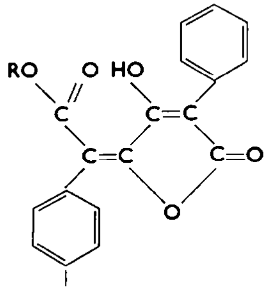
subjected to dehydration, yielded the same 4-methoxypulvinic dilactone (II). There is therefore no doubt that the two compounds are closely related.

In order to investigate if the isomerism was due to the difference in position of the nuclear methoxyl group, each of the isomers was condensed with *o*-phenylenediamine,[4] and the iminazole derivative obtained in each case was subjected to fission with potassium hydroxide; the same 4-methoxybenzylbenziminazole was formed. Hence it could be concluded that the nuclear methoxyl was attached to the same phenyl ring near to the ester group in both cases. It would therefore follow that the isomerism is stereoisomerism and hence the new low-melting isomer is named *iso*pinastric acid. More information about the isomer was provided by the following observations:

(1) Methylation of the dilactone (II) under mild conditions, the use of strong alkali being avoided, yielded only *iso*pinastric acid derivatives. With 1 mole of methyl sulphate and potassium carbonate in boiling acetone solution, a mixture of *iso*pinastric acid and its methyl ether was obtained, some of the dilactone remaining unchanged. With 2 moles of methyl sulphate the product was only *iso*pinastric acid methyl ether.

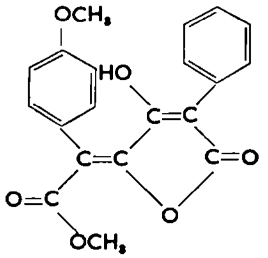
(2) *iso*Pinastric acid, when subjected to heat or heated with N-dimethylaniline or treated with absolute methanolic potash in the cold, underwent slow conversion into pinastric acid.

These observations are satisfactorily explained if *iso*pinastric acid (IIIb) is considered to be the *trans–trans* form of the 1:4-diphenylbutadiene system and pinastric acid (IV) to be the *cis–trans* form. This conclusion is supported by the ultra-violet absorption spectra (Fig. 1). The dilactone (*trans–trans*, II) and *iso*pinastric acid (IIIb) agree closely in the nature of the curves and positions of the maxima (270 and 310 mμ). Pinastric acid (*cis–trans*) has the maximum at a lower wavelength (295 mμ); as was earlier found in unsubstituted 1:4-diphenylbutadiene,[5] here also the lowering is 15 mμ. In the case of *trans-* and *cis*-stilbenes also the same difference is found. The infra-red spectra of the isomers do not have marked differences.



(III)

(*trans–trans*)



(IV)

(*cis–trans*)

(a) R = H (b) R = CH_3

In contrast with unsubstituted 1:4-diphenylbutadiene in which the *trans–trans* form is the stablest under the influence of chemical catalysts, in the present case the

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[4] O. P. Mittal and T. R. Seshadri, *J. Chem. Soc.* 3053 (1955).

[5] J. H. Pinkard, B. Wille and L. Zechmeister, *J. Amer. Chem. Soc.* **70**, 1938 (1948).

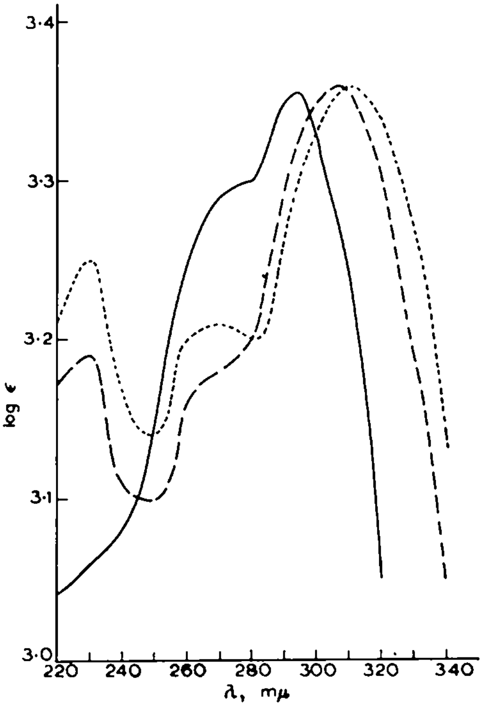
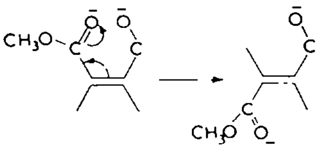
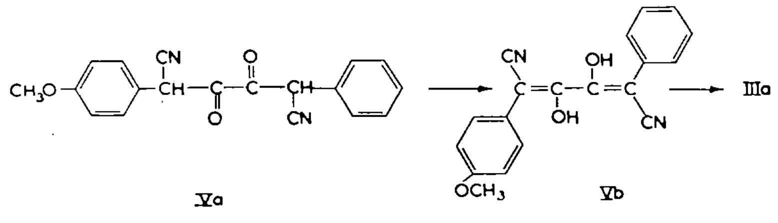


FIG. 1. Ultra-violet spectra in methanol solution; ——— pinastric acid; — — — *iso*pinastric acid; - - - - - - 4-methoxypulvinic dilactone.

cis-trans form seems to be somewhat more stable. This could be attributed to polar influences between the —CO_2R and —OH groups, which may tend to repel each other and provide the driving force for the inversion. The mechanism can be represented as given below:



The change from *trans-trans* to *cis-trans* seems to be more easily effected under the conditions of the lactone ring fission by means of alcoholic potash or hydrochloric acid. In the course of this work the observation was made that 4-methoxydiphenylketipinic acid dinitrile (Va), prepared as an intermediate in the synthesis of 4-methoxypulvinic dilactone, yields on acid hydrolysis mostly 4-methoxypulvinic acid (*trans-trans* form) along with a small amount of the *cis-trans* form. This would indicate



that the *trans-trans* structure (Vb) of the dinitrile is probably the most stable and that isomeric change takes place only to a small extent in the course of the acid hydrolysis.

EXPERIMENTAL

Preparation of pinastric acid (IV) *and* iso*pinastric acid* (IIIb)

(i) 4-Methoxypulvinic dilactone (0·5 g) was dissolved in 2% absolute methanolic potash (150 ml) and the solution was allowed to stand for ½ hr. It was cooled in ice and acidified with dilute hydrochloric acid. The solid that separated was filtered off, dried and boiled with methanol and the solution was filtered. The undissolved portion crystallised from benzene as orange rectangular plates, m.p. 202-204°; the mixed m.p. with pinastric acid was undepressed. It agreed in all its properties with pinastric acid. The filtrate was concentrated, when a pale-orange coloured solid separated as fine needles (*iso*pinastric acid), m.p. 120-121° (Found: C, 68·3; H, 4·8; —OCH_3, 17·5. $C_{20}H_{10}O_6$ requires C, 68·2; H, 4·5; —OCH_3, 17·6 per cent). The two compounds were obtained in almost equal amounts.

(ii) The dilactone (0·5 g) was heated under reflux with methanol (25 ml) and hydrochloric acid (2 ml) for ½ hr. Methanol was removed under reduced pressure and water was added. The solid product was found to be the same as obtained in expt. (i) and the yields of the two acids were equal.

Carboxylic acid derivatives

(i) *Hydrolysis of* iso*pinastric acid. iso*Pinastric acid (0·1 g) was heated under reflux with 2% barium hydroxide (20 ml) for 10 min. The solution was cooled and acidified. The solid that separated was filtered off, dried and recrystallised from a mixture of ether and light petroleum (boiling range 40–60°) to yield orange coloured rectangular prisms of *trans-trans*-4-methoxypulvinic acid, m.p. 207–209° (Found: C, 67·8; H, 3·7; $C_{19}H_8O_6$ requires C, 67·5; H, 4·1 per cent). Hydrolysis of pinastric acid also gave a carboxylic acid having m.p. 207–209° (*cis-trans*). However, the mixed m.p. with the sample from *iso*pinastric acid was depressed (189–195°).

(ii) *Hydrolysis of 4-methoxydiphenylketipinic acid dinitrile*[3] (Va). The dinitrile (0·5 g), glacial acetic acid (5 ml), concentrated sulphuric acid (2 ml) and water (4 ml) were heated under reflux for 2 hr, cooled and diluted with water. The solid that separated was filtered off, dried and recrystallised from a mixture of chloroform and light petroleum (boiling range 40–60°), to give a product having m.p. 207–209°. It agreed in all its properties with the sample (*trans-trans*-carboxylic acid) obtained by the hydrolysis of *iso*pinastric acid with barium hydroxide; the mixed m.p. was undepressed.

The crude carboxylic acid obtained in the above described experiment (0·2 g), m.p. 172–184° was heated under reflux with acetone (20 ml), potassium carbonate (1 g) and dimethyl sulphate (0·03 ml, 1 mole) for 3 hr. After the potassium salts had been filtered off, acetone was distilled off from the filtrate and water was added to the residue. The solid product was treated with 5% aqueous sodium bicarbonate. The undissolved portion was dried and recrystallised from ethyl acetate and light petroleum (boiling range 40–60°) to yield yellow rhombohedral prisms (50 mg), m.p. 129–131°. The mixed m.p. with *iso*pinastric acid methyl ether was undepressed. The bicarbonate extract was acidified and the solid that separated was filtered off, dried and boiled with methanol. A small amount that remained undissolved crystallised from benzene and light petroleum (boiling range 40–60°) as orange plates (15 mg), m.p. 202–204° (pinastric acid). The filtrate was concentrated, when orange coloured needles separated (70 mg), m.p. 120–121° (*iso*pinastric acid). The formation of *iso*pinastric (*trans–trans*) and pinastric (*cis–trans*) acids was therefore in the ratio of 8 to 1 and the yield of the *trans–trans* and *cis–trans* carboxylic acids should also have been in the same ratio.

The carboxylic acid (*trans–trans*) obtained by the ester hydrolysis of *iso*pinastric acid was heated under reflux with acetic anhydride (5 ml) for ½ hr. Acetic anhydride was removed under reduced pressure and the solid was recrystallised from benzene to yield yellow needles, m.p. 194–196°. The mixed m.p. with an authentic sample of 4-methoxypulvinic dilactone was undepressed.

iso*Pinastric acid methyl ether*

(i) *iso*Pinastric acid (0·1 g), acetone (20 ml), potassium carbonate (2 g) and excess of methyl iodide were heated under reflux for 3 hr. The solid product was dried and recrystallised from a mixture of ethyl acetate and light petroleum (boiling range 40–60°) to yield yellow thick rectangular prisms, m.p. 129–131° (Found: C, 68·6; H, 5·1; $C_{21}H_{18}O_6$ requires C, 68·8; H, 4·9 per cent). M.p. of pinastric acid methyl ether is 150–151°.

(ii) The carboxylic acid (*trans–trans*) (0·1 g) obtained by the two methods mentioned above, acetone (20 ml), potassium carbonate (2 g) and excess of methyl iodide were used and the product was worked up as described in (i) above. The yellow solid was dried and recrystallised from a mixture of ether and light petroleum (boiling range 40–60°) to yield yellow thick rectangular prisms, m.p. 129–131°. The mixed m.p. with the sample prepared as described in (i) was undepressed.

(iii) The dilactone when treated with 1 mole of dimethyl sulphate under the same conditions as mentioned below gave a mixture of *iso*pinastric acid and its methyl ether, some dilactone remaining unchanged. *iso*Pinastric acid was separated from the mixture with 5% aqueous bicarbonate. The methyl ether was separated from the dilactone by fractional crystallisation from ethyl acetate and light petroleum (boiling range 40–60°), when the methyl ether crystallised first and the dilactone later. 4-Methoxypulvinic dilactone (II) (0·2 g), acetone (40 ml), potassium carbonate (4 g) and dimethyl sulphate (2 moles, 1 ml) were heated under reflux for 3 hr. The product was crystallised from a mixture of ethyl acetate and light petroleum (boiling range 40–60°) to yield yellow stout rhombohedral prisms, m.p. 129–131° (Found: C, 68·7; H, 5·1; $C_{21}H_{18}O_6$ requires C, 68·8; H, 4·9 per cent).

iso*Pinastric acid acetate*

*iso*Pinastric acid (0·1g), acetic anhydride (5 ml) and two drops of dry pyridine were heated under reflux for ½ hr. The product was crystallised from ethyl acetate to yield yellow thin rectangular plates, m.p. 159–161°. The mixed m.p. with pinastric acid acetate (m.p. 170–171°) was considerably depressed (144–150°) (Found: C, 66·7; H, 4·7; $C_{22}H_{18}O_7$ requires C, 67·0; H, 4·6 per cent.)

Demethylation of iso*pinastric acid (4-acetoxypulvinic dilactone)*

*iso*Pinastric acid (0·5 g), glacial acetic acid (10 ml), hydriodic acid (2 moles, 1 ml) were heated under reflux at 140° for 5 hr. The mixture was cooled and poured over crushed ice and extracted repeatedly with ether. The ether extract was washed first with water and then extracted with 5% sodium bicarbonate. The sodium bicarbonate extract was acidified, and the red solid obtained was collected, dried and heated under reflux with acetic anhydride (5 ml) for ½ hr. Acetic anhydride was removed under reduced pressure and the yellow solid was recrystallised from ethyl acetate to yield yellow stout rectangular prisms, m.p. 212–213°. Pinastric acid on similar treatment gave a yellow compound, m.p. 212–213°; the mixed m.p. with the above sample was undepressed.

Condensation of iso*pinastric acid with* o*-phenylenediamine*

*iso*Pinastric acid (1 g), *o*-phenylenediamine (0·44 g) and N-dimethylaniline (36 ml) were heated at 200° in an oil bath for 4 hr. The mixture was cooled and poured over crushed ice containing hydrochloric acid. The brown solid was collected, dried and recrystallised from a mixture of ethyl acetate and light petroleum (boiling range 40–60°) to yield thin orange-red rectangular plates, m.p. 296–298° (Found: C, 73·3; H, 4·8; $C_{25}H_{18}O_4N_2$ requires C, 73·2; H, 4·4 per cent).

The above product (0·3 g) was heated under reflux with 15% absolute alcoholic potash (15 ml) for 5 hr. The colourless potassium salts that separated were filtered off. Alcohol was removed from the filtrate under reduced pressure and water was added. The colourless solid was collected, dried and recrystallised from a mixture of ethyl acetate and light petroleum (boiling range 40–60°), m.p. 165–167°. The mixed m.p. with an authentic sample of 4-methoxybenzylbenziminazole was undepressed.

Conversion of iso*pinastric acid into pinastric acid*

(i) *iso*Pinastric acid (0·1 g) was heated in a test tube at 160° in an oil bath for 3 hr. The tube was cooled and the solid was boiled with methanol. The undissolved portion crystallised from a mixture of ether and light petroleum (boiling range 40–60°) as orange plates (yield 10 per cent), m.p. 202–204°; the mixed m.p. with pinastric acid was undepressed. Moreover it was observed that no dilactone was formed. *iso*Pinastric acid was recovered from the filtrate.

(ii) *iso*Pinastric acid (0·1 g) was dissolved in 2% absolute methanolic potash (50 ml) and the solution was kept in the cold for ½ hr. It was cooled in ice and acidified with dilute hydrochloric acid. The solid product was collected, dried and boiled with methanol. The undissolved portion crystallised from benzene as orange plates (yield 11 per cent), m.p. 202–204°. It agreed in all its properties with pinastric acid. *iso*Pinastric acid was recovered from the filtrate.

(iii) *iso*Pinastric acid (0·1 g) and N-dimethylaniline (11 ml) were heated at 180° in an oil bath for 3 hr. The mixture was cooled and poured over crushed ice mixed with hydrochloric acid. The pale-orange solid was washed first with cold dilute hydrochloric acid and then with cold water. The product dissolved completely in 5% sodium bicarbonate, showing that no dilactone was formed. It was also treated with hot methanol, and the undissolved portion crystallised as orange plates from benzene (yield 8 per cent), m.p. 202–204°. The mixed m.p. with pinastric acid was undepressed. The filtrate was concentrated, when *iso*pinastric acid crystallised out.

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