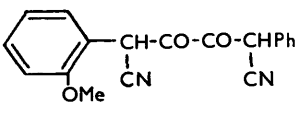
340. *Synthesis of Leprapinic Acid and Constitution of Pinastric Acid.*

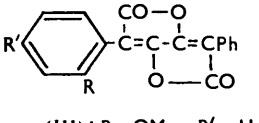
By O. P. Mittal and T. R. Seshadri.

Leprapinic acid has been synthesised by hydrolysis of α-*o*-methoxyphenyl-α′-phenylketipinic dinitrile to 2-methoxypulvinic dilactone followed by methanolysis. The nuclear methoxyl group of pinastric acid should be located in the phenyl ring near the ester grouping since the product of its condensation with *o*-phenylenediamine and subsequent hydrolysis contains a methoxyl group.

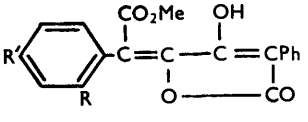
In an earlier communication,[1] leprapinic acid was shown to be 2-methoxyvulpinic acid (I). This has now been confirmed by its synthesis employing Asano's modification [2,3] (two stage) of Volhard's method.[4]



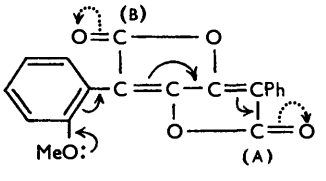
(II)



(III): R = OMe, R′ = H.
(V): R = H, R′ = OMe.

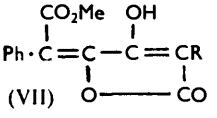


(I): R = OMe, R′ = H.
(VI): R = H, R′ = OMe.

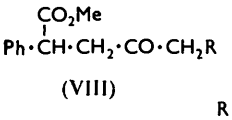


(IV)

α-*o*-Methoxyphenyl-α′-phenylketipinic dinitrile[3] (II) was refluxed with sulphuric–acetic acid and then acetic anhydride. 2-Methoxypulvinic dilactone (III) was obtained, which when treated with methanolic potassium hydroxide yielded 2-methoxyvulpinic acid (I), identical with leprapinic acid.

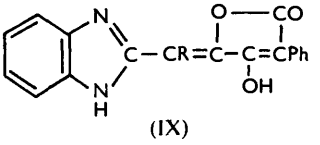


(VII)

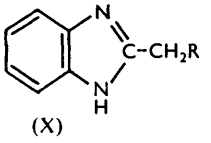


(VIII)

R = *p*-C$_6$H$_4$·OMe



(IX)



(X)

It follows that, of the two lactone rings in (III), the one closer to the substituted benzene nucleus is more easily opened. This seems to be according to expectations based on the availability of electrons in the bridging chain (cf. IV). Methoxyl being an electron source,

[1] Mittal and Seshadri, *J.*, 1955, 3053.
[2] Asano and Kameda, *Ber.*, 1934, **67**, 1522.
[3] *Idem*, *Ber.*, 1935, **68**, 1565.
[4] Volhard, *Annalen*, 1894, **282**, 1.

the positive charge on the carbon atom (A) will be considerably less than that on the carbon atom (B) which consequently receives the attack of the methoxide ion preferentially.

Since a similar method has been used [2] in the synthesis of pinastric acid from 4-methoxypulvinic dilactone (V), and since a *p*-methoxyl group will produce a similar electromeric effect, it is reasonable to expect that, in this synthesis also, the lactone ring near the substituted benzene ring should have undergone fission and hence this acid should also contain the methoxyl group in the phenyl ring near the ester group, as in (VI). This is, however, not in conformity with the findings of Asano and Kameda [3] who concluded that pinastric acid was 4'-methoxyvulpinic acid (VII) from a study of its reduction products, one of which was assigned the structure (VIII). To throw more light on this question the method suggested by Schönberg [5] and used earlier by Mittal and Seshadri [1] in the case of leprapinic acid has now been used with pinastric acid. This acid has been condensed with *o*-phenylenediamine and then subjected to fission with absolute alcoholic potassium hydroxide. The final product is 2-4'-methoxybenzylbenziminazole (X), identical with a synthetic sample obtained from *p*-methoxyphenylacetic acid, thus showing that the methoxyl group in pinastric acid also is attached to the benzene ring which is close to the ester group, *i.e.*, it is 4-methoxyvulpinic acid (VI).

Experimental

2-Methoxypulvinic Dilactone.—α-*o*-Methoxyphenyl-α'-phenylketipinic dinitrile was prepared according to the method of Asano and Kameda.[3] The intermediate ethyl cyano-*o*-methoxyphenylpyruvate melted at 95—96° (lit.[3], 104—105°) (Found: C, 62·5; H, 5·3. Calc. for $C_{13}H_{13}O_4N$: C, 63·1; H, 5·3%).

The dinitrile (0·5 g.), acetic acid (6 c.c.), concentrated sulphuric acid (3·3 c.c.), and water (4 c.c.) were heated under reflux for 2 hr. A reddish-brown oil gradually separated. When cooled and treated with water the oil solidified. The solid was filtered off, dried, and refluxed with acetic anhydride (5 c.c.) for ½ hr. The excess of the anhydride was decomposed with ice-water, and the yellow precipitate filtered off and dried (yield 0·5 g.). It crystallised from benzene as yellow needles, m. p. 172—173° (Found: C, 71·5; H, 3·7. Calc. for $C_{19}H_{12}O_5$: C, 71·2; H, 3·8%). The mixed m. p. with 2-methoxypulvinic dilactone obtained from leprapinic acid was undepressed.

Methyl 2-Methoxypulvinate (*Leprapinic Acid*).—2-Methoxypulvinic dilactone (0·25 g.) was dissolved in absolute methanolic potassium hydroxide (50 c.c.; 2%), kept at room temperature for ½ hr., diluted with water (150 c.c.), and acidified. The precipitate crystallised from methanol as golden-yellow rectangular tablets, m. p. 159—160° alone or mixed with leprapinic acid obtained from *Lepraria citrina* Schaer (Found: C, 67·6; H, 4·9. Calc. for $C_{20}H_{16}O_6$: C, 68·2; H, 4·6%).

Condensation of Pinastric Acid with o-*Phenylenediamine.*—Pinastric acid (0·7 g.), *o*-phenylenediamine (0·5 g.), and *NN*-dimethylaniline (25 c.c.) were refluxed at 200—210° for 4 hr. and, after cooling, poured into dilute acid (200 c.c.). The dark brown 2-(α-2-*benziminazolyl*-4-*methoxybenzylidene*)-3-*hydroxy*-5-*oxo*-4-*phenylfuran* (IX) was filtered off, washed with dilute acid, then with water, and dried. It crystallised from ethyl acetate–light petroleum as brown-red rhombohedral plates, m. p. 292—293° (decomp.) (yield 0·3 g.) (Found: C, 73·4; H, 4·2. $C_{25}H_{18}O_4N_2$ requires C, 73·2; H, 4·4%). It dissolves with difficulty in benzene and ethyl alcohol and easily in ethyl acetate and in dilute alkali.

Hydrolysis. This product (150 mg.) was refluxed with absolute alcoholic potassium hydroxide (7 c.c.; 10%) for 5 hr. The insoluble potassium salts were filtered off and the filtrate was concentrated under reduced pressure. Ice-water (30 c.c.) was added, the semi-solid mass extracted with ether, and the ether extract dried and evaporated. The residual 2-4'-*methoxybenzylbenziminazole* crystallised from ethyl acetate as colourless rectangular plates, m. p. 165—166° (Found: OCH_3, 12·4. $C_{15}H_{14}ON_2$ requires OCH_3, 13·1%) alone or mixed with a sample prepared from *p*-methoxyphenylacetic acid and *o*-phenylenediamine.

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[5] Schönberg and Sina, *J.*, 1946, 601.