# STUDIES IN THE BIOCHEMISTRY OF MICRO-ORGANISMS---V\*

# THE STRUCTURE AND SYNTHESIS OF CURVULIC ACID AND CURVIN, METABOLIC PRODUCTS OF CURVULARIA SIDDIQUI, SP. NOVO

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#### (Received 8 June 1964)

Abstract—Curvulic acid and curvin, metabolic products of Curvularia Siddiqui sp. novo, are shown to be 2-acetyl-3,5-dihydroxy-4-methoxyphenylacetic acid (III) and ethyl 2-acetyl-3,5-dihydroxy-4-methoxyphenylacetate (IV) respectively. These structures are confirmed by synthesis of the metabolites.

EARLIER communications described the isolation of curvulic acid,<sup>1,2</sup> m.p. 154°, curvin,<sup>2</sup> m.p. 123° and other compounds<sup>1-4</sup> from culture media of *Curvularia Siddiqui* sp. novo.<sup>5</sup> The present evidence necessitates revision of the molecular formula of curvulic acid, previously given<sup>2</sup> as  $C_{12}H_{14}O_7$ , to  $C_{11}H_{12}O_6$ . The compound was shown<sup>2</sup> to be an aliphatic carboxylic acid with pK 4·7, containing one methoxyl group, one C-methyl group, and an aromatic ring with an unsubstituted position *para* to a phenolic hydroxyl group. IR absorption (in Nujol) indicated the presence of both free and H-bonded hydroxyl groups (3320, 3198 cm<sup>-1</sup> respectively), the carboxyl group (3500–2350, 1704 cm<sup>-1</sup>), and a H-bonded aromatic ketone (1643 cm<sup>-1</sup>). NMR spectra of curvulic acid showed singlet proton resonances in pyridine at  $\tau$ 7·03, 6·24, and 5·82, and in acetone at  $\tau$ 3·42, corresponding in chemical shift and in intensity to an aromatic methyl ketone, an aromatic methoxyl group, a phenylacetyl



\* Part IV, A. Kamal and M. Akram Sandhu, Tetrahedron Letters 611 (1963).

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<sup>1</sup> A. Kamal, N. Ahmad, M. Ali Khan and I. H. Qureshi, Tetrahedron 18, 433 (1962).

- <sup>3</sup> A. Kamal, A. Ali Qureshi, M. Ali Khan and F. Mohd Khan, Tetrahedron 19, 117 (1963).
- <sup>3</sup> A. Kamal, M. Ali Khan and A. A. Qureshi, Tetrahedron 19, 111 (1963).
- <sup>4</sup> A. Kamal and M. Akram Sandhu, Tetrahedron Letters 611 (1963).

<sup>&</sup>lt;sup>5</sup> S. Iftikhar Ahmad and M. Sayeed Qureshi, Pakistan J. Sci. Ind. Res. 3, (3), 177 (1960).

methylene group and a benzenoid hydrogen respectively. These combined data are represented in formula I for curvulic acid.

Methylation experiments provided confirmation of the nature of the oxygen functions in curvulic acid (I). Brief treatment with diazomethane gave the compound, m.p. 139°, previously described<sup>2</sup> as "dehydrocurvulic acid,"  $C_{12}H_{12}O_{6}$ . This compound is, in fact, curvulic acid methyl ester,  $C_{12}H_{14}O_6$ , a structure in better agreement with analyses (Found: C, 56.7; H, 5.68; O, 37.6; OMe, 23.8. C12H14Og requires: C, 56.7; H, 5.5; O, 37.8; 2OMe, 24.4%), and which is confirmed by IR absorption (in Nujol) at 3375 (free OH), 3170 (H-bonded OH), 1731 (aliphatic ester) and 1647 cm<sup>-1</sup> (H-bonded aromatic ketone), and by PMR absorption (in  $CDCl_3$ ) at  $\tau - 0.06$  (H-bonded OH), 4.30 (free OH), 3.63 (ArH), 6.10 (ArOCH<sub>3</sub>), 6.18 (ArCH<sub>2</sub>CO), 6.30 (CO<sub>2</sub>CH<sub>3</sub>), and 7.38 (ArCOCH<sub>3</sub>). Further methylation of this methyl ester with methyl iodide and potassium carbonate in acetone,<sup>2</sup> or prolonged treatment of curvulic acid itself with diazomethane, afforded O,O-dimethylcurvulic acid methyl ester m.p. 62°,  $C_{14}H_{18}O_6$ , previously described<sup>2</sup> as "dimethyldehydrocurvulic acid," an oil  $C_{14}H_{16}O_6$ . IR spectroscopy (in CCl<sub>4</sub>) now showed a non-bonded aromatic ketone,  $v_{max}$  1682 cm<sup>-1</sup>, in addition to the aliphatic ester,  $v_{max}$  1733 cm<sup>-1</sup>, while the analytical figure of four methoxyl groups was confirmed by NMR absorption (in CDCl<sub>2</sub>) at  $\tau$  6.07, 6.10 and 6.11 (3ArOCH<sub>3</sub>) and 6.30 (CO<sub>2</sub>CH<sub>3</sub>), the remaining benzenoid, methylene and acetyl protons also being visible in the spectrum at  $\tau 3.45$ , 6.32, and 7.46 respectively. Alkaline hydrolysis of O,O-dimethylcurvulic acid methyl ester gave O,O-dimethylcurvulic acid, which showed proton resonances (in CDCl<sub>3</sub>) at  $\tau$ 3.52 (ArH), 6.08 (3ArOCH<sub>2</sub>), 6.31 (ArCH<sub>2</sub>CO), and 7.31 (ArCOCH<sub>3</sub>), confirming the previous methyl ether and methyl ester proton assignments.

Reaction of O,O-dimethylcurvulic acid methyl ester with hot 50% sulphuric acid yielded an acid  $C_{11}H_{14}O_5$ , m.p. 120°,  $v_{max}$  (in Nujol) 3300-2400 and 1707 cm<sup>-1</sup> (CO<sub>2</sub>H), which with diazomethane gave the corresponding methyl ester,  $C_{12}H_{16}O_5$ ,  $v_{max}$  (liquid film) 1745 cm<sup>-1</sup> (CO<sub>2</sub>Me). The NMR spectrum of this acid (in CDCl<sub>3</sub>) showed, in addition to singlets at  $\tau$ -0.45 (CO<sub>2</sub>H) and 6.42 (ArCH<sub>2</sub>CO), two identical benzenoid protons (singlet at  $\tau$ 3.44) and three methoxyl groups in similar environments (singlet at  $\tau$  6.15). This indicated that the acid was 3,4,5-trimethoxyphenylacetic acid, which was confirmed by direct comparison with authentic material. Formation of this acid clearly involves deacetylation of the aromatic ring by a reverse Friedel-Crafts mechanism,<sup>6,7</sup> together with hydrolysis of the methyl ester.

The representation I for curvulic acid can now be revised to II, in which the positions of the methyl ether and one hydroxyl group remain to be established. Treatment of curvulic acid itself or its methyl ester with hot 50% sulphuric or hydriodic acid gave a dihydroxymethoxyphenylacetic acid,  $C_9H_{10}O_5$ , m.p. 130°,  $\nu_{max}$  (in Nujol) 3380 (OH), 3270 (OH), 3100–2350 and 1707 cm<sup>-1</sup> (CO<sub>2</sub>H). The two benzenoid proton resonances in the NMR spectrum (in acetone) of this acid occurred as a singlet at  $\tau 3.43$ . The absence of spin coupling between these *m*-related hydrogen nuclei implies that they are in identical environments, and that the acid  $C_9H_{10}O_5$  is therefore the symmetrically substituted 3,5-dihydroxy-4-methoxyphenyl-acetic acid, rather than the alternative, unsymmetrical 3,4-dihydroxy-5-methoxy acid.

A. J. Birch, O. C. Musgrave, R. W. Rickards and H. Smith, J. Chem. Soc. 3146 (1959).

<sup>7</sup> A. J. Birch, B. Moore and R. W. Rickards, J. Chem. Soc. 220 (1962).



This conclusion was confirmed by direct comparison with synthetic 3,5-dihydroxy-4methoxyphenylacetic acid, prepared by catalytic hydrogenolysis of the known<sup>8</sup> 3,5-dibenzyloxy-4-methoxyphenylacetic acid. The isomeric, 3,4-dihydroxy-5-methoxyphenylacetic acid, m.p. 160°, was prepared by Arndt-Eistert synthesis from 3,4diacetoxy-5-methoxybenzoic acid,<sup>9</sup> followed by hydrolysis of the resulting methyl 3,4-diacetoxy-5-methoxyphenylacetate. As expected on theoretical grounds, the *m*-oriented benzenoid protons in the NMR spectrum (in acetone) of this unsymmetrical acid gave rise to an AB quartet (J<sub>AB</sub> = 2 c/sec) centered at  $\tau 2.77$ .

Curvulic acid is accordingly 2-acetyl-3,5-dihydroxy-4-methoxyphenylacetic acid (III).

O-methylcurvulic acid methyl ester,  $C_{13}H_{16}O_6$ , m.p. 81°, obtained together with O,O-dimethylcurvulic acid methyl ester from treatment of curvulic acid with diazomethane for five days, is clearly methyl-2-acetyl-3,4-dimethoxy-5-hydroxyphenylacetate. This compound gives a brown ferric test in ethanol, in contrast to the blue-green reaction of compounds in this series containing a H-bonded hydroxyl. That the H-bonded hydroxyl has been methylated follows also from IR absorption (in CCl<sub>4</sub>) characteristic of a free hydroxyl group (3420 cm<sup>-1</sup>) and a non-bonded aromatic ketone (1681 cm<sup>-1</sup>) in addition to the ester absorption (1732 cm<sup>-1</sup>). The NMR spectrum, showing singlet resonances (in CDCl<sub>2</sub>) at  $\tau 2\cdot 29$  (free OH), 3.66 (ArH), 6.11 (2ArOCH<sub>3</sub>), 6.25 (ArCH<sub>2</sub>CO), 6.31 (CO<sub>2</sub>CH<sub>3</sub>) and 7.41 (ArCOCH<sub>3</sub>), was in agreement with this formulation.

Curvin,  $C_{13}H_{16}O_6$ , is the ethyl ester (IV) of curvulic acid, since alkaline hydrolysis yields curvulic acid (III), which can be re-esterified with ethanol to curvin. The IR spectrum of curvin (in Nujol) reveals both free and H-bonded hydroxyl groups (3420 and 3170 cm<sup>-1</sup> respectively), an aliphatic ester (1730 cm<sup>-1</sup>) and a H-bonded aromatic ketone (1646 cm<sup>-1</sup>). PMR absorption (in CDCl<sub>3</sub>) at  $\tau$ 0.0 (H-bonded OH), 3.62 (ArH), 4.05 (free OH), 5.80 and 8.70 (a quartet and triplet respectively, J = 6 c/sec, CO<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 6.11 (ArOCH<sub>3</sub>), 6.18 (ArCH<sub>2</sub>CO) and 7.38 (ArCOCH<sub>3</sub>) provided full confirmation of this formulation (IV), which is also in agreement with evidence presented previously.<sup>2</sup> Analysis showed the presence in curvin of two C-methyl groups, and correction of the previously-quoted methoxyl analysis to allow for the presence of both methoxyl and ethoxyl groups gives an alkoxyl value of 27.7% compared with the required 28.3%. Methylation<sup>2</sup> of curvin with methyl iodide and potassium carbonate in acetone gave O,O-dimethylcurvin,  $C_{15}H_{20}O_6$ . which on warming with sulphuric acid yields 3,4,5-trimethoxyphenylacetic acid.

Acetylation of 3,5-dihydroxy-4-methoxyphenylacetic acid under Friedel-Crafts conditions gave curvulic acid (III). Since this acid had already been converted into the corresponding ethyl ester, this also constitutes a formal synthesis of curvin (IV), and confirms the structures of the two metabolites.

<sup>\*</sup> C. Schopf and L. W. Winterhalder, Liebig's Ann. 544, 62 (1940).

<sup>&</sup>lt;sup>9</sup> W. Bradley, R. Robinson and G. Schwarzenbach, J. Chem. Soc. 133, 793 (1930).

Curvulic acid (III) and curvin (IV) represent an interesting biosynthetic variation, involving introduction of an additional hydroxyl function which is then methylated, of the direct polyacetate pathway leading to curvulinic acid<sup>3,4</sup> (V) and curvulin<sup>3,4</sup> (VI), which are also metabolites of *Curvularia Siddiqui*. The natural occurrence of ethyl esters, such as curvin and curvulin, is rare, previous examples being the isolation of ethyl acetate from *Penicillium digitatum*<sup>10</sup> and of monoethyl dipicolinate from *Bacillus cereus* var. *mycoides* and *B. megaterium*.<sup>11</sup>

In vivo studies on the synthesis and interconversion of the metabolites of Curvularia Siddiqui will be reported in a separate communication.

### **EXPERIMENTAL**

M.ps are uncorrected. Light petroleum refers to the fraction b.p. 40-60°. UV spectra were measured in EtOH on Beckman DB and Unicam SP500 spectrophotometers. IR spectra were determined with Beckman IR 5A and Unicam SP200 instruments. NMR spectra were recorded for ca. 12% solutions containing tetramethylsilane as internal reference on a Varian Associates A60 machine. Microanalyses were carried out by Dr. A. Bernhardt, Mulheim, West Germany.

Interconversion of curvin and curvulic acid. Saponification of curvin (134 mg) in ethanolic KOH at room temp for 8 hr gave curvulic acid (78 mg), m.p. 152–153° from ethyl acetate-light petroleum, identified by mixed m.p. and IR spectrum in comparison with authentic material, m.p. 154°.

Curvulic acid (120 mg) on refluxing in EtOH (15 ml) containing conc.  $H_2SO_4$  (0.3 ml) for 16 hr afforded curvin (105 mg), m.p. 123° from benzene, identified by mixed m.p. and IR spectrum in comparison with authentic material, m.p. 123°.

O,O-Dimethylcurvulic acid methyl ester. Treatment of curvulic acid methyl ester<sup>2</sup> (480 mg) with an excess of ethereal diazomethane for 7 days gave O,O-dimethylcurvulic acid methyl ester (460 mg) m.p. 62°, purified by distillation at 178-180°/0·1 mm and crystallization from ether-light petroleum,  $\nu_{max}$  (in CCl<sub>4</sub>) 1733 (CO<sub>8</sub>Me) and 1682 cm<sup>-1</sup> (ArCO) (Found: C, 59·5; H, 6·69; O, 33·8; OMe, 44·0; C<sub>14</sub>H<sub>18</sub>O<sub>8</sub> requires: C, 59·6; H, 6·43; O, 34·0; 4 OMe, 43·9%.) The compound gave positive iodoform and hydroxamic acid tests. Comparison of IR and UV spectra showed this compound to be identical with the previously-described "dimethyldehydrocurvulic acid."<sup>2</sup>

O,O-Dimethylcurvulic acid. Hydrolysis of O,O-dimethylcurvulic acid methyl ester (282 mg) in ethanolic KOH (10 ml 10%) on the steam-bath for 4 hr afforded O,O-dimethylcurvulic acid (180 mg, 67%), needles m.p. 102° from ether-light petroleum, pKa (in aqueous EtOH) 4·3,  $\lambda_{max}$  215, 270 mµ (log  $\varepsilon$  4·02, 3·17),  $\nu_{max}$  (in Nujol) 3500-2400 and 1696 (CO<sub>2</sub>H), 1685 cm<sup>-1</sup> (ArCO), (Found: C, 58·2; H, 6·01; O, 35·9. C<sub>13</sub>H<sub>16</sub>O<sub>6</sub> requires: C, 58·2; H, 6·01; O, 35·8%.) The compound gives a positive iodoform test.

O-Methylcurvulic acid methyl ester. The product from reaction of curvulic acid (480 mg) with an excess of ethereal diazomethane for 5 days was distilled at  $150^{\circ}/0.5$  mm. The crystals which separated from the distillate were washed with ether and recrystallized from benzene to give O-methylcurvulic acid methyl ester (78 mg), needles m.p. 81°,  $\lambda_{max}$  273 m $\mu$  (log  $\varepsilon$  3.21),  $\nu_{max}$  (in CCl<sub>4</sub>) 3420 (free OH), 1732 (CO<sub>2</sub>Me), 1681 cm<sup>-1</sup> (ArCO). (Found: C, 58.2; H, 5.95. C<sub>18</sub>H<sub>18</sub>O<sub>6</sub> requires: C, 58.3; H, 5.90%.) O,O-Dimethylcurvulic acid methyl ester (370 mg), m.p. 60°, identified by mixed m.p. and IR spectrum, was obtained from the remaining distillate and ether washings.

Fission of O,O-dimethylcurvulic acid methyl ester with sulphuric acid. The methyl ester (282 mg) was heated with dil. H<sub>2</sub>SO<sub>4</sub> (10 ml, 1:1) on the steam-bath for 7 hr. Extraction with ethyl acetate and recovery afforded an acid (142 mg), m.p. 120° from ether-light petroleum,  $\lambda_{max}$  270 m $\mu$  (log  $\varepsilon$  3·57),  $\nu_{max}$  (in Nujol) 3300-2400 and 1707 cm<sup>-1</sup> (CO<sub>2</sub>H). (Found: C, 58·4; H, 6·16; O, 35·5. C<sub>11</sub>H<sub>14</sub>O<sub>5</sub> requires: C, 58·4; H, 6·24; O, 35·4%.) A mixed m.p. with authentic 3,4,5-trimethoxy-phenylacetic acid (prepared after Hadáček *et al.*<sup>12</sup>) showed no depression, and IR spectra were identical.

The acid (452 mg) with ethereal diazomethane gave methyl 3,4,5-trimethoxyphenylacetate (390 mg,

<sup>10</sup> J. H. Birkinshaw and H. Raistrick, Trans. Roy. Soc. B220, 331 (1931).

- <sup>11</sup> J. J. Perry and J. W. Foster, J. Bacteriology 72, 295 (1956).
- 12 J. Hadáček, J. Michalský and L. Macholán, Chem. Listy 49, 271 (1955).

81%), b.p. 148°/0.5 mm,  $\lambda_{max}$  277 m $\mu$  (log  $\varepsilon$  3.82),  $\nu_{max}$  (liquid film) 1745 cm<sup>-1</sup> (CO<sub>2</sub>Me). (Found: C, 59.9; H, 6.32; O, 33.8; OMe, 44.0 Calc for C<sub>12</sub>H<sub>10</sub>O<sub>5</sub>: C, 60.0; H, 6.71; O, 33.3; 4OMe 51.6%) Hadáček *et al.*<sup>12</sup> report b.p. 172–182°/10 mm for this ester.

Fission of curvulic acid and curvulic acid methyl ester with sulphuric acid. Treatment of curvulic acid (240 mg) with  $H_2SO_4$  as above for 2 hr gave an acid (160 mg, 87%), needles m.p. 130° on crystallization from ethyl acetate-light petroleum, pKa 3·3 (in EtOHaq), identified as 3,5-dihydroxy-4-methoxyphenylacetic acid by m.p. and spectroscopic comparison with authentic material prepared as described below.

Treatment of curvulic acid methyl ester with  $H_2SO_4$  under similar conditions, or of curvulic acid (240 mg) with HI (5 ml) and red P (100 mg) on the steam-bath for 1 hr, afforded the same acid, m.p. 130° (78% and 28% yield respectively).

3,5-Dihydroxy-4-methoxyphenylacetic acid. Hydrogen was passed into a solution of 3,5-dibenzyloxy-4-methoxyphenylacetic acid (126 mg, m.p. 138°, prepared by Schopf and Winterhalder's method<sup>8</sup>) in acetic acid (15 ml) containing Pd-C (100 mg, 5%). After 16 hr the catalyst was filtered off, the solvent removed under red. press., and the residue crystallized from ether to yield 3,5dihydroxy-4-methoxyphenylacetic acid (36 mg, 53%), needles m.p. 130°,  $\lambda_{max}$  275 m $\mu$  (log  $\varepsilon$  3·20),  $\nu_{max}$  (in Nujol) 3380 (OH), 3270 (OH), 3100-2350 and 1707 cm<sup>-1</sup> (CO<sub>2</sub>H). (Found: C, 54·7; H, 5·09; O, 40·4; OMe, 15·1. C<sub>9</sub>H<sub>10</sub>O<sub>5</sub> requires: C, 54·5; H, 5·09; O, 40·4; 10Me, 15·6%.)

3,4-Dihydroxy-5-methoxyphenylacetic acid. 3-O-Methylgallic acid, m.p. 220°,  $\lambda_{max}$  217, 275 m $\mu$  (log  $\varepsilon$  4·53, 4·12),  $\nu_{max}$  (in Nujol) 3230 (OH), 3500–2350 and 1660 cm<sup>-1</sup> (CO<sub>2</sub>H),  $\tau$  (in acetone) 2·70, 2·79 (doublets, benzenoid protons in an AB system,  $J_{AB} = 2$  c/s), and 6·12 (ArOCH<sub>2</sub>), was prepared after Bradley et al.,<sup>9</sup> and also by oxidation of 3,4-dihydroxy-5-methoxybenzaldehyde,<sup>9,13</sup> with alkaline Ag<sub>2</sub>O by Pearl's method.<sup>14</sup> This acid was converted as described by Bradley et al.<sup>9</sup> into  $\omega$ -diazo-3,4-diacetoxy-5-methoxyacetophenone, m.p. 90–91°,  $\lambda_{max}$  213, 247, 293 m $\mu$  (log  $\varepsilon$  4·54, 4·07, 3·61),  $\nu_{max}$  (in Nujol) 2090 (COCHN<sub>2</sub>), 1770 (ArOCOMe), 1718 cm<sup>-1</sup> (ArCOCHN<sub>2</sub>).

The diazoketone was rearranged according to the method of Schopf and Winterhalder.<sup>8</sup> To the diazoketone (1.75 g) in MeOH (40 ml) at 55° was added Ag<sub>2</sub>O [from AgNO<sub>3</sub> (200 mg) and NaOH]. The addition was repeated 4 times at hourly intervals, and the reaction was then left at room temp overnight. After filtration and removal of the solvent, distillation at 160–165°/0.03 mm gave methy/3,4-diacetoxy-5-methoxyphenylacetate (1.42 g, 82%), colourless crystals m.p. 100–100.5° from ether,  $\lambda_{max}$  212, 246, 294 mµ (log  $\varepsilon$  4.47, 3.94, 3.41),  $\nu_{max}$  (in Nujoł) 1760 (ArOCOMe) 1710 cm<sup>-1</sup> (CO<sub>2</sub>Me). (Found: C, 55.8; H, 5.70; C<sub>14</sub>H<sub>16</sub>O<sub>7</sub> requires: C, 56.7; H, 5.44%.)

Hydrolysis of methyl 3,4-diacetoxy-5-methoxyphenylacetate with 10% ethanolic KOH at room temp overnight gave 3,4-dihydroxy-5-methoxyphenylacetic acid, needles m.p. 160° from ether-CHCl<sub>3</sub>,  $\lambda_{max}$  216, 270 m $\mu$  (log  $\varepsilon$  4·46, 4·02),  $\nu_{max}$  (in Nujol) 3240 (OH), 3500-2350 and 1675 cm<sup>-1</sup> (CO<sub>2</sub>H). (Found: C, 53·9; H, 5·00. C<sub>9</sub>H<sub>10</sub>O<sub>5</sub> requires: C, 54·5; H, 5·09%.)

2-Acetyl-3,5-dihydroxy-4-methoxyphenylacetic acid. To 3,5-dihydroxy-4-methoxyphenylacetic acid (99 mg) in nitrobenzene (10 ml) containing acetyl chloride (0.6 ml) was added with stirring during 15 min, powdered anhydrous AlCl<sub>s</sub> (1.0 g), maintaining the reaction at 0°. After stirring for a further 2 hr, ice and conc. HCl were added and the mixture extracted with ethyl acetate. The extract was washed with NaHCO<sub>3</sub>aq, and the washings acidified and re-extracted with ethyl acetate. Recovery gave 2-acetyl-3,5-dihydroxy-4-methoxyphenylacetic acid (62 mg, 51%) needles m.p. 154° from ethyl acetate-light petroleum,  $\lambda_{max}$  285 m $\mu$  (log  $\varepsilon$  3.25),  $\nu_{max}$  (in Nujol) 3320 (non-bonded OH), 3198 (H-bonded OH), 3500-2350 and 1704 (CO<sub>2</sub>H), and 1645 cm<sup>-1</sup>(H-bonded C=O). (Found: C, 55·2; H, 5·40. C<sub>11</sub>H<sub>13</sub>O<sub>6</sub> requires: C, 55·0; H, 5·00). A mixed m.p. with curvulic acid showed no depression, and IR spectra of the 2 compounds were superimposable.

Acknowledgements—We are indebted to the Pakistan Council of Scientific and Industrial Research for granting study leave to A. A. Q., to Mr. A. Smith and Miss M. Murphy for the determination of NMR spectra, and to Professor A. J. Birch for his interest in this work.

<sup>13</sup> R. L. Shriner and P. McCutchan, J. Amer. Chem. Soc. 51, 2193 (1929).
<sup>14</sup> I. A. Pearl, J. Amer. Chem. Soc. 68, 429 (1946).