Steroid Intermediates. Synthesis and Transformations of 7-Aryl-4,7-dioxoheptanoic Acids

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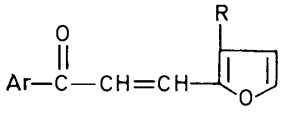
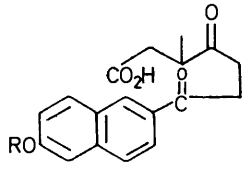
The 7-aryl-3-methyl-4,7-dioxoheptanoic acids [(5)—(7)] have been synthesized in an attempt to provide steroid precursors with a built-in angular C(13)-methyl group. The acids undergo various transformations with basic and acidic reagents, but fail to undergo the next cyclization step in the Robinson sequence. A convenient method for preparing 3-methyl-2-furaldehyde, one of the key reactants, is described. Further, the 1,2-dihydrocyclopenta-[*a*]naphthalen-3-ones [(21)—(24)], carrying oxygen-functions at the 5-, 7-, and 9-positions, have been synthesized as part of a projected route to ring-B-oxygenated steroids.

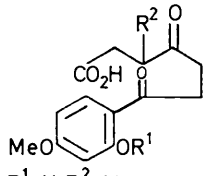
ROBINSON'S route to steroids [1] has been further explored through the synthesis of the 4,7-dioxoheptanoic acids (5) and (7)—(9). The acids with a 3-methyl substituent were prepared in an attempt to introduce a





(1) Ar = 6-OMe-2-naphthyl, R=Me
(2) Ar = 2-OH-4-OMe-phenyl, R=Me
(3) Ar = 2-OH-4-OMe-phenyl, R=H
(4) Ar = 2,4-$(OMe)_2$-phenyl, R=H

(5) R=Me
(6) R=H

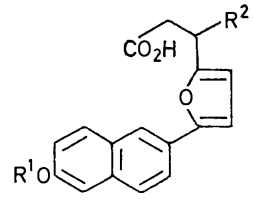


(7) R^1=H, R^2=Me
(8) R^1=R^2=H
(9) R^1=Me, R^2=H

built-in steroidal angular C(13) methyl group. The acid (8), lacking the 3-methyl group, was prepared to test the feasibility of Robinson's method for compounds possessing a hydroxy-group *ortho* to the heptanoic acid chain. The acid (8) is a potential precursor to ring-B-oxygenated steroids, and the hydroxy-acid (8) and its methyl ether (9) have been further cyclized to the cyclopentanaphthalenes [(21)—(24)].

3-Methyl-2-furaldehyde, the relatively inaccessible initial reactant, was prepared from methyl 3-methyl-2-furoate by treating the corresponding hydrazide with sodium periodate in aqueous ammonia. The method is based on that of Wingfield, Harlan, and Hanmer,[2] but was modified in order to suppress side-reactions leading to 3-methyl-2-furamide and to 3-methyl-2-furaldehyde 3-methyl-2-furoylhydrazone.

The methoxide-catalyzed condensation of 3-methyl-2-furaldehyde with 2-acetyl-6-methoxynaphthalene afforded the enone (1). The latter on acidic hydrolysis gave a mixture of three main products: the desired heptanoic acid (5), the corresponding furan-acid (10), and the demethylated heptanoic acid (6). The acid (10) showed a single carbonyl peak at 1710 cm^{-1} and peaks at 1630, 1610, 1600, and 1550 cm^{-1}, the characteristic pattern found in all the furan-acids prepared in this work. Although the existence of an equilibrium between the dioxoheptanoic acid and the furan-acid under the reaction conditions had been indicated in previous studies,[1,3-5] only one of the acids was actually isolated. This is one of the few instances [6,7] when both acids have been obtained. In contrast, Robinson's heptanoic acid lacking the 3-methyl substituent was not transformed into the corresponding furan-acid (12) under these conditions. The acid (12), prepared from the heptanoic acid by treatment with cold acetic acid–sulphuric acid, was completely converted back into the heptanoic acid with hot hydrochloric acid–acetic acid–water. The pure furan-acid (10) gave the same mixture of acids (5), (6), and (10) on treatment with aqueous acid. The 3-methyl substituent apparently directs the equilibrium composition in acidic media towards the



(10) R^1=Me, R^2=Me
(11) R^1=H, R^2=Me
(12) R^1=Me, R^2=H

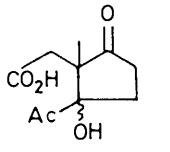
furan-acid, and this may result from the enhanced enolization of the 4-carbonyl group. The equilibrium also depends to a great extent on the nature of substitution in the aromatic ring. For instance, the phenolic furan-acid (11), though easily prepared from (6) using

[1] R. Robinson, *J. Chem. Soc.*, 1938, 1390.
[2] H. N. Wingfield, W. R. Harlan, and H. R. Hanmer, *J. Amer. Chem. Soc.*, 1952, **74**, 5796.
[3] R. H. Martin and R. Robinson, *J. Chem. Soc.*, 1943, 497.
[4] D. L. Turner, *J. Amer. Chem. Soc.*, 1949, **71**, 612.
[5] F. D. Popp, W. R. Schleigh, and L. E. Katz, *J. Chem. Soc.* (*C*), 1968, 2253.
[6] F. W. Short and G. M. Rockwood, *J. Heterocyclic Chem.*, 1969, **6**, 713.
[7] M. M. Coombs and (Mrs) S. B. Jaitly, *J. Chem. Soc.* (*C*), 1971, 230.

cold acetic acid–sulphuric acid, could not be isolated from the hot aqueous acid solution.

The acidic hydrolysis of the furfurylidene compound (2) yielded the heptanoic acid (7) as the sole product in 65% yield. It seems reasonable that strongly electron releasing substituents in the aromatic ring deactivate the aromatic carbonyl group towards nucleophilic attack, thus shifting the equilibrium towards the heptanoic acid. In this case, the heptanoic acid is also more stable relative to the furan-acid owing to chelation. In fact, attempts to effect its conversion into the furan-acid with various acidic reagents were not successful.

The heptanoic acids (5)—(7) resisted the next step in the usual Robinson sequence. Attempts to effect ring-closure across the 3- and 7-positions through aldol-type reactions were carried out under different basic and acidic conditions, and also using enamine intermediates. While the heptanoic acid (7) was recovered unchanged after treatment with alkaline reagents,



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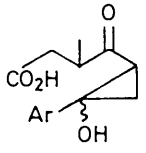

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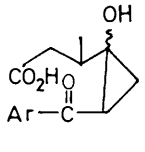

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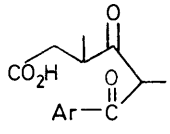
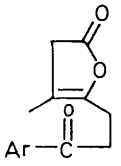


(28)

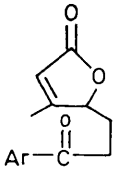
Ar = 6-OMe-2-naphthyl

the naphthylheptanoic acids (5) and (6) gave complex mixtures of products. The acid (5) yielded some yellow non-crystallizable lactones; two yellow glassy fractions comprising acids, which undergo, among other changes, easy lactonization; and the degradation products 2-acetyl-6-methoxynaphthalene and 6-methoxy-2-naphthoic acid. Fractional crystallization or chromatography of the acids or their esters, and of the lactones did not yield characterizable products. Spectra and analyses of these glassy products indicate that they are not formed by cleavage. It is reasonable that they contain the cyclic ketols (25)—(27) (hydroxy-band in the i.r. spectra of the esters), mixed with products of their further transformations. The three-membered cyclic ketols in particular could undergo dehydration or rearrange through collapse of the strained ring to the β-diketone (28) or to other products.

With acidic reagents the heptanoic acid (5) was invariably transformed into the furan-acid (10). In contrast, the acid (7) was unchanged when treated with cold acetic acid–sulphuric acid mixtures and transformed into the lactone (15) ($\nu_{max.}$ 1760 cm^{-1}) on boiling with toluene-*p*-sulphonic acid in benzene or toluene. The lactone (15) was converted into the lactone (16) with pyridine–acetic anhydride. With refluxing acetic anhydride, the acid (7) was converted into the lactone (14) ($\nu_{max.}$ 1795 cm^{-1}). The acid (5) was also converted into the enol-lactone (13) ($\nu_{max.}$ 1800, 1710, 1675, and 1625 cm^{-1}) with boiling acetic anhydride. The peak at 1710 cm^{-1} appears to be due to aromatic carbonyl absorption, shifted to a higher frequency by a possible



(13) Ar = 6-OMe-2-naphthyl
(14) Ar = 2-OAc-4-OMe-phenyl



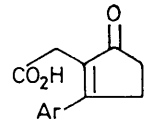
(15) Ar = 2-OH-4-OMe-phenyl
(16) Ar = 2-OAc-4-OMe-phenyl

interaction with the lactone oxygen. The lactone (13) also gave the furan-acid (10) when treated with acids.

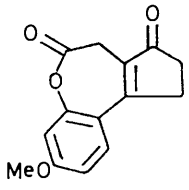
The heptanoic acid (5) gave under the enamine reaction conditions (toluene, acetic acid, and piperidine) only the piperidide of the acid.

2′,4′-Dimethoxyacetophenone condensed with furfural to give the furfurylidene compound (4), which on acidic hydrolysis gave the heptanoic acid (9). The latter smoothly cyclized in alkali to the cyclopentenone acid (17) which in boiling acetic anhydride formed the cyclopentanaphthalene (21); this latter was easily hydrolysed to the phenol (22).

In an analogous synthesis starting with 2′-hydroxy-4′-methoxyacetophenone, the dioxoheptanoic acid (8)



(17) Ar = 2,4-$(OMe)_2$-phenyl
(18) Ar = 2-OH-4-OMe-phenyl
(19) Ar = 2-OBz-4-OMe-phenyl



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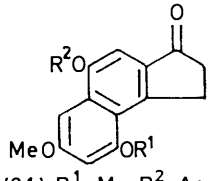

(21) R^1 = Me, R^2 = Ac
(22) R^1 = Me, R^2 = H
(23) R^1 = Bz, R^2 = Ac
(24) R^1 = R^2 = H

was obtained in 75% yield (yields of 30—40% are usual in these reactions). The high yield in this case and in the preparation of acid (7) can be attributed to the increased stability of the product due to chelation between the C(7)-carbonyl and the *ortho*-hydroxy-group. The acid (8) easily cyclized in alkali to the cyclopentenone acid (18), but the subsequent further cyclization

presented difficulties. Treatment with boiling acetic anhydride gave the lactone (20) and the usual Friedel–Crafts reagents were not effective. The desired ring-closure could however be achieved by protection of the *ortho*-hydroxy-group by benzoylation, followed by treatment with boiling acetic anhydride. The tricyclic product (23) was carefully hydrolysed in cold sulphuric acid to 5,9-dihydroxy-7-methoxy-1,2-dihydrocyclopenta[*a*]naphthalen-3-one (24).

EXPERIMENTAL

Spectra were recorded on Perkin-Elmer i.r. 237B and 257 spectrophotometers and a Perkin-Elmer u.v.–visible 137 spectrophotometer.

3-*Methyl*-2-*furohydrazide*.—To hydrazine hydrate (80%; 17 ml) heated on a steam-bath, methyl 3-methyl-2-furoate [8] (25 g) was gradually added, and heating was continued for 6 h. The crystalline mass was washed with alcohol and crystallized from benzene (16·2 g; further crop, 7—8 g), as needles, m.p. 108—109° (lit.,[9] 103—105°).

3-*Methyl*-2-*furaldehyde*.—To a well-stirred solution of sodium periodate (35 g) in water (480 ml), aqueous ammonia (4%; 160 ml) was added gradually (45 min) at 0°. Ether (150 ml) was then added and the mixture cooled to 0°. A solution of the above hydrazide (10 g) in water (160 ml) was added slowly (45 min) to the periodate solution, stirring and cooling being continued for a further 30 min. The aqueous layer was treated with barium acetate solution (24%; 160 ml). The white precipitate was filtered off, and the filtrate was nearly neutralized with acetic acid and saturated with sodium chloride. The filtrate was extracted with ether (5—6 times), and the extract washed with sodium hydrogen carbonate in saturated aqueous sodium chloride, and finally with saturated sodium chloride solution. 3-Methyl-2-furaldehyde (2·87 g) distilled at 60—64° at 12—13 mmHg (lit.,[10a] 60—61° at 12 mmHg); 2,4-*dinitrophenylhydrazone*, m.p. 207—208°.

From the residue, 3-methyl-2-furamide (0·5 g) was isolated by several extractions with hexane, m.p. 88—90° (lit.,[10b] 90—90·5°). The amide could be quantitatively converted into the hydrazide in refluxing hydrazine hydrate. When the procedure of Wingfield *et al.*[2] was used, 3-*methyl*-2-*furaldehyde* 3-*methyl*-2-*furoylhydrazone*, m.p. 192—195°, was the main product.

6-*Methoxy*-2-*naphthyl* 2-(3-*Methyl*-2-*furyl*)*vinyl Ketone* (1).—To a warm solution of 3-methyl-2-furaldehyde (2·87 g) and 2-acetyl-6-methoxynaphthalene (3·5 g) in methanol (30 ml), sodium methoxide in methanol (4%; 6 ml) was added. On keeping overnight, yellow needles of the *furfurylidene compound* (1) separated, m.p. 117—119° (4·52 g), $\nu_{max.}$ (Nujol) 1655, 1625, 1601, and 1568 cm^{-1} (Found: C, 78·35; H, 5·4. $C_{19}H_{16}O_3$ requires C, 78·1; H, 5·5%).

7-(6-*Methoxy*-2-*naphthyl*)-3-*methyl*-4,7-*dioxoheptanoic Acid* (5).—The furfurylidene compound (1) (2·9 g) in ethanol (50 ml) and conc. hydrochloric acid (12 ml) was refluxed for 15 h; the alcohol was distilled off, and the tarry residue was extracted with a mixture of conc. hydrochloric acid (31 ml), acetic acid (38 ml), and water (76 ml) by gently refluxing the solution for 2—3 h. The hot solution was decanted from the tar and cooled. The residual tar was re-extracted eight times, using fresh hydrochloric acid–acetic acid–water mixtures after every two extractions. The crude crops showed on t.l.c. [silica gel containing traces of sodium silicate; 20% methanol–benzene and n-butanol–water–ammonia (95 : 5 : 1) systems] mainly three compounds. The combined product was subjected to fractional crystallization: on warming with benzene and cooling, white crystals of 7-(6-*hydroxy*-2-*naphthyl*)-3-*methyl*-4,7-*dioxoheptanoic acid* (6) (0·170 g), m.p. 140—142°, separated. These gave cream needles (from ethanol–benzene), m.p. 143—145°, $\nu_{max.}$ (KBr) 3440sh, 3320, 1738, 1690, 1666, and 1620 cm^{-1} (Found: C, 68·6; H, 5·75. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·75%). The *hydrate* crystallised from water, m.p. 165—166°, $\nu_{max.}$ KBr 3400sh, 3240, 1740, 1700sh, 1680, and 1620 cm^{-1} (Found: C, 66·25; H, 6·35. $C_{18}H_{18}O_5,0{\cdot}5H_2O$ requires C, 66·85; H, 5·9%). The acetate had m.p. 141—144°, and the methyl ester m.p. 135—137°. On concentration of the mother-liquor and dilution with hexane, the *heptanoic acid* (5) separated as white clusters of needles (0·320 g), m.p. 125—127° (from benzene–hexane, $\nu_{max.}$ (KBr) 1692, 1680, 1625, and 1602 cm^{-1} (Found: C, 69·75; H, 6·4. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·15%). The methyl ester of (5) melted at 78—80°, the dioxime at 241—242°, and the semicarbazone at 201—202°. Further dilution of the mother-liquors with hexane gave white needles of 3-[5-(6-*methoxy*-2-*naphthyl*)-2-*furyl*]*butanoic acid* (10) which crystallized from benzene in creamy white needles, m.p. 173—174°, $\nu_{max.}$ (KBr) 1710, 1628, 1610, 1599, and 1550 cm^{-1}, $\lambda_{max.}$ (ethanol) 220 (ε 27,000), 236 (22,670), 264 (24,220), 273 (23,780), 307 (27,970), and 321 nm (25,330) (Found: C, 74·05; H, 6·2. $C_{19}H_{18}O_4$ requires C, 73·5; H, 5·85%). The methyl ester of (10) melted at 98—99°. The combined mother-liquors on further dilution with hexane gave more of the acid (5) (0·210 g).

Conversion of the Furan-acid (10) *into the Heptanoic Acid* (5).—On refluxing the acid (10) (0·05 g) dissolved in hydrochloric acid (*d* 1·178; 0·9 ml), acetic acid (1 ml), and water (2 ml) for 5 h, a white crystalline solid melting in the range 65—75° was obtained, which, on fractional crystallization as described above for (5), gave the acids (5) and (6), and a small amount of (10).

3-[5-(6-*Hydroxy*-2-*naphthyl*)-2-*furyl*]*butanoic Acid* (11).—The acid (6) (0·05 g) was dissolved in acetic acid (2 ml) containing conc. sulphuric acid (0·03 ml) and left at room temperature for 48 h. Dilution with ice-cold water gave the *furan-acid* (11) as yellow crystals from benzene, m.p. 166—168°, $\nu_{max.}$ (KBr) 3425, 1705, 1630, 1612, 1600, and 1550 cm^{-1} (Found: C, 73·5; H, 5·85. $C_{18}H_{16}O_4$ requires C, 72·95; H, 5·45%).

3-[5-(6-*Methoxy*-2-*naphthyl*)-2-*furyl*]*propanoic Acid* (12).—7-(6-Methoxy-2-naphthyl)-4,7-dioxoheptanoic acid prepared by Robinson's method had m.p. 138—140° (lit.,[1] 142—143°). It was dissolved in acetic acid (4·5 ml) and sulphuric acid (98%; 0·5 ml) and set aside for 2 days. The *furan-acid* (12) crystallized from benzene in yellow needles, m.p. 184—185°, $\nu_{max.}$ (KBr) 1695, 1630, 1610, 1598, 1552, and 1500 cm^{-1} (Found: C, 73·4; H, 5·3. $C_{18}H_{16}O_4$ requires C, 73·0; H, 5·4%).

Base-catalysed Reactions of the Heptanoic Acid (5).—

[8] D. M. Burness, *Org. Synth.*, 1963, Coll. Vol. IV, p. 649.

[9] H. L. Yale, K. Losee, J. Martins, M. Holsing, F. M. Ferry, and J. Bernstein, *J. Amer. Chem. Soc.*, 1953, **75**, 1933.

[10] A. P. Dunlop and F. N. Peters, 'The Furans,' Reinhold, New York, 1953 (*a*) p. 404, (*b*) p. 548.

(*a*) Reactions with aqueous sodium hydroxide or potassium hydroxide were carried out under a wide range of conditions: the concentration of acid (5) was varied from 0·003 to 0·3 molar, that of alkali from 0·02 to 5%, the reaction time from 3 to 48 h, and the temperature from 30 to 100°. The reaction mixture was acidified and extracted with ether or ether–benzene. The waxy yellow product, dried by azeotropic distillation with benzene, was fractionated on a column of silica gel (containing traces of sodium silicate; activated at 120° for 6 h). The benzene fraction (i) yielded a small quantity of 2-acetyl-6-methoxynaphthalene. Elution with chloroform gave a yellow glassy solid (ii) which appeared to be a lactone; $\nu_{max.}$ ($CHCl_3$) 1780, 1710, 1675, 1623, and 1530 cm^{-1}. The next two fractions (iii, iv), eluted with 25% ethyl acetate–benzene, were mixtures of lactones. Subsequent fractions were acidic. Fraction (v) (50% ethyl acetate–benzene) gave 6-methoxy-2-naphthoic acid, m.p. 197—200°, identical with an authentic sample prepared by the sodium hypoiodite oxidation of 2-acetyl-6-methoxynaphthalene. Fraction (vi) (ethyl acetate) gave unchanged dioxoheptanoic acid (5), m.p. 122—124°, mixed with traces of the yellow products. Elution with methanol–benzene gave salt-like residues which were extracted, after acidification, with ether–benzene. 20% Methanol–benzene gave a bright yellow uncrystallizable residue (vii) which melted in the range 105—125°, $\nu_{max.}$ ($CHCl_3$) 1780sh, 1712, 1675sh, and 1625 cm^{-1} (Found: C, 70·0; H, 6·2. Calc. for $C_{19}H_{20}O_5$ C, 69·5; H, 6·15%). Esterification of (vii) using methanol–sulphuric acid gave the methyl ester which distilled over slowly at 150—180° and 0·04—0·01 mmHg to give a deep yellow semi-solid distillate which showed $\nu_{max.}$ 3340br, 1730, 1710, 1675, and 1625 cm^{-1} (Found: C, 70·0; H, 7·0. Calc. for $C_{20}H_{22}O_5$ C, 70·15; H, 6·5%). Fraction (vii) could be separated into a neutral and acidic fractions by means of sodium hydrogen carbonate. The i.r. spectrum of the neutral component showed $\nu_{max.}$ ($CHCl_3$) 1780, 1712, 1675sh, and 1625 cm^{-1}. The acidic component showed $\nu_{max.}$ ($CHCl_3$) 1710, 1675sh, and 1625 cm^{-1}. Elution with 50% methanol–benzene, again gave a deep yellow uncrystallizable solid (viii), $\nu_{max.}$ ($CHCl_3$) 1712, 1630, and 1535 cm^{-1} (Found: C, 70·8; H, 6·45. Calc. for $C_{19}H_{20}O_5$ C, 69·5; H, 6·15%).

(*b*) The acid (5) was treated with sodium methoxide and with potassium t-butoxide in solutions of the corresponding alcohols, over a wide range of concentrations, temperatures, and time. Chromatography revealed product mixtures similar to that obtained in (*a*). In runs with potassium t-butoxide the proportion of the cleavage product (6-methoxy-2-naphthoic acid) showed a considerable increase. Reactions with potassium t-butoxide in benzene gave results similar to those obtained under aqueous alkaline conditions. However, in dimethylformamide the starting material was completely recovered.

Acid-catalysed Reactions of the Acid (5).—(a) *Sulphuric acid.* When treated with 50% aqueous sulphuric acid at 95—100° or with sulphuric acid in acetic acid (20—30%) at room temperature, the acid (5) afforded the furan-acid (10).

(b) *Toluene*-p-*sulphonic acid.* A mixture of the acid (5) (0·164 g), toluene-*p*-sulphonic acid (0·5 g), and dry benzene (or toluene, xylene, or acetic acid) (30—40 ml) was refluxed for 3 h. The product was again the furan-acid (10).

7-(6-*Methoxy*-2-*naphthyl*)-3-*methyl*-7-*oxohept*-3-*en*-4-*olide* (13).—Acid (5) was refluxed gently with acetic anhydride for 0·5 h. Acetic anhydride was removed under vacuum, and the sticky product was taken up in ether, washed with sodium hydrogen carbonate solution, and dried. The lactone (13), obtained as a pale yellow soft solid, was pure by t.l.c. but could not be crystallized; $\nu_{max.}$ (CCl_4) 1800, 1710, 1675, 1625, and 1505 cm^{-1}.

2,4-*Dimethoxyphenyl* 2-(2-*Furyl*)*vinyl Ketone* (4).—A mixture of freshly distilled 2-furaldehyde (4·2 g) and 2′,4′-dimethoxyacetophenone (7·7 g) was added to methanolic sodium methoxide (1%; 10 ml) with shaking and cooling in ice–water and left overnight. The product crystallized from aqueous ethanol in orange needles, m.p. 61—65° (lit.,[11] 59·5—60°).

7-(2,4-*Dimethoxyphenyl*)-4,7-*dioxoheptanoic Acid* (9).—The furfurylidene compound (4) (20 g) in ethanol (200 ml) and conc. hydrochloric acid (50 ml) was refluxed for 18 h. The solvent was distilled off and the residue was extracted with a mixture of conc. hydrochloric acid (40 ml), glacial acetic acid (50 ml), and water (100 ml) under gentle reflux for 2 h. The hot solution was decanted and cooled, and the reddish brown needles of the dioxoheptanoic acid (9) were filtered off. The mother-liquor was re-used for extracting the residual tar, and the process was repeated until no more compound separated. The total extract (8 g) was crystallized from methanol (charcoal) to give white *needles*, m.p. 122—124°, $\nu_{max.}$ (Nujol) 1710, 1690, 1650, 1592, and 1570 cm^{-1} (Found: C, 61·35; H, 6·3. $C_{15}H_{18}O_6$ requires C, 61·25; H, 6·15%).

2-(2,4-*Dimethoxyphenyl*)-5-*oxocyclopent*-1-*enylacetic Acid* (17).—The acid (9) (3 g) in 2% potassium hydroxide solution (300 ml) was heated on a steam-bath for 8 h. On acidification and cooling, the *cyclopentenone-acid* (17) (2·57 g) separated. It crystallized from aqueous methanol (charcoal) in pale yellow cubes, m.p. 150—152°, $\nu_{max.}$ (Nujol) 1739, 1645, 1600, and 1570 cm^{-1}, $\lambda_{max.}$ (ethanol) 230 (ε 13,280), 285 (10,330), and 308 nm (11,560) (Found: C, 65·25; H, 6·2. $C_{15}H_{16}O_5$ requires C, 65·15; H, 5·85%). Its 2,4-*dinitrophenylhydrazone* melted at 220—221°.

5-*Acetoxy*-7,9-*dimethoxy*-1,2-*dihydrocyclopenta*[a]*naphthalen*-3-*one* (21).—A solution of (17) (0·5 g) in acetic anhydride (5 ml) was refluxed for 4 h. The *ketone* (21) (0·410 g) crystallized from ethanol (charcoal) in cream needles, m.p. 215—216°, $\nu_{max.}$ (Nujol) 1765, 1695, 1615, and 1590 cm^{-1} (Found: C, 68·1; H, 5·65. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·35%).

5-*Hydroxy*-7,9-*dimethoxy*-1,2-*dihydrocyclopenta*[a]*naphthalen*-3-*one* (22).—The acetate (21) in 5% sodium hydroxide solution (containing 3% alcohol) was warmed on a steam-bath for 2 h. On acidification, the tricyclic *keto-phenol* (22) separated, and was crystallized from pyridine–acetic acid as brown needles, m.p. 305°, $\nu_{max.}$ (Nujol) 3330, 1670, 1619, and 1590 cm^{-1} (Found: C, 69·75; H, 5·9. $C_{15}H_{14}O_4$ requires C, 69·75; H, 5·45%).

2-*Hydroxy*-4-*methoxyphenyl* 2-(2-*Furyl*)*vinyl Ketone* (3).—Prepared as (4) above, this ketone crystallized from methanol in yellow needles, m.p. 116° (lit.,[12] 112°).

7-(2-*Hydroxy*-4-*methoxyphenyl*)-4,7-*dioxoheptanoic Acid* (8).—Prepared as (9) above, this acid was obtained in 75% yield after only 2—3 extractions. It crystallized from

[11] V. J. Lavrushin, S. V. Tsukerman, and A. I. Artemenko, *Zhur. obshchei Khim.*, 1961, **31**, 3037 (*Chem. Abs.*, 1962, **56**, 15454b).

[12] S. Courant and S. V. Kostanecki, *Ber.*, 1906, **39**, 4032 (*Chem. Abs.*, 1907, **1**, 563).

ethanol in white needles, m.p. 163° (lit.,[13] 165°), $\nu_{max.}$ (Nujol) 1710sh, 1700sh, 1692, 1625, and 1575 cm^{-1} (Found: C, 60·2; H, 6·05. Calc. for $C_{14}H_{16}O_6$: C, 59·95; H, 5·75%).

2-(2-Hydroxy-4-methoxyphenyl)-5-oxocyclopent-1-enylacetic Acid (18).—The dioxoheptanoic acid (8) (2·5 g) in 4% potassium hydroxide solution (250 ml) was heated on a steam-bath for 15 h, sodium chloride (10 g) was added and the mixture was acidified with conc. hydrochloric acid. On keeping overnight, long brown needles of the *cyclopentenylacetic acid* (18) (1·86 g) separated and crystallized from methanol in yellow needles, m.p. 172—173°, $\nu_{max.}$ (Nujol) 3200br, 3160, 1710, 1660, 1610, and 1585 cm^{-1} (Found: C, 63·75; H, 5·85. $C_{14}H_{14}O_5$ requires C, 64·1; H, 5·4%). Its 2,4-dinitrophenylhydrazone melted at 192—193°, the methyl ester at 135—137°, and the ethyl ester, obtained from the lactone (20) by heating the latter in ethanol for 15—20 min, melted at 125°.

8-Methoxy-1,4-dihydro-6-oxabenzo[a]cyclopenta[c]cycloheptene-3(2H),5-dione (20).—The cyclopentenylacetic acid (18) (0·5 g) in acetic anhydride (5 ml) was refluxed for 5 h, cooled and poured into ice. The product crystallized from ethanol as white flakes, m.p. 133°, $\nu_{max.}$ (Nujol) 1760, 1687, 1635, 1615, 1557, and 1512 cm^{-1} (Found: C, 69·1; H, 5·25. $C_{14}H_{12}O_4$ requires C, 68·85; H, 4·95%). The 2,4-dinitrophenylhydrazone melted at 259—260°.

2-(2-Benzoyloxy-4-methoxyphenyl)-5-oxocyclopentenylacetic Acid (19).—To the cyclopentenone-acid (18) (4 g) dissolved in 10% sodium hydroxide solution (20 ml), benzoyl chloride (3 g) was added, and the mixture was stirred vigorously for 8 h and then acidified. The oily product was washed with hot water and taken up in benzene. The solution was concentrated and diluted with hexane. The *benzoyloxy-derivative* (19) (1·8 g) melted at 140—141°, $\nu_{max.}$ (Nujol) 1738, 1700, 1643, and 1615 cm^{-1} (Found: C, 68·55; H, 4·55. $C_{21}H_{18}O_6$ requires C, 68·8; H, 4·95%).

5-Acetoxy-9-benzoyloxy-7-methoxy-1,2-dihydrocyclopenta[a]naphthalen-3-one (23).—The benzoyloxy-derivative (19) (2 g) was refluxed with acetic anhydride (20 ml) for 6 h, cooled, and poured into ice–water. The resulting *cyclopentanaphthalene derivative* (23) (0·92 g) crystallized from alcohol in white needles, m.p. 186—187°, $\nu_{max.}$ (Nujol) 1770, 1740, 1700, 1630, 1605sh, and 1580sh cm^{-1} (Found: C, 70·1; H, 4·55. $C_{23}H_{18}O_6$ requires C, 70·75; H, 4·65%). It gave a characteristic green fluorescence in 50% sulphuric acid.

5,9-Dihydroxy-7-methoxy-1,2-dihydrocyclopenta[a]naphthalen-3-one (24).—A solution of (23) (0·5 g) in conc. sulphuric acid (3—4 ml) was set aside overnight and poured into crushed ice. The precipitated *dihydroxy-ketone* (24) crystallized from methanol in yellow needles, m.p. 323—325°, $\nu_{max.}$ (Nujol) 3360, 3150, 1660, 1620, and 1590 cm^{-1} (Found: C, 68·7; H, 5·55. $C_{14}H_{12}O_4$ requires C, 68·85; H, 4·95%). It gave a green fluorescence in 50% sulphuric acid. The diacetate melted at 226—227°.

2-Hydroxy-4-methoxyphenyl 2-(3-Methyl-2-furyl)vinyl Ketone (2).—Sodium methoxide in methanol (2%; 6 ml) was added slowly to an ice-cold solution of 3-methyl-2-furaldehyde (2·76 g) and 2′-hydroxy-4′-methoxyacetophenone (4 g). Overnight yellow needles of the *furfurylidene derivative* (2) separated. More crops (3—4) were obtained by neutralization of the mother-liquor with acetic acid and concentration (combined yield 2·80 g). The ketone (2) crystallized from methanol in yellow needles, m.p. 115—116°, $\nu_{max.}$ (KBr) 1635, 1580, 1560, and 1505 cm^{-1} (Found: C, 69·95; H, 5·2. $C_{15}H_{14}O_4$ requires C, 69·7; H, 5·45%).

7-(2-Hydroxy-4-methoxyphenyl)-3-methyl-4,7-dioxoheptanoic Acid (7).—Prepared as (8) above, this was obtained in 65% yield in 2—3 extractions. The acid (7) crystallized from benzene–hexane in white *needles*, m.p. 123—124°, $\nu_{max.}$ (KBr) 1710sh, 1700, 1630, 1580, and 1503 cm^{-1} (Found: C, 61·35; H, 5·6. $C_{15}H_{18}O_6$ requires C, 61·25; H, 6·15%). The *acetate* of (7) melted at 125—127°, $\nu_{max.}$ (Nujol) 1770, 1710, 1695, 1675, 1615, 1575, and 1500 cm^{-1} (Found: C, 60·7; H, 6·35. $C_{17}H_{20}O_7$ requires C, 60·7; H, 6·0%). It gave a dioxime, m.p. 234—235.

7-(2-Hydroxy-4-methoxyphenyl)-3-methyl-7-oxohept-2-en-4-olide (15).—A mixture of the acid (7) (0·28 g), toluene-*p*-sulphonic acid (0·170 g), and dry benzene (30 ml) was refluxed for 3 h. The solvent was distilled off and the residue was taken up in ether and washed with sodium hydrogen carbonate solution. The soft solid residue of the lactone (15) gave a deep reddish brown colour with ferric chloride, and its i.r. spectrum (Nujol) showed peaks at 1760, 1635, 1583, and 1510 cm^{-1}.

Acetylation of the Lactone (15).—The lactone (15), when treated with pyridine and acetic anhydride at room temperature, was converted into the *lactone* (16), $\nu_{max.}$ (CCl_4) 1760, 1675, 1625, 1605, 1575, and 1500 cm^{-1}.

7-(2-Acetoxy-4-methoxyphenyl)-3-methyl-7-oxohept-3-en-4-olide (14).—The acid (7) was refluxed with acetic anhydride for 1 h, cooled, and poured into ice. The sticky mass was extracted with ether, and the extract was washed with dilute sodium hydroxide and water. The residue of lactone (14) could not be crystallized but was pure by t.l.c., $\nu_{max.}$ (CCl_4) 1795, 1760, 1675, 1625sh, 1610, 1565, and 1490 cm^{-1}.

Both lactones (14) and (16) were found to undergo mutual isomerization on silica gel columns, and on heating with activated charcoal.

[3/323 *Received*, 13*th February*, 1973]

[13] G. B. Marini-Bettolo, *Gazzetta*, 1941, **71**, 635 (*Chem. Abs.*, 1943, **37**, 123).