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FRIEDEL-CRAFTS CONDENSATION OF ETHYL ALLYLMALONATE WITH ANISOLE*

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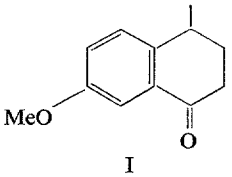
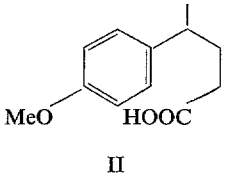
Abstract—Chemical and spectroscopic data, has shown that the major product from Friedel-Crafts condensation of anisole with ethyl allylmalonate, followed by saponification and decarboxylation is γ-(*o*-anisyl)valeric acid and not the *para*-isomer, as concluded earlier by different groups of workers.

IN CONNECTION with some projected synthetic work, the preparation of 4-methyl-7-methoxytetralone (I) was undertaken. An obvious method for its preparation appeared to be the cyclization of the γ-(*p*-anisyl)valeric acid (II). Colonge and Grimaud[1] effected the Friedel-Crafts alkylation of anisole with ethyl allylacetate and isolated a product (21% yield) which after saponification furnished a monocarboxylic acid, m.p.



I



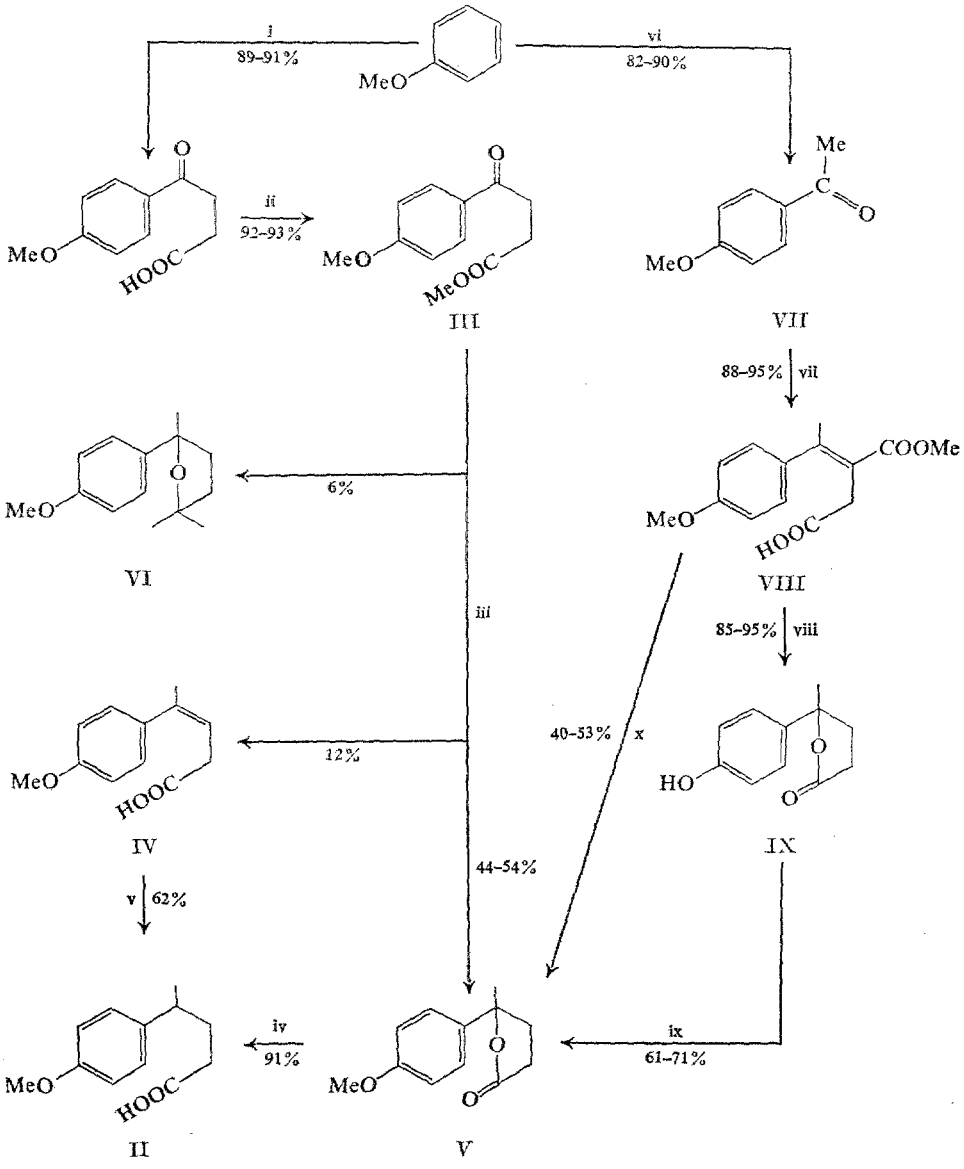
II

65° formulated as γ-(*p*-anisyl)valeric acid (II). These authors also showed that the acid obtained earlier[2] by alkylation with ethyl allylmalonate followed by saponification and decarboxylation was identical with their compound. More recently, Mukherjee *et al.*[3] apparently unaware of the earlier work, investigated the condensation of anisole with ethyl allylacetate and isolated a product, which on saponification gave a liquid which was also assigned the structure II. Both groups of workers reported the oxidation of their products to *p*-anisic acid.

In view of these reports, the preparation[2] of γ-(*p*-anisyl)valeric acid was undertaken and in agreement with the authors an acid m.p. 64–66°, of expected structure II was obtained. However, this acid failed to cyclize smoothly with polyphosphoric acid (PPA) and only a resinous product resulted under the conditions[4] which gave an 88% yield of 7-methoxytetralone from γ-(*p*-anisyl)butyric acid. The cyclization could be accomplished, though in only 10–15% yield, by the action of PPA at 165° [5] or by aluminium chloride cyclization of its acid chloride.[3] This cast strong doubts on the structure II assigned to the acid. On the other hand, these results are inconsistent with

* Communication No. 1001, National Chemical Laboratory, Poona.

[1] J. Colonge and E. Grimaud, *Bull. Soc. Chim. Fr.* 439 (1951).
[2] E. Fourneau and P. Baranger, *Bull. Soc. Chim. Fr.* **49**, 1167 (1931).
[3] S. M. Mukherjee, O. P. Vig and N. K. Maheshwari, *J. Indian Chem. Soc.* **34**, 9 (1957).
[4] G. S. Krishna Rao and Sukh Dev, *J. Indian Chem. Soc.* **34**, 255 (1957).
[5] W. Cocker, B. E. Cross, J. T. Edward, D. S. Jenkinson and J. McCrormick, *J. Chem. Soc.* 2362 (1963).



Reagents: (i) Succinic anhydride, $AlCl_3$; (ii) MeOH, H^+; (iii) MeMgI; (iv) Pd–C, HOAc, H_2; (v) Raney Ni + NaOH; (vi) Acetic acid + PPA; (vii) Dimethyl succinate, t-BuOK, t-BuOH; (viii) HBr–Acetic acid; (ix) Me_2SO_4, NaOH; (x) Sulphosalicylic acid.

FIG. 1. Synthesis of γ-(*p*-anisyl)valeric acid.

the reported oxidation of this acid to *p*-anisic acid. When the oxidation of this product was carried out with potassium permanganate, under the conditions[6] reported[3] no anisic acid could be obtained.

When the condensation of anisole with ethyl allylacetate was carried out according to the directions[3] an acid indistinguishable (m.p., mixed m.p.) from the acid obtained by the earlier method resulted.

Synthesis of γ-(p-anisyl)valeric acid

The above results clearly show that the acid of m.p. 65° of these authors must be different from γ-(*p*-anisyl)valeric acid (II). This has been confirmed by an unequivocal synthesis of II (Fig. 1).

Action of methyl magnesium iodide on methyl β-(*p*-anisoyl)propionate (III) furnished, besides the expected lactone V and the unsaturated acid[7] IV, a small amount of a neutral compound, $C_{14}H_{20}O_2$, which on the basis of its IR spectrum (no CO or OH absorption) is formulated as the tetrahydrofuran VI, the formation of which is readily understood. This structure is in full accord with its PMR spectrum: 3 quaternary methyls attached to carbon linked to oxygen, sharp 3H singlets at 71, 77, 83 cps; OCH_3, sharp 3H singlet at 224 c/s; a 4H signal between 395 and 443 c/s exhibiting an AB splitting pattern assignable to the aromatic protons of *p*-substituted benzene nucleus.

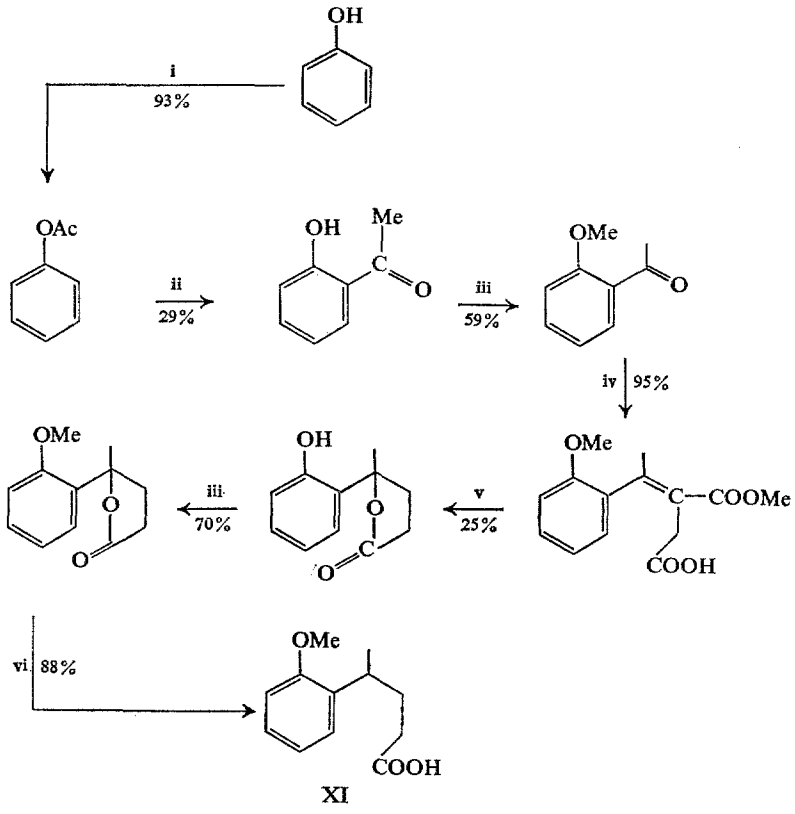
The lactone V was also prepared by the alternate route shown in Fig. 1. *p*-Methoxyacetophenone[8] (VII) on Stobbe condensation[9] with dimethyl succinate, furnished the half ester VIII as a mixture of isomers, from which one isomer m.p. 101–102·5° could be separated. This displayed its UV absorption peak at 369 mμ (ε, 13,450), which is in conformity with its formulation as VIII.[10] The crude half-ester mixture VIII was decarboxylated and lactonized by refluxing with HBr–acetic acid to give, after methylation, the lactone V; this conversion to lactone V could be more conveniently carried out by refluxing with sulphosalicylic acid in acetic acid; under these conditions little demethylation occurred.

The lactone V on hydrogenolysis with Pd–C in acetic acid containing a trace of perchloric acid[11] furnished the required γ-(*p*-anisyl)valeric acid (II) in high yield. This preparation, m.p. 39–40·5° and its IR spectrum is completely different from that of the acid of m.p. 64–66° described earlier. As expected, this preparation of γ-(*p*-anisyl)valeric acid readily cyclized with PPA to give the tetralone (I) (λ_{max} 253, ε 10,590) in about 80% yield.

Nature of the product of condensation of anisole with ethyl allylmalonate and synthesis of γ-(o-anisyl)valeric acid

Of the various structures possible for the acid m.p. 64–66°, the possibility of its being δ-(*p*-anisyl)valeric acid[12] (X) was ruled out on the basis of the m.p. (113–114·5°)

[6] Colonge and Grimaud[1] do not give details of the oxidation experiments.
[7] C. Rai and Sukh Dev, *J. Indian Chem. Soc.* **34**, 178 (1957).
[8] Sukh Dev, *J. Indian Chem. Soc.* **33**, 703 (1956).
[9] W. S. Johnson and G. H. Daub in *Organic Reactions* (Edited by R. Adams) Vol. VI, p. 2. Wiley, New York (1951).
[10] cf. Dorfmann, *Chem. Rev.* **53**, 703 (1956).
[11] K. W. Rosenmund and E. Karg, *Ber. Dtsch. Chem. Ges.* **75**, 1850 (1942).
[12] Fourneau and Baranger[2] had assigned this structure to their acid.



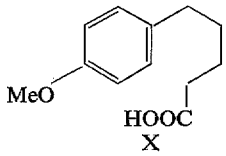
XI

Reagents: (i) Acetic anhydride, NaOH; (ii) $AlCl_3$; (iii) Me_2SO_4, NaOH; (iv) Succinic anhydride, t-BuOK, t-BuOH; (v) HBr, acetic acid; (vi) Pd–C, acetic acid, H_2.

FIG. 2. Synthesis of γ-(*o*-anisyl)valeric acid.

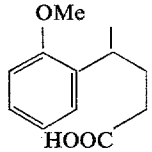
TABLE 1. COMPARISON OF THE PROPERTIES OF COLONGE-GRIMAUD'S AND MUKHERJEE *et al.* ACIDS WITH AUTHENTIC SAMPLES

	γ-(*p*-Anisyl)-valeric acid	γ-(*o*-Anisyl)-valeric acid	Acid obtained *via* Friedel-Crafts alkylation		
			Colonge and Grimaud	Mukherjee *et al.*	Present work
Acid:					
m.p.	39–40·5°	63–65°	65°	Liquid	64–66°
m.p. of its S-benzyl-thiuronium salt	149–150°	128–129°	—	125–126°	128–129°
PPA cyclization to tetralone:					
Yield %	80	Resin	—	—	Resin
m.p. of 2,4 DNP	220–222°	—	—	—	—
$AlCl_3$ *cyclization to the tetralone:*					
Yield %	—	—	—	44	15
m.p. 2,4 DNP	—	—	—	215–216°	230–232°

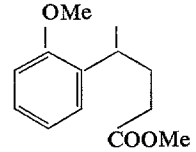


X

recorded for the latter acid, synthesized by an unambiguous method.[13] An examination of the IR spectrum of this acid shows the presence of a strong band at 755 cm^{-1} assignable to the out-of-plane deformation of four adjacent hydrogens of the benzene nucleus[14] and on this basis, the acid was suspected to be the *o*-isomer XI. This is



XI



XII

fully supported by the PMR spectra of the methyl esters of the two acids. Both show signals recognizable for CH_3—CH, OCH_3, $COOCH_3$. The 1H quartet centred at 157 c/s (J = 6·5 c/s) in the spectrum of the ester from *p*-acid and assigned to the benzylic tertiary proton, occurs centred at 191 c/s (J = 6·5 c/s) in the spectrum of the ester from acid of m.p. 64–66°; this down-field shift is understandable if this compound has the structure XII, in which case, the paramagnetic shift will be induced by the proximity of the OMe grouping and the benzylic tertiary proton; the fact that the CH_3—CH signals occur at identical field-strength in both the spectra is understandable on the basis of the preferred conformation expected for the molecules, in which the bulkier Me group is no longer in the plane of the benzene ring. The PMR spectrum of the *p*-isomer shows the expected AB splitting pattern for the aromatic protons (e.g. compare PMR spectrum of *p*-methyl anisole[15]) while, the pattern observed for aromatic proton signals for the other ester is consistent only with structure XII (e.g. compare PMR spectra of salicaldoxime, coumarin, indene[16]). Thus the acid resulting from the Friedel-Crafts alkylation of anisole with ethyl allylmalonate, followed by saponification and decarboxylation, must be formulated as the γ-(*o*-anisyl)valeric acid (XI). This is fully confirmed by its unambiguous synthesis, schematically shown in Fig. 2.

In order to see, if besides the *o*-compound, any other isomer is produced during the Friedel-Crafts alkylation of anisole with ethyl allylmalonate, the mother liquors (accounting for ~20% of the total saponification product) obtained during the crystallization of the malonic acid (m.p. 143–144°) were separately decarboxylated to furnish a product, the IR spectrum of which showed strong bands at 829, 756 cm^{-1} (out-of-plane deformation of aromatic ring protons[14]) characteristic of the *p*- and the *o*-isomer respectively. The extent of *p*-alkylation was, next, computed from the GLC of the methyl ester derived from the total decarboxylation acids which showed it to consist of approximately 9:1 mixture of *o*- and *p*-isomers.

Table 1 shows a comparison of the properties of the acids obtained by Colonge

[13] P. D. Gardner, W. J. Horton, G. Thompson and R. R. Twelves, *J. Am. Chem. Soc.* **74**, 5527 (1952).
[14] L. J. Bellamy, *The Infrared spectra of complex Molecules* p. 65. Methuen, London (1958).
[15] *NMR spectra Catalog* Vol. I, Spectrum No. 205. Varian Associates, Palo Alto (1962).
[16] Ref. 15, Spectra Nos. 156, 225, 227.

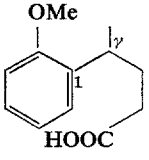
and Grimaud and by Mukherjee *et al.* with those of γ-(*p*-anisyl)valeric acid (II) and its *o*-isomer XI. It is clear from this that both of these authors were dealing with the *o*-compound as has been established in the present investigation.

DISCUSSION

Two points of interest arise: firstly, the need to rationalize the predominantly *ortho*-alkylation of anisole with ethyl allylmalonate and secondly, the failure of the γ-(*o*-anisyl)valeric acid to cyclize smoothly with PPA.

Regarding the orientation in the alkylation, no straight-forward explanation is apparent. A literature survey shows that aluminium chloride catalyzed alkylation of anisole gives predominantly *p*-products with cyclopentene[17] while with cyclohexene, the major alkylation product is the *o*-cyclohexyl-anisole.[17] These results indicate that the *o*-isomer is preferentially formed in a kinetically faster reaction involving a molar tertiary complex of anisole, olefin and aluminium chloride, in which the oxygen of the anisole and the π-electrons of the olefin are complexing with the *same* molecule of aluminium chloride. Such a complex may be expected to furnish a predominantly *ortho*-alkylation by virtue of the proximity of the *ortho*-position; the situation may be likened to that operating in intramolecular alkylation. The *para*-product may arise from a direct alkylation at the *para*-position by the usual pathway.[18,19]

The failure of γ-(*o*-anisyl)valeric acid to undergo smooth intramolecular cyclization with PPA, in contrast to that of the *p*-isomer, though in both cases the ring closure will be taking place *meta* to the MeO, may be assigned to steric factors only. Apparently the steric overlap between the MeO and the Me group in the *o*-isomer, which would be relieved in the free acid by adapting a suitable conformation by rotation



about the C_1—C_γ bond, would become serious in the transition state required for the tetralone with the result that intermolecular acylation, leading to a polymeric product, takes precedence over the usual intramolecular acylation.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Pet. ether refers to fraction b.p. 40–60°. All solvent extracts were dried over Na_2SO_4.

UV spectra were taken on a Perkin–Elmer spectrophotometer (model 350) in 95% EtOH. IR spectra were recorded as smears (liquids) or in KBr (solids) on a Beckman IR 4 instrument. The PMR spectra were taken in 10–20% CCl_4 soln with TMS as internal standard on a Varian A-60 spectrometer. The signals are reported in c/s from TMS.

The $C_{12}H_{16}O_3$ acid of Fourneau and Baranger

(i) *By condensation with ethyl allylmalonate.* In this condensation according to the directions,[2] anisole (351 g, 3·25M) in pet. ether (650 ml) was placed in a 3-necked flask fitted with a Herschberg

[17] S. H. Patenkin and B. S. Friedman in *Friedel-Crafts and Related Reactions* (Ed. G. A. Olah) Vol. II, Part I, p. 226. Interscience, New York (1964).

[18] Ref. 17, p. 3.

[19] Under the reaction conditions used for the alkylation experiments, *o*-product does not undergo any isomerization.

stirrer and a $CaCl_2$ guard-tube. Anhyd $AlCl_3$ (553 g, 4·15M) was added in small lots with stirring and the resulting light-brown coloured soln stirred for another 25 min and diethyl allylmalonate[20] (130 g, 0·65M) added slowly with stirring at room temp (30°). The stirring was continued for a further 9 hr and the reaction mixture decomposed by pouring on to iced water (2·5 l.) containing 400 ml conc. HCl. This was then extracted with ether (4 × 300 ml), washed with brine (3 × 30 ml), dried and stripped of solvent. The residue was fractionally distilled and the fraction b.p. 155–160°/1–2 mm collected separately, n_D^{32} 1·4910, yield 94·6 g (47%) (Lit.[2] b.p. 209°/20 mm, yield 30%).

The above diester (89 g) was saponified by refluxing with alcoholic KOH (100 g, in 1 l. EtOH) for 4 hr and worked up to give the acid (ether extraction), m.p. 135–138°, yield 73·6 g. A small sample of this product was converted into the methyl ester (CH_2N_2) and analyzed by GLC (Perkin–Elmer Vapour Fractometer, model 154D, 20% diethylene glycol succinate on Chromosorb W, 2 meters column, H_2, 200°, 15 lbs p.s.i.). The crude acid was recrystallized from benzene to give a solid (and mother liquors M) m.p. 143–144°, yield 61·4 g (Lit.[2] m.p. 144–145°). IR spectrum: COOH 3448, 2710, 928, 900, 1754, 1715 cm^{-1}; OMe 1245 cm^{-1}; aromatic ring H, 755 cm^{-1}. (Found: C, 62·1; H, 6·2. $C_{13}H_{16}O_5$ requires: C, 61·89; H, 6·39%.)

The above malonic acid was decarboxylated by heating at 160–170° till the evolution of CO_2 ceased (3 hr). The product was finally distilled: b.p. 153–154°/0·9 mm, m.p. 61–65°, yield 82%; it was recrystallized from pet. ether to give colorless needles, m.p. 64–66° (Lit.,[2] m.p. 65°).

The S-*benzylthiuronium salt* was prepared in the usual manner and after two crystallizations from dil. EtOH had m.p. 128–129°. (Found: N, 7·2. $C_{20}H_{26}O_3N_2S$ requires: N, 7·5%.)

The malonic acid from *mother liquors M* was decarboxylated in the same way and the product distilled: b.p. 145–150°/0·5 mm, yield 9·67 g (16·4% on the wt of the ester). IR spectrum: COOH 2685, 946, 1711 cm^{-1}; OMe 1029 cm^{-1}; aromatic ring H, 829, 756 cm^{-1}.

(ii) *By condensation with allylacetic acid.* Anisole (4·32 g, 0·04M) and allylacetic acid[20] (2·0 g, 0·02M) were taken in a flask fitted with a Herschberg stirrer and a reflux condenser carrying a $CaCl_2$ guard-tube. $AlCl_3$ (2·93 g, 0·022M) was added slowly with stirring and the reaction mixture left at room temp for 24 hr and then heated for 2 hr on a water bath. The complex was decomposed by pouring on powdered ice (10 g) and HClaq (10 ml) and extracted with ether. The ether extract was thoroughly extracted with 10% NH_4OH (3 × 15 ml) and the soln filtered through activated charcoal and acidified (HClaq). The mixture was extracted with ether (3 × 10 ml), washed with brine (5 ml) and dried. After removing the solvent, the residue was distilled: b.p. 160–165°/2 mm, n_D^{27} 1·5140, yield 1·8 g. The product solidified after a few days, m.p. 62–64°. Mixed m.p. with the specimen obtained by method (i) was undepressed. (Found: C, 69·08; H, 7·52; $C_{12}H_{16}O_3$ requires: C, 69·20; H, 7·74%.)

The S-*benzylthiuronium salt* prepared in the usual manner had m.p. 128–129°; mixed m.p. with the previous specimen from (i) was undepressed.

(iii) *By condensation with ethyl allylacetate.* In the procedure adopted,[3] dry, freshly distilled anisole (75 ml) was cooled to −10° and $AlCl_3$ (30 g) was added in 5 portions during an interval of 45 min. After each addition of $AlCl_3$, ethyl allylacetate was added in small portions (total 14 g). After the additions, the mixture was stirred for 2 hr at 0° and then for 1 hr at 5° and then left overnight (19 hr) at room temp (~25°). The reaction mixture was worked up in the usual manner to give a product: b.p. 158–160°/10 mm n_D^{27} 1·4970, yield 11·65 g (Lit.[3] b.p. 152–154°/10 mm, yield 8·0 g).

The above ester (11·6 g) was hydrolyzed by refluxing with alcoholic KOH (6·7 g of KOH in 147 ml EtOH) for 12 hr and then worked up to give a product b.p. 160–164°/2 mm n_D^{24} 1·5160, yield 8·65 g. It failed to crystallize during several weeks till seeded with the product obtained by the method of French workers m.p. 63–65°. Mixed m.p. of this solid with that obtained by method (i) was undepressed.

Cyclization of the $C_{12}H_{16}O_3$ *acid*

(i) *With polyphosphoric acid at* 80°.[4] To PPA (from 7 g of P_2O_5 and 3 ml of syrupy phosphoric acid) maintained at 80°, the acid (1 g) was added and thoroughly mixed. The reaction mixture was maintained at that temp for 1 hr and the practically colourless reaction mixture diluted with iced water (20 ml) and worked up in the usual manner to give only a small amount of a neutral fraction which could not be distilled.

[20] R. P. Linstead and H. N. Rydon, *J. Chem. Soc.* 580 (1933).

(ii) *With polyphosphoric acid at* 165°.[5] 1·0 g of the acid was added to PPA, prepared from 3 g of P_2O_5 and 4 g of syrupy phosphoric acid at 165°. The reaction mixture was kept at this temp with vigorous stirring for 5 min and then worked up to give the tetralone: b.p. 112–114°/0·7 mm, n_D^{26} 1·5624, yield 0·1 g (11·5%). IR spectrum was identical with that of the sample obtained under (iii) below.

(iii) *By the Friedel-Crafts method.*[3] To PCl_5 (5 g) covered with benzene (12 ml), 5 g of the acid was added with cooling. The reaction was completed by occasional warming on waterbath till the PCl_5 had almost disappeared. $AlCl_3$ (3·8 g) covered with dry heptane (10 ml) was cooled to −10° and the acid chloride soln prepared as above, added in one lot and the reaction allowed to continue at room temp. It was finally completed by occasional warming on a water bath (3 hr). The reaction mixture was worked up to give a neutral fraction: b.p. 112–114°/0·8 mm, n_D^{26} 1·5602, yield 0·73 g (15·9%); λ_{max} 257 mμ (ε 10230). IR spectrum: C=O 1692 cm^{-1}, OMe 1259 cm^{-1}; aromatic ring H, 800, 746 cm^{-1}. (Found: C, 74·9; H, 7·49. $C_{12}H_{14}O_2$ requires: C, 75·76; H, 7·42%.)

2,4-*Dinitrophenylhydrazone* (H_2SO_4 method), red needles (benzene–hexane) m.p. 230–232°. (Found: N, 15·13. $C_{18}H_{18}O_5N_4$ requires: N, 15·13%.)

γ-(p-Anisyl)valeric acid

Methyl β-(p-anisoyl)propionate (III). *β-(p*-Anisoyl)propionic acid[4] (190 g, m.p. 146–148°), MeOH (200 ml), dry benzene (200 ml) and conc. H_2SO_4 (10 ml) were refluxed for 10 hr and worked up to give the required ester: b.p. 160–161°/1 mm m.p. 47–48·5°, yield 188 g (Lit.[21] m.p. 46–47°). IR spectrum: C=O, 1689 cm^{-1}; COOMe 1745 cm^{-1}; OMe 1271, 1255 cm^{-1}; aromatic ring H, 833 cm^{-1}.

Action of methyl magnesium iodide on the above ester. To a soln of the keto ester (22·2 g, 0·1M) dissolved in dry ether (150 ml) and chilled to 0°, MeMgI in ether (from Mg 4·13 g, ether 100 ml and MeI 25·6 g in 50 ml ether) was added (N_2) in a thin stream with continuous stirring during a period of 45 min. A sticky mass separated and after stirring for another 2 hr, the product was left overnight at room temp. Next day, the material was refluxed for 4 hr and after cooling worked up with HClaq (1:1, 120 ml). The ethereal soln was separated washed with 100% $Na_2S_2O_3$aq (50 ml) followed by water (2 × 50 ml) and then extracted with sat Na_2CO_3aq (4 × 50 ml). The alkaline extracts were cooled and acidified (HClaq, 1:1) and extracted with ether (3 × 50 ml) and the ether extracts washed with brine (20 ml) and dried. On removing the solvent, the unsaturated acid IV was obtained as a viscous liquid, yield 2·58 g (12·5%). This was used as such in the next step (see below).

The ethereal soln containing the neutral products was washed with brine (20 ml), dried and solvent removed to give crude lactone (7·9 g). This was purified as under:

KOH (10 g) in EtOH (120 ml) was added to the lactone (17·9 g) and the mixture refluxed for 4 hr and then separated into acidic and neutral fractions. The neutral portion was distilled to give VI b.p. 103–105°/3 mm, n_D^{30} 1·5062, yield 0·89 g (~6%) λ_{max} 224 (ε 13080), 276 (ε 3375) and 283 mμ (ε 2846). IR spectrum: OMe 1252 cm^{-1}; —C—O—C— 1087, 1079 cm^{-1}; $\begin{matrix}Me\\Me\end{matrix}$ > 1364 cm^{-1}. (Found: C, 75·67; H, 8·74. $C_{14}H_{20}O_2$ requires: C, 76·32; H, 9·15%.)

The alkaline soln (after charcoal treatment) was acidified with HClaq and warmed on the water-bath for 2 hr cooled, extracted with ether (4 × 100 ml), the ether extracts washed with sat $NaHCO_3$aq (3 × 50 ml) [from the bicarbonate soln was recovered in the usual way 3·87 g of acid, identified—m.p., mixed m.p.—as *β-(p*-Anisoyl)propionic acid], washed with brine (3 × 15 ml), dried and stripped of solvent to give after distillation V, b.p. 140–142°/1·5–2 mm, n_D^{30} 1·5318, yield 11·19 g (54·3%) λ_{max} 225 (ε 12,450), 276 (ε 2085) and 282 mμ (ε 1640). IR spectrum: γ lactone 1760 cm^{-1}; OMe 1247 cm^{-1}; aromatic ring H, 833 cm^{-1}. (Found: C, 69·59; H, 6·72. $C_{12}H_{14}O_3$ requires: C, 69·84; H, 6·84%.)

Condensation of p-*methoxyacetophenone with dimethyl succinate*

Dimethyl succinate (21·9 g, 0·15M) and *p*-methoxyacetophenone[8] (15·0 g, 0·1M) were mixed and added to a soln of $KOBu^t$ (from 4·3 g K) in t-BuOH (100 ml); an additional amount of t-BuOH (20 ml) was used for rinsing in the reactants. The yellow soln was refluxed for 45 min (N_2), cooled to room temp and then acidified with HClaq (1:1). The alcohol was removed by distillation using a water-pump and the oily residue treated with excess 10% NH_4OHaq and extracted with ether (4 × 50 ml). The alkaline extract was cooled, acidified with HClaq, extracted with ether (4 × 50 ml) and

[21] G. Bargellini and M. Giua, *Gazz. Chim. Ital.* **42**, 197 (1912).

dried. After distilling the solvent, the crude VIII was obtained which was purified by distillation: b.p. 175–177°/0·1 mm n_D^{31} 1·5575, yield 23·2 g (87·9%). It solidified on keeping for several days, m.p. 60–70°. Repeated crystallizations of a sample from benzene–pet. ether (1:1) gave a product, white solid m.p. 101–102·5°; λ_{max} 269 mμ (ε 13,450). (Found: C, 63·52; H, 6·1; neut. equiv. 261·4. $C_{14}H_{16}O_5$ requires: C, 63·63; H, 6·06%; neut. equiv. 264.)

γ-(p-Anisyl)γ-methylbutyrolactone (V)

(i) *With hydrobromic acid in acetic acid.* The above half-ester (13·5 g, m.p. 60–70°) was refluxed (N_2) with AcOH (48 ml), 48% HBraq (32 ml) and water (16 ml) for 17 hr. The volatile acids were removed by distillation on a waterbath under suction and the oily residue taken up in ether (400 ml) and washed with sat $NaHCO_3$aq (4 × 40 ml). This bicarbonate extract on acidification yielded an acid (3·23 g) which was mixed with the next lot of the half-ester and again subjected to acid treatment as above. The ether extract after bicarbonate extraction was washed with brine, dried and stripped of the solvent to give the crude lactone (6·22 g).

The above lactone (14·5 g) was dissolved in NaOHaq (5 g in 50 ml H_2O) and treated with Me_2SO_4 (8·5 g). The mixture was stirred at room temp for 1 hr and later on a waterbath for 1 hr. The reaction product was charcoaled and the clarified soln extracted with ether (3 × 50 ml), the ether extract washed with brine, dried and solvent removed to give 0·4 g of a liquid identified as *p*-methoxyacetophenone. The alkaline extract was acidified with HClaq extracted with ether (3 × 50 ml), washed with brine and dried. After solvent removal, the product was distilled to give V, b.p. 133–136°/0·5 mm, yield 11·05 g (71·3%).

(ii) *With sulphosalicylic acid in acetic acid.* The above half-ester (5·0 g) dissolved in AcOH (18·0 g) was refluxed with sulphosalicylic acid (1·0 g) and water (4·0 ml) under N_2 for 24 hr. AcOH was removed by distillation from a water-bath under suction and residue worked up to give besides 0·57 g of an acid, 3·36 g of the required crude lactone which was further purified by treatment with ethanolic KOH as described for the crude lactone obtained by Grignard method. The neutral (0·11 g) and the acid (0·03 g) materials were rejected and the *lactone* (V) thus obtained was finally purified by distillation: b.p. 140–142°/1·5 mm, yield 2·1 g (53·3%).

IR spectra of the two preparations was superimposable on that of the product from the inverse Grignard method.

γ-(p-Anisyl)valeric acid (II)

(i) *From γ-(p-anisyl)γ-methylbutyrolactone* (V). The lactone (7·89 g) in gl. AcOH (60 ml) was hydrogenated over reduced 10% Pd–C (1 g) in presence of perchloric acid (60%, 0·6 ml) at 25°/710 mm. The reaction was stopped at the end of 20 hr when the theoretical amount of H_2 had been absorbed. The reaction mixture was worked up to give the required acid: b.p. 147–150°/0·2–0·3 mm, $n_D^{26.5}$ 1·5168, yield 7·18 g (91%). The product solidified (m.p. 37–39°) on standing and after 3 crystallizations from pet. ether had m.p. 39–40·5°. (Found: C, 69·06; H, 7·67. $C_{12}H_{16}O_3$ requires: C, 69·20; H, 7·74%.)

S-*Benzylthiuronium salt* of this acid was prepared in the usual way and after one crystallization from dil. EtOH furnished a white crystalline powder m.p. 149–150°. (Found: N, 7·39. $C_{20}H_{26}N_2SO_3$ requires: N, 7·52%.)

(ii) *From γ-(p-anisyl)γ-methylvinylacetic acid* (IV). The acid IV (4·95 g) was reduced with Raney Ni–Al alloy and alkali[22] following closely the directions of Sukh Dev[23] to give in 70% yield the reduced acid, b.p. 170–175°/2 mm, m.p. 38–40°, n_D^{32} 1·5175; S-*benzylthiuronium salt*, m.p. 149–150°.

4-*Methyl-7-methoxytetralone* (I)

The above acid was cyclized with PPA at 80° in the way described earlier. The product was obtained as a colourless oil, b.p. 138–140°/1·5 mm, n_D^{30} 1·5560, yield 0·8 g (80%); λ_{max} 253 mμ (ε 10,580) IR Spectrum: C=O 1689 cm^{-1}; OMe 1236, aromatic ring H, 880, 824 cm^{-1}. (Found: C, 75·88; H, 7·79. $C_{12}H_{14}O_2$ requires: C, 75·76; H, 7·42%.)

The 2,4-*dinitrophenylhydrazone* (H_2SO_4 method) red needles (benzene–hexane), m.p. 220–222°. (Found: N, 15·03. $C_{18}H_{18}O_5N_7$ requires: N, 15·13%.)

[22] E. Schwenk, D. Papa, B. Whitman and H. F. Ginsberg, *J. Org. Chem.* **9**, 175 (1944).
[23] Sukh Dev, *J. Indian Chem. Soc.* **32**, 518 (1955).

Stobbe condensation

o-Methoxyacetophenone[24–26] (15 g) was condensed with dimethyl succinate (21·9 g) in presence of t-BuOK in t-BuOH (from 4·3 g K and 100 ml t-BuOH) in the manner described earlier for the *p*-isomer and then worked up to give 25·3 g (yield 95·8%) of the crude half-ester which was used as such in the next step.

γ-(o-Anisyl)γ-methylbutyrolactone

The half-ester (crude, 10 g) was refluxed with 48% HBraq (24 ml) in AcOH (36 ml) for 17 hr and then worked up exactly as described for the *p*-isomer. In this way crude lactone was obtained which was methylated with Me_2SO_4 (2 ml) and NaOHaq (1·4 g, 12 ml of H_2O). On working up, the required lactone distilled as a colourless liquid, b.p. 129–131°/0·6 mm, n_D^{26} 1·5311; yield 1·7 g (21·8%). IR spectrum: γ-lactone 1776 cm^{-1}; OMe 1250 cm^{-1}; aromatic ring H, 757 cm^{-1}. (Found: C, 69·28; H, 7·19. $C_{12}H_{14}O_3$ requires: C, 69·84; H, 7·74%.)

γ-(o-Anisyl)valeric acid

The above lactone (1·0 g) was hydrogenated with 10% Pd–C (0·12 g) in presence of AcOH (10 ml) and 60% perchloric acid aq (0·1 ml) at room temp and press and then worked up to yield the hydrogenated product, b.p. 138–140°/0·6 mm, m.p. 58–62°, yield 0·88 g (87·5%). A portion after crystallization from pet. ether had m.p. 63–65°, mixed m.p. with the acid obtained *via* ethyl allylmalonate condensation remained undepressed. (Found: C, 69·5; H, 7·9. $C_{12}H_{16}O_3$ requires: C, 69·2; H, 7·74%.)

S-*Benzylthiuronium salt* crystallized from dil. EtOH as a white powder, m.p. 128–129°, mixed m.p. with the corresponding deriv of the acid obtained *via* Friedel-Crafts alkylation remained undepressed.

[24] K. V. Auwers, *Liebigs Ann.* **408,** 245 (1915).
[25] K. W. Rosenmund and W. Schnurr, *Liebigs Ann.* **460,** 88 (1928).
[26] A. I. Vogel, *Practical Organic Chemistry* p. 669. Longman, London (1956).