# 462. *β-Aroylpropionic Acids. Part XV.* The Preparation and Lactonisation of β-Aroyl-α- and -β-arylpropionic Acids.*

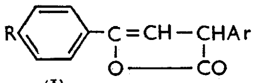
By F. G. Baddar and Sayad Sherif.

Chlorobenzene with phenyl- and *p*-methoxyphenyl-succinic anhydride in presence of aluminium chloride gives, in the former case, β-*p*-chlorobenzoyl-β-phenylpropionic acid, and in the latter a mixture of β-*p*-chlorobenzoyl-α- and -β-*p*-hydroxyphenylpropionic acid.

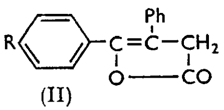
β-Aroyl-α- and -β-arylpropionic acids are converted by hot acetic–sulphuric acid into βγ-unsaturated γ-lactones.

Condensation of phenylsuccinic anhydride with chlorobenzene in presence of anhydrous aluminium chloride gave rise to β-*p*-chlorobenzoyl-β-phenylpropionic acid as sole product. Its structure was established by the facts that with chromic acid it gave *p*-chlorobenzoic acid, and it differed from β-*p*-chlorobenzoyl-α-phenylpropionic acid. The latter acid was prepared from β-*p*-chlorophenyl styryl ketone by addition of hydrogen cyanide and subsequent hydrolysis.[1] β-*p*-Chlorobenzoyl-α-phenylpropionic acid was reduced to γ-*p*-chlorophenyl-α-phenylbutyric acid, then cyclised to 7-chloro-2-phenyl-1-tetralone, which with methylmagnesium iodide gave 7-chloro-1,2,3,4-tetrahydro-1-methyl-2-phenyl-1-naphthol (III), whose tetralol structure was inferred from its infrared spectrum.

*p*-Methoxyphenylsuccinic anhydride with chlorobenzene in presence of aluminium chloride gave a mixture of β-*p*-chlorobenzoyl-β- and -α-*p*-hydroxyphenylpropionic acid, the former predominating, together with 3% of β-*p*-chlorobenzoyl-α-*p*-methoxyphenylpropionic acid. The β-*p*-chlorobenzoyl-α-*p*-hydroxyphenyl- and -α-*p*-methoxyphenylpropionic acid were identical with authentic specimens. The structure of the β-*p*-chlorobenzoyl-β-*p*-hydroxyphenylpropionic acid was established by elemental analysis and oxidation to *p*-chlorobenzoic acid. The presence of the hydroxyl group in the two acids was established by the infrared spectra.



(I)



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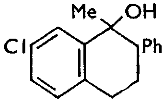

(III)

When the β-aroyl-α- and -β-aryl-propionic acids were heated with acetic–sulphuric acid, they were converted into the corresponding βγ-unsaturated γ-lactones (I and II, respectively). The lactone structure was established by the appearance of its characteristic stretching frequency[2] in the infrared spectra of these compounds (1775—1730 cm.$^{-1}$) (see Table).

The results of the present investigation and of Wali *et al.*[3] show that electron-attracting substituents in either reactant favour the formation of the β-aroyl-β-arylpropionic acids. On the other hand, electron-repelling substituents lead to the predominant formation of the α-substituted acids.[4]

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* Part XIV, *Egypt. J. Chem.*, in the press.

[1] Allen and Frame, *Canad. J. Res.*, 1932, **6**, 605.

[2] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1956, p. 153.

[3] Wali, Khalil, Bhatia, and Ahmad, *Proc. Indian Acad. Sci.*, 1941, **14**, *A*, 139.

[4] Baddar, Fahim, and Fleifel, *J.*, 1955, 2199; Baddar, Fleifel, and Sherif, *J. Chem.* (*U.A.R.*), in the press (formerly *Egypt. J. Chem.*

## EXPERIMENTAL

Infrared spectra were measured by Perkin–Elmer Infracord spectrophotometer model 137, by the Nujol mull technique.

β-*p-Chlorobenzoyl-α-phenylpropionitrile.*—A solution of *p*-chlorophenyl styryl ketone (30 g.), in ethanol (250 ml.) was treated with aqueous potassium cyanide (20 g. in 50 ml.) and glacial acetic acid (10 ml.). The mixture was heated to the b. p., then allowed to cool. The product (32 g.) was filtered off and crystallised from benzene–light petroleum (b. p. 50—70°), to give β-*p*-chlorobenzoyl-α-phenylpropionitrile, m. p. 126—127° (Allen and Frame[1] give m. p. 122°) (Found: C, 70·6; H, 4·55; Cl, 12·3; N, 4·85. Calc. for $C_{16}H_{12}ClNO$: C, 71·2; H, 4·45; Cl, 13·2; N, 5·2%).

β-p-*Chlorobenzoyl-α-phenylpropionic Acid.*—β-*p*-Chlorobenzoyl-α-phenylpropionitrile (30 g.) was refluxed in methanol (200 ml.) and concentrated sulphuric acid (40 ml.) for 6 hr. The *ester*, which solidified on cooling, was filtered off (32 g.) and crystallised from benzene; it had m. p. 113—114° (Found: C, 67·7; H, 4·9; Cl, 11·6; OMe, 10·5. $C_{17}H_{15}ClO_3$ requires C, 67·4; H, 5·0; Cl, 11·7; OMe, 10·2%). The ester (15 g.) was hydrolysed with 10% aqueous potassium hydroxide (200 ml.) (1 hr., reflux) to β-*p*-chlorobenzoyl-α-phenylpropionic acid (13 g.), m. p. 159—160° (from ethanol) (Akhnookh *et al.*[5] give m. p. 160°) (Found: C, 66·2; H, 4·5; Cl, 12·3. Calc. for $C_{16}H_{13}ClO_3$: C, 66·7; H, 4·5; Cl, 12·3%). The acid and its ethyl ester[1] gave the same yellow 2,4-*dinitrophenylhydrazone*, m. p. 164—165° (from acetic acid) (Found: C, 58·1; H, 4·3; N, 11·2. $C_{24}H_{21}ClN_4O_6$ requires C, 58·0; H, 4·2; N, 11·3%).

γ-p-*Chlorophenyl-α-phenylbutyric Acid.*—β-*p*-Chlorobenzoyl-α-phenylpropionic acid (5 g.) was reduced by the Martin–Clemmensen method (48 hr.) to γ-p-*chlorophenyl-α-phenylbutyric acid* (4 g.), m. p. 82—83° [from light petroleum (b. p. 50—70°)] (Found: C, 70·1; H, 5·4; Cl, 12·4. $C_{16}H_{15}ClO_2$ requires C, 70·0; H, 5·5; Cl, 12·9%).

7-*Chloro*-2-*phenyl*-1-*tetralone.*—A mixture of γ-*p*-chlorophenyl-α-phenylbutyric acid (5 g.), concentrated sulphuric acid (15 ml.), and acetic acid (7 ml.) was heated on a boiling-water bath for 1·5 hr. with stirring and then worked up as usual.

7-*Chloro*-2-*phenyl*-1-*tetralone* (2·5 g.) had m. p. 85—86° [from light petroleum (b. p. 50—70°)] (Found: C, 74·8; H, 4·9; Cl, 13·7. $C_{16}H_{13}ClO$ requires C, 74·85; H, 5·1; Cl, 13·8%). Its orange-red 2,4-*dinitrophenylhydrazone* had m. p. 229—230° (from acetic acid) (Found: C, 60·4; H, 3·6; Cl, 7·9; N, 12·8. $C_{22}H_{17}ClN_4O_4$ requires C, 60·5; H, 3·9; Cl, 8·1; N, 12·8%).

7-*Chloro*-1,2,3,4-*tetrahydro*-1-*methyl*-2-*phenyl*-1-*naphthol.*—The above tetralone (1·5 g.) in ether was added gradually to ethereal methylmagnesium iodide [from methyl iodide (5 g.) and magnesium (0·4 g.)], refluxed for 5 hr., left overnight, and worked up in the usual manner. The *tetralol* (1·5 g.) was extracted with boiling light petroleum (b. p. 50—60°), then crystallised from benzene; it had m. p. 139—140° (Found: C, 74·35; H, 6·4; Cl, 13·1. $C_{17}H_{17}ClO$ requires C, 74·9; H, 6·2; Cl, 13·0%), $\nu_{max.}$ 3570 cm.$^{-1}$ (OH).[6]

β-p-*Chlorobenzoyl*-β-*phenylpropionic Acid.*—Phenylsuccinic anhydride (17·6 g., 1 mol.) in chlorobenzene (20 ml.) was added gradually to a cooled and stirred mixture of anhydrous aluminium chloride (27 g., 2 mols.), and chlorobenzene (30 ml.). The mixture was heated on a boiling-water bath for 3 hr. The product (18 g., 62%) crystallised from benzene, to give β-p-*chlorobenzoyl*-β-*phenylpropionic acid*, m. p. 147—148°, depressed to 120—127° when admixed with the α-phenyl isomer (Found: C, 67·1; H, 4·6; Cl, 11·7. $C_{16}H_{13}ClO_3$ requires C, 66·7; H, 4·5; Cl, 12·3%). With chromic oxide in acetic acid it gave *p*-chlorobenzoic acid, m. p. and mixed m. p. 239°. Its *methyl ester* had m. p. 97—98° [from light petroleum (b. p. 50—70°)] (Found: C, 67·45; H, 4·9; Cl, 11·5; OMe, 10·5. $C_{17}H_{15}ClO_3$ requires C, 67·4; H, 5·0; Cl, 11·7; OMe, 10·2%).

p-*Chlorophenyl* 4-*Methoxystyryl Ketone.*—A mixture of *p*-chloroacetophenone (15·5 g.), ethanol (25 ml.), water (40 ml.), sodium hydroxide (5 g.), and *p*-anisaldehyde (13·5 g.) was stirred at 20—25° for 1·5 hr., then diluted with water and filtered. The *chalcone* (25 g.) was obtained in pale lemon-yellow needles, m. p. 124—125°, from ethanol (Found: C, 70·4; H, 4·7; Cl, 13·0; OMe, 11·5. $C_{16}H_{13}ClO_2$ requires C, 70·45; H, 4·8; Cl, 13·0; OMe, 11·4%).

β-p-*Chlorobenzoyl*-α-p-*methoxyphenylpropionitrile.*—To a solution of the chalcone (10 g.), in ethanol (100 ml.), glacial acetic acid (5 ml.) and aqueous potassium cyanide (7 g. in 15 ml.) were added. The mixture was boiled to obtain a clear solution, then left overnight. The *nitrile*

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[5] Akhnookh, Awad, and Baddar, *J.*, 1959, 1015.

[6] Ref. 2, p. 84.

(11 g.) had m. p. 120—121° (from ethanol) (Found: C, 67·85; H, 4·55; Cl, 11·7; N, 4·7; OMe, 10·1. $C_{17}H_{14}ClNO_2$ requires C, 68·1; H, 4·7; Cl, 11·85; N, 4·7; OMe, 10·35%).

β-p-*Chlorobenzoyl*-α-p-*methoxyphenylpropionic Acid.*—The preceding nitrile (12 g.), methanol (80 ml.), and concentrated sulphuric acid (15 ml.) were refluxed for 8 hr., giving *methyl* β-p-*chlorobenzoyl*-α-p-*methoxyphenylpropionate* (12 g.), m. p. 69—70° [from benzene–light petroleum (b. p. 50—70°)] (Found: C, 65·0; H, 5·2; Cl, 10·8; OMe, 18·6. $C_{18}H_{17}ClO_4$ requires C, 65·0; H, 5·1; Cl, 10·7; 2OMe, 18·6%). The ester (7 g.) was hydrolysed with 10% aqueous potassium hydroxide (100 ml.) (2 hr.) to the acid (5·5 g.), m. p. 153—154° (from ethanol) (Akhnookh *et al.*[7] give the same m. p.) (Found: C, 64·0; H, 4·9; Cl, 10·8; OMe, 9·6. Calc. for $C_{17}H_{15}ClO_4$: C, 64·05; H, 4·7; Cl, 11·1; OMe, 9·7%), giving with concentrated sulphuric acid a red colour which changed to blue after few minutes. When the acid or its ethyl ester was warmed with 2,4-dinitrophenylhydrazine in ethanol and concentrated sulphuric acid, the yellow 2,4-*dinitrophenylhydrazone* of the ethyl ester was obtained, having m. p. 197—198° (from glacial acetic acid) (Found: C, 57·0; H, 4·5; Cl, 6·9; N, 10·5. $C_{25}H_{23}ClN_4O_7$ requires C, 57·0; H, 4·4; Cl, 6·7; N, 10·6%).

γ-p-*Chlorophenyl*-α-p-*methoxyphenylbutyric Acid.*—β-*p*-Chlorobenzoyl-α-*p*-methoxyphenylpropionic acid (5 g.) was reduced by the modified Clemmensen method (36 hr.). γ-p-*Chlorophenyl*-α-p-*methoxyphenylbutyric acid* (4·5 g.) had m. p. 94—95° [from light petroleum (b. p. 50—70°)] (Found: C, 66·4; H, 5·4; Cl, 11·1; OMe, 10·0. $C_{17}H_{17}ClO_3$ requires C, 67·0; H, 5·6; Cl, 11·7; OMe, 10·2%).

β-p-*Chlorobenzoyl*-α-p-*hydroxyphenylpropionic Acid.*—A mixture of β-*p*-chlorobenzoyl-α-*p*-methoxyphenylpropionic acid (5 g.), aluminium chloride (10 g.), and chlorobenzene (30 ml.) was stirred at 100° for 2 hr., then worked up as usual. The product (4 g.) was crystallised from dilute ethanol, then from benzene, to give β-p-*chlorobenzoyl*-α-p-*hydroxyphenylpropionic acid*, m. p. 154—155° depressed to 130—135° on admixture with β-*p*-chlorobenzoyl-α-*p*-methoxyphenylpropionic acid. It gave a yellow colour with concentrated sulphuric acid which changed to green after few minutes (Found: C, 63·1; H, 4·2; Cl, 11·4. $C_{16}H_{13}ClO_4$ requires C, 63·05; H, 4·3; Cl, 11·65%). It had $\nu_{max.}$ 3570 cm.$^{-1}$ (OH).

*Condensation of Chlorobenzene with* p-*Methoxyphenylsuccinic Anhydride.*—The product from chlorobenzene (150 ml.), *p*-methoxyphenylsuccinic anhydride (20·6 g., 1 mol.), and aluminium chloride (27 g., 2 mol.) (2 hr. on a boiling-water bath) was fractionally crystallised from benzene, then from dilute acetic acid, to give β-p-*chlorobenzoyl*-β-p-*hydroxyphenylpropionic acid*, m. p. 200—201° (14 g., 44%) (Found: C, 63·2; H, 4·4; Cl, 10·6. $C_{16}H_{13}ClO_4$ requires C, 63·05; H, 4·3; Cl, 11·65%), $\nu_{max.}$ 3570 (OH) and 1680 cm.$^{-1}$ (C=O),[8] oxidised by chromic oxide in acetic acid to *p*-chlorobenzoic acid.

| | Lactone | | Acid | AcOH | $H_2SO_4$ | | | | Yield | $\nu_{max.}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| | Ar | R | (g.) | (ml.) | (ml.) | Temp. | Solvent | M. p. | (%) | (cm.$^{-1}$) † |
| I | Ph | H | 10 | 20 | 40 | 100° | $PhNO_2$ | 285° * | 90 | 1770 |
| I | Ph | Me | 2 | 10 | 10 | 100 | Xylene | 265 | 70 | 1765 |
| I | Ph | Cl | 2·5 | 5 | 10 | 100 | Xylene | 245 § | 90 | 1775 |
| I | *p*-MeO·$C_6H_4$ | Cl | 2 | 15 | 7 | 65—70 | Ethanol | 140 | 80 | 1730 |
| II | — | H | 10 | 20 | 40 | 100 | Ethanol | 157 | 90 | 1750 |
| II | — | Me | 5 | 10 | 20 | 100 | $C_6H_6$–Pet ‡ | 133 | 60 | 1740 |
| II | — | Cl | 2·5 | 5 | 10 | 100 | $C_6H_6$–Pet ‡ | 141 | 90 | 1775 |

* Not depressed when admixed with an authentic specimen.[9] † Stretching frequency for βγ-unsaturated γ-lactones. ‡ Pet = light petroleum (b. p. 50—70°). § Decomp.

| | Lactone | | | Found (%) | | | | Required (%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Ar | R | Formula | C | H | Cl | OMe | C | H | Cl | OMe |
| I | Ph | Me | $C_{17}H_{14}O_2$ | 81·1 | 5·6 | — | — | 81·6 | 5·6 | — | — |
| I | Ph | Cl | $C_{16}H_{11}ClO_2$ | 70·7 | 4·2 | 13·1 | — | 70·9 | 4·1 | 13·1 | — |
| I | *p*-MeO·$C_6H_4$ | Cl | $C_{17}H_{13}ClO_3$ | 67·5 | 4·4 | 11·8 | 10·3 | 67·9 | 4·3 | 11·8 | 10·3 |
| II | — | H | $C_{16}H_{12}O_2$ | 81·2 | 5·2 | — | — | 81·3 | 5·1 | — | — |
| II | — | Me | $C_{17}H_{14}O_2$ | 81·1 | 5·8 | — | — | 81·6 | 5·6 | — | — |
| II | — | Cl | $C_{16}H_{11}ClO_2$ | 71·1 | 4·3 | 12·6 | — | 70·9 | 4·1 | 13·1 | — |

The benzene mother-liquor was evaporated, and the residue was crystallised from dilute

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[7] Akhnookh, Awad, and Baddar, *Egypt. J. Chem.*, in the press.

[8] Ref. 2, p. 114.

[9] Hann and Lapworth, *J.*, 1904, **85**, 1355.

ethanol, to give β-*p*-chlorobenzoyl-α-*p*-hydroxyphenylpropionic acid, m. p. and mixed m. p. 154—155° (3 g., 9%). Concentration of the ethanol mother-liquor gave β-*p*-chlorobenzoyl-α-*p*-methoxyphenylpropionic acid (1 g. 3%), m. p. and mixed m. p. 153—154°.

*Lactonisation of* β-*Aroyl*-α- *and* -β-*arylpropionic Acids.*—The solution of the acid in acetic acid was heated with concentrated sulphuric acid for 1·5 hr. and, after cooling, poured into water. The solid was filtered off and washed with dilute sodium carbonate solution. The *lactone* then crystallised from a suitable solvent (see Table).

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