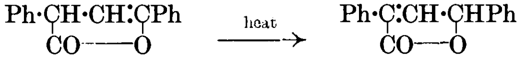
CXXII.—*The Hydrolysis of γ-Keto-nitriles of the Type* R·CH(CN)·CH$_2$·COPh.

By MARJORIE ROBERTSON and HENRY STEPHEN.

ANSCHUTZ and MONTFORT (*Annalen*, 1895, **284**, 2; *Ber.*, 1895, **28**, 63) investigated the hydrolysis of β-benzoyl-α-phenylpropionitrile, Ph·CH(CN)·CH$_2$·COPh, and obtained β-benzoyl-α-phenylpropionic acid (compare Rupe and Schneider, *Ber.*, 1895, **28**, 960; Hann and Lapworth, J., 1904, **85**, 1355; Lapworth and Wechsler, J., 1910, **97**, 39). This keto-acid yields two isomeric lactones derived from the enolic form of the acid, (I) (m. p. 109°; Anschutz and Montfort) and (II) (m. p. 284—286°; Lapworth and Wechsler), αγ-diphenyl*iso*crotonolactone and αγ-diphenylcrotonolactone respectively.

(I.)  (II.)

$$\text{(I.)}\quad \begin{array}{l}\text{Ph·}\underset{|}{\text{C}}\text{H·CH:}\underset{|}{\text{C}}\text{Ph}\\ \quad\ \text{CO——O}\end{array} \xrightarrow{\text{heat}} \begin{array}{l}\text{Ph·}\underset{|}{\text{C}}\text{:CH·}\underset{|}{\text{C}}\text{HPh}\\ \quad\ \text{CO——O}\end{array}\quad \text{(II.)}$$

The relationship between these lactones is analogous to that of vinylacetic acid and crotonic acid, the conversion of the former into the latter by heating alone or in solution being an established fact. The constitution of (I) was proved (Anschutz and Montfort, *loc. cit.*) by reducing the acid, which gave αγ-diphenylbutyrolactone (m. p. 103°)*. The structure (II) was proposed by Lapworth and Wechsler, who state that the lactone does not revert again to the keto-acid by hydrolytic fission, but appears to give an acid resembling phenylacetic acid. We have confirmed that phenylacetic acid is produced when (II) is carefully fused with potassium hydroxide. During the course of our experiments we have observed that the lactone (I) is labile, being converted into the higher-melting form (II) by the action of heat or by repeated crystallisation from solvents, from which (II), being much less soluble, usually separates during the process of solution.

A third substance, isomeric with the above lactones, was obtained

---

* In their publication, Anschutz and Montfort have reversed the melting points of this lactone and the unsaturated lactone (II), and the same error is repeated by Hann and Lapworth (*loc. cit.*). We have prepared lactone (II) and confirmed the melting point, 109° (Found: C, 81·4; H, 5·3. Calc. for $C_{16}H_{12}O_2$: C, 81·35; H, 5·1%).

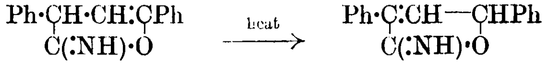
by treating a solution of β-benzoyl-α-phenylpropionitrile in acetic acid with hydrogen chloride. This compound melts at 206°, and shows the same tendency to change into the higher-melting form during crystallisation. When it was boiled with aqueous sodium hydroxide solution, acetophenone, identified by its *p*-nitrophenylhydrazone, was obtained, showing that partial fission of the compound had taken place. A similar fission applies to the lactone (I). The alkaline solution on acidification gave β-benzoyl-α-phenylpropionic acid.

The hydrolysis of β-benzoyl-α-phenylpropionitrile and of *β-benzoyl-α-(*p*-methoxyphenyl)propionitrile* to give the respective *keto-acids* is best done by warming the nitriles at 80° with 50% sulphuric acid, but this method is not applicable to *β-benzoyl-α-(3 : 4-methylenedioxyphenyl)propionitrile,* which is readily decomposed by sulphuric acid, the methylene group being attacked. The corresponding *acid* in this case was prepared by saturating an alcoholic solution of the nitrile with hydrogen chloride, and hydrolysing the ester formed.

Conversion of the Above Acids into Lactones.—In all three cases, two isomeric lactones were obtained, the *iso*crotonic forms, always the lower-melting isomerides, being prepared by boiling solutions of the acids in acetic anhydride. The higher-melting crotonic forms were obtained (*a*) by the action of heat on the acids, which lose 1 mol. of water quantitatively above the melting point, and (*b*) by boiling solutions of the lower forms in alcohol or acetic acid.

β-Benzoyl-α-phenylpropionamide (Rupe and Schneider, *loc. cit.*) and *β-benzoyl-α-(*p*-methoxyphenyl)propionamide* are readily prepared by treatment of the respective nitriles with 75% sulphuric acid at the ordinary temperature for 15 minutes. *β-Benzoyl-α-(3 : 4-methylenedioxyphenyl)propionamide* was prepared by treating a solution of the nitrile in acetic acid with hydrogen chloride.

Conversion of the Nitriles and Amides into Imino-lactones.—Two isomeric *imino-lactones* (III) and (IV) corresponding to the above lactones have been obtained :

(III.)  (IV.)

$$\text{(III.)}\quad \begin{array}{c}\text{Ph}\cdot\text{CH}\cdot\text{CH:CPh}\\ \text{C(:NH)}\cdot\text{O}\end{array} \xrightarrow{\text{heat}} \begin{array}{c}\text{Ph}\cdot\text{C:CH}\text{—}\text{CHPh}\\ \text{C(:NH)}\cdot\text{O}\end{array}\quad \text{(IV.)}$$

The lower-melting form (III) is obtained by the action of acetic anhydride on the corresponding amide, and (IV) by (*a*) heating the amide a few degrees above the melting point, (*b*) boiling a solution of (III) in acetic acid, and (*c*) treating the nitrile with concentrated sulphuric acid.

EXPERIMENTAL.

β-Benzoyl-α-phenyl-, β-benzoyl-α-(*p*-methoxyphenyl)-, and β-benzoyl-α-(3 : 4-methylenedioxyphenyl)-propionitriles were prepared from the corresponding arylideneacetophenones by the method of Hann and Lapworth (*loc. cit.*). The second nitrile showed the greatest, and the third nitrile the least, tendency to condense with their corresponding arylideneacetophenones to give very sparingly soluble *cyclo*pentane derivatives, as stated by Hann and Lapworth, although a large excess of potassium cyanide and a higher temperature were employed in the latter case.

β-*Benzoyl*-α-(p-*methoxyphenyl*)*propionitrile* forms pale yellow plates, m. p. 118° (Found : C, 76·9; H, 5·6. $C_{17}H_{15}O_2N$ requires C, 77·0; H, 5·7%), and β-*benzoyl*-α-(3 : 4-*methylenedioxyphenyl*)-*propionitrile* straw-coloured plates, m. p. 129° (Found : C, 73·0; H, 4·7. $C_{17}H_{13}O_3N$ requires C, 73·1; H, 4·7%).

β-*Benzoyl*-α-(p-*methoxyphenyl*)*propionic acid* was prepared by warming a solution of 2·6 g. of the nitrile in 20 c.c. of 50% sulphuric acid. It became pale green and slowly dark green and when a solid began to separate the mixture was poured on ice. The white precipitate was separated, dissolved in sodium bicarbonate solution at 40°, recovered from the filtered solution, and crystallised from dilute alcohol, the keto-acid being obtained as colourless needles, m. p. 155° (Found : C, 72·0; H, 5·65. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%).

β-*Benzoyl*-α-(3 : 4-*methylenedioxyphenyl*)*propionic acid* was prepared by the method of Rupe and Schneider (*loc. cit.*) and obtained as fine white needles, m. p. 134°, from dilute alcohol (Found : C, 68·6; H, 4·5. $C_{17}H_{14}O_5$ requires C, 68·45; H, 4·7%).

α-(p-*Methoxyphenyl*)-γ-*phenyl*iso*crotonolactone* was prepared by boiling a solution of the corresponding acid (1 g.) in excess of acetic anhydride for 3 hours. A finely divided solid separated, which was filtered off, the filtrate being poured into cold water. The solid was crystallised from dilute alcohol and proved to be the insoluble crotonolactone (0·25 g.) (see below). The aqueous solution of the filtrate deposited the *iso*crotonolactone, which formed needles, m. p. 96°, from methyl alcohol (Found : C, 76·8; H, 5·2. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3%). The insoluble *crotonolactone* crystallised from acetic acid in needles, which sublimed at 266° and melted at 270—275° (decomp.) (Found : C, 76·3; H, 5·0. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3%). This lactone is obtained in larger yield (0·4 g.) if acetyl chloride is used as the dehydrating agent. The lower-melting lactone above is converted by prolonged boiling in alcohol into the less soluble, higher-melting form. The latter is also formed quantitatively by heating the acid for 2 hours at 180—220° (Found : loss of H_2O, 6·55. $C_{17}H_{16}O_4$ requires loss, 6·34%).

α-(3 : 4-*Methylenedioxyphenyl*)-γ-*phenyl*iso*crotonolactone*, prepared from the corresponding acid in a manner similar to the above, crystallised from dilute methyl alcohol in flat white needles, m. p. 143° (Found: C, 72·7; H, 4·1. $C_{17}H_{12}O_4$ requires C, 72·85; H, 4·3%). The *crotonolactone* was prepared from the former by boiling a solution of it in acetic acid for 3 hours. The precipitate, after being washed with ether, appeared under the microscope as minute needles, m. p. 285—290° (decomp.; showing a tendency to sublime at 280°) (Found: C, 72·5; H, 4·0. $C_{17}H_{12}O_4$ requires C, 72·85; H, 4·3%).

β-*Benzoyl*-α-*phenylpropionamide* was prepared by treating the nitrile with 75% sulphuric acid, the temperature being maintained at 15° by cooling in water. After 15 minutes the mixture was poured on ice, and the precipitated amide filtered. Crystallisation from dilute methyl alcohol gave needles, m. p. 149° (Found: C, 75·6; H, 5·8; volatile NH_3, 7·1. $C_{16}H_{15}O_2N$ requires C, 75·9; H, 5·9; volatile NH_3, 7·1%). A weighed amount of the amide was heated at 190° for an hour, and the loss in weight determined. The residue crystallised from nitrobenzene in minute needles, which decomposed above 290°; analysis indicated that the substance was *αγ-diphenylcrotonoiminolactone* (Found: loss 1 mol. H_2O, 7·5. $C_{16}H_{15}O_2N$ requires loss 7·2%. Found: C, 81·8; H, 5·5. $C_{16}H_{13}ON$ requires C, 81·7; H, 5·5%). *αγ-Diphenyl*iso*crotonoiminolactone* was obtained by boiling the above amide with excess of acetic anhydride for two hours; the solution was then poured into cold water. The oil obtained slowly solidified and then crystallised from dilute methyl alcohol in small plates, m. p. 122° (Found: volatile NH_3, 6·85. $C_{16}H_{13}ON$ requires NH_3, 7·2%). The iminolactone is isomerised to the higher-melting isomeride by prolonged boiling with acetic acid.

β-*Benzoyl*-α-(p-*methoxyphenyl*)*propionamide* was readily obtained in 60% yield by dissolving the nitrile in 75% sulphuric acid cooled to 5°. It crystallised from dilute alcohol in needles, m. p. 153°; a mixed m. p. determination with the corresponding acid (m. p. 155°) showed a depression of 30° (Found: C, 72·2; H, 6·2; volatile NH_3, 6·1. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·0; NH_3, 6·0%). The amide, when heated at 165°, lost exactly 1 equiv. of water, giving a product which had an indefinite melting point (270—280°) and was insufficiently pure for analysis (Found: loss 1 mol. H_2O, 6·3. $C_{17}H_{17}O_3N$ requires loss, 6·4%).

When the amide was heated with acetic anhydride it gave α-(p-*methoxyphenyl*)-γ-*phenyl*iso*crotonoiminolactone*, which formed plates, m. p. 114°, from dilute methyl alcohol (Found: volatile NH_3, 6·3. $C_{17}H_{15}O_2N$ requires NH_3, 6·4%).

β-*Benzoyl*-α-(3:4-*methylenedioxyphenyl*)*propionamide* was prepared by saturating a solution of the nitrile in glacial acetic acid with dry hydrogen chloride. The yellow solution became dark red and was kept over-night in the refrigerator. When it was poured into water, a dark greenish oil separated, which slowly hardened : this was unchanged nitrile. The mother-liquor after 3 days deposited colourless needles which, recrystallised from dilute alcohol, melted at 149° (Found : C, 68·55 ; H, 5·1 ; volatile NH_3, 5·7. $C_{17}H_{15}O_4N$ requires C, 68·7 ; H, 5·05 ; NH_3, 5·7%). A weighed quantity of the amide, heated at 150—170°, melted to a green liquid, the colour of which gradually disappeared and the liquid solidified (Found : loss 1 mol. H_2O, 6·05. $C_{17}H_{15}O_4N$ requires loss, 6·1%). The residue was boiled repeatedly with glacial acetic acid : the insoluble white powder, m. p. (rapidly heated) 265°, proved to be α-(3 : 4-*methylenedioxyphenyl*)-γ-*phenylcrotonoiminolactone* (Found : C, 73·4 ; H, 4·8. $C_{17}H_{13}O_3N$ requires C, 73·1 ; H, 4·7%).

THE UNIVERSITY OF THE WITWATERSRAND,
JOHANNESBURG, SOUTH AFRICA.
[*Received, February 2nd*, 1931.]