99. *The Chemistry of the Triterpenes. Part VIII. The α- and β-Amyrenes.*

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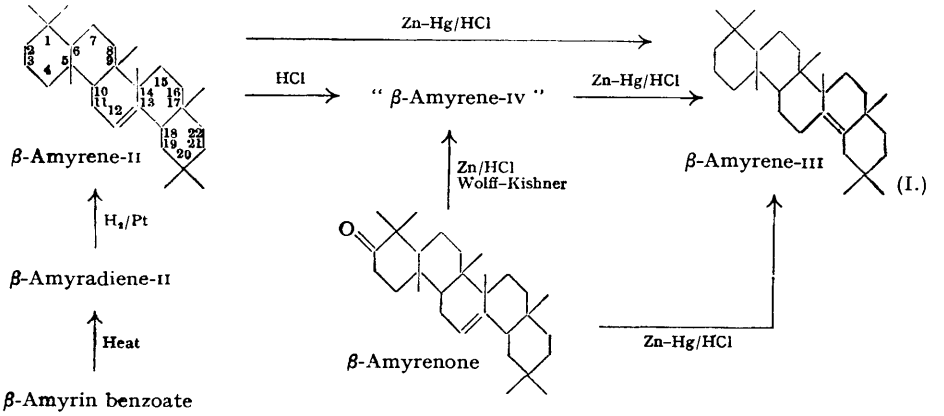
A review of the chemistry of the α- and β-amyrenes in the light of current structures for α-amyrin, β-amyrin, and lupeol indicated a number of anomalies. These have been investigated and resolved. In the course of the investigations it has been found that the conditions which give rise to the isomerisation of the double bond in derivatives of β-amyrin have no effect upon the double bond in those of α-amyrin.

In the investigations leading to the discovery of the inter-relationship of the β-amyrin and lupeol groups of triterpenes described in the preceding paper, the $C_{30}H_{50}$ hydrocarbon, β-amyrene-III, was obtained from both groups. This compound was first obtained by Winterstein ond Stein (*Annalen*, 1933, **502**, 233) by the reduction of β-amyrenone with amalgamated zinc and hydrochloric acid and also by the isomerisation of β-amyrene-II with the same reagents. The β-amyrene-II was prepared by hydrogenation of β-amyradiene-II (β-amyrilene-II), obtained by pyrolysis of β-amyrin benzoate.

β-Amyrene-III (δ-amyrene) is now known (see preceding paper) to be the parent hydrocarbon of δ-amyrenol (Ruzicka and Jeger, *Helv. Chim. Acta*, 1941, **24**, 1243), with the structure indicated (I). β-Amyrene-II should be the parent hydrocarbon of β-amyrin, with the ethylenic linkage in the 12 : 13 position, its formation from β-amyradiene-II being the result of the hydrogenation of the double bond formed on pyrolysis of the benzoate. This is probably a *cis*-elimination of benzoic acid, not involving a structural rearrangement (*cf.* Barton, *J.*, 1949



2174). The formation of β-amyrene-III from β-amyrene-II can be imagined as proceeding *via* a carbonium ion as indicated in the preceding paper, and from β-amyrenone by the same mechanism, the isomerisation accompanying the reduction of the carbonyl group. If this mechanism is correct then the conversion of β-amyrene-II into β-amyrene-III should be able to proceed in the presence of acid alone and should not require the presence of amalgamated zinc. Indeed, Winterstein and Stein found that β-amyrene-II could be isomerised in the presence of hydrochloric acid alone, but the product they obtained was not β-amyrene-III, but an isomer, " β-amyrene-IV," with an optical rotation lying approximately midway between those of β-amyrene-II and -III. β-Amyrene-IV was also obtained by Winterstein and Stein by reduction of β-amyrenone with pure zinc and hydrochloric acid, and they record that it could be isomerised further by amalgamated zinc and hydrochloric acid to β-amyrene-III.

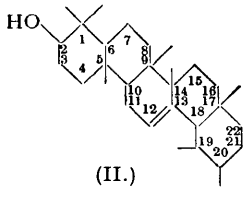
Ruzicka, Schellenberg, and Goldberg (*Helv. Chim. Acta*, 1937, **20**, 791) have also reported the preparation, from β-amyrenone by Wolff–Kishner reduction, of a compound which is said to be probably identical with β-amyrene-IV. This conversion and the reactions described by Winterstein and Stein are indicated in the accompanying reaction scheme, in which are given the structures which are now acceptable for β-amyrenes-II and -III and for β-amyrenone. It is clear that the formulation of any structure for β-amyrene-IV, as an intermediate in the con-

version of β-amyrene-II into β-amyrene-III, is well-nigh impossible. This anomaly became very obvious during the course of the work described in the preceding paper and a reinvestigation of the reactions involved seemed to be highly desirable.

β-Amyrene-II was obtained by hydrogenation of β-amyradiene-II, prepared according to Winterstein and Stein's method, and its constants agreed with those previously reported. Repetition of the reduction of β-amyrenone by the procedure used by Ruzicka *et al.* (*loc. cit.*) and also by a modified Wolff–Kishner method, resulted in the formation in both cases, not of β-amyrene-IV, but of β-amyrene-II, with constants identical with those of the β-amyrene-II prepared from β-amyradiene-II. This result was in accord with our expectation that no isomerisation would occur under the conditions of Wolff–Kishner reductions.

A reinvestigation of the isomerisation of β-amyrene-II in glacial acetic acid, hydrochloric acid being used alone as the catalyst, in the absence of zinc or mercury, showed that if the isomerisation was carried to completion, β-amyrene-III was the sole product. (The β-amyrene-III had a rotation of $[\alpha]_D$ −33° as compared with the figure of −22° reported by Winterstein and Stein. We believe that this is due to our product being purer.) If, however, the isomerisation was not carried to completion products of variable rotation were obtained, with some of the rotations corresponding to those reported for the supposed β-amyrene-IV. It was also found that as the isomerisation proceeded the rotation of the products gradually fell. These results lead to the conclusion that Winterstein and Stein's so-called "β-amyrene-IV" was a mixture of β-amyrene-II and β-amyrene-III. They also show that neither zinc, nor mercury, is necessary for the acid-induced isomerisation of β-amyrene-II to β-amyrene-III, thus confirming the ideas implicit in the mechanism proposed for the formation of β-amyrene-III. Further confirmation is provided by the acid-induced isomerisation of β-amyrenone to δ-amyrenone, when only the double bond is affected, and the Wolff–Kishner reduction of the carbonyl group of the δ-amyrenone giving β-amyrene-III, described in the preceding paper.

In view of the conversion of β-amyrenone into δ-amyrenone, described in the preceding paper, and the discovery by Winterstein and Stein of the formation of β-amyrene-III by Clemmensen reduction of β-amyrenone, it was of interest to study comparable reactions with α-amyrenone, since the structure (II) which has been suggested for α-amyrin (Meisels, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1949, **32**, 1075; 1950, **33**, 700) admits of the possibility of double-bond migration analogous to that observed in the β-amyrin series.



(II.)

Winterstein and Stein have already described a Clemmensen reduction of α-amyrenone and report the formation of α-amyrene-II, which is also obtained by hydrogenation of α-amyradiene-II, the diene obtained by the pyrolysis of α-amyrin benzoate. They further report that α-amyrene-II is a mixture of two α-amyrenes, one melting at 120—122° ($[\alpha]_D$ +98·9°) and the other melting at 110—112° ($[\alpha]_D$ +88·8°). Whilst the isolation of two α-amyrenes from the Clemmensen reduction can easily be explained by assuming isomerisation of the 12 : 13 double bond, the production of the same two α-amyrenes by hydrogenation of α-amyradiene-II is difficult to understand. The hydrocarbon corresponding to the structure (II) for α-amyrin should be obtainable by the Wolff–Kishner reduction of α-amyrenone. This reaction has already been carried out by way of the semicarbazone by Ruzicka, Muller, and Schellenberg (*Helv. Chim. Acta*, 1939, **22**, 758) who isolated a hydrocarbon, m. p. 124°, $[\alpha]_D$ +95°, which they considered to be identical with the higher-melting form of α-amyrene-II obtained by Winterstein and Stein.

We have carried out a Wolff–Kishner reduction of α-amyrenone *via* the hydrazone and obtained the same hydrocarbon, and it is also produced by the Clemmensen reduction of α-amyrenone. No form melting at *ca.* 110° was obtained. Repetition of Winterstein and Stein's procedure for the preparation of α-amyrene-II gave this compound as platelets which, under the microscope, were observed to melt partially at 115°, the melt then crystallised in short needles which melted at 123·5—124°. There were no depressions of melting point on admixture of this compound and the products from α-amyrenone. It is clear, therefore, that there is only one compound, α-amyrene-II, formed from α-amyrin benzoate by pyrolysis and hydrogenation, and from α-amyrenone either by Wolff–Kishner or Clemmensen reduction; but that the hydrocarbon is dimorphic. The results also reveal the important fact that the double bond in α-amyrin is not isomerised under the conditions of the Clemmensen reduction. Attempts to isomerise the double bond in α-amyrenone using the conditions which have been found to isomerise β-amyrenone to δ-amyrenone proved unsuccessful, α-amyrenone being recovered in

good yield after treatment in benzene solution with sulphuric acid in acetic acid for 15 days. The use of more drastic conditions have, as yet, led only to extensive degradation of the α-amyrenone.

The absence of isomerisation provides yet another example of the extraordinary lack of reactivity shown by the double bond of α-amyrin, as compared with that of β-amyrin. Meisels, Jeger, and Ruzicka (*loc. cit.*) ascribe this lack of reactivity to steric hindrance by the methyl group sited at C_{19}. As indicated in the preceding paper, however, it is possible that α- and β-amyrin possess different configurations at C_{18} and that this difference accounts, in part, at least, for the difference in reactivity of the double bonds of the two compounds.

Experimental.

(Rotations were measured in chloroform. Melting points were determined on the Kofler block and are corrected.)

*β-Amyrene-*II.—(a) *From β-amyradiene-*II. β-Amyradiene-II (500 mg.) (Winterstein and Stein, *loc. cit.*) was hydrogenated for 45 minutes at 20° in acetic acid (30 c.c.)–ethyl acetate (10 c.c.), Adams's platinum oxide (50 mg.) being used as catalyst. Water was then added and the product isolated by benzene extraction. Crystallisation from ethyl acetate–methanol gave needles (350 mg.), m. p. 159—162° raised by further recrystallisation from acetone and from chloroform–methanol to 160—162·5°, $[\alpha]_D^{20}$ +96° (*c*, 0·803).

(b) *From β-amyrenone by Wolff–Kishner reduction.* (i) β-Amyrenone semicarbazone (400 mg.) was added to sodium ethoxide, prepared from sodium (0·75 g.) in absolute ethanol (10 c.c.), and the mixture was heated for 20 hours at 185° in a small autoclave. The product (400 mg.) was isolated by benzene extraction. It was dissolved in pentane and chromatographed on a column of neutral alumina (50 g.; activity I). The column was washed with pentane (60 c.c.), and a fraction (350 mg.) was then obtained, by elution with pentane (70 c.c.), which, on crystallisation from chloroform–methanol, gave needles of β-amyrene-II, m. p. 161—162·5° undepressed on admixture with authentic β-amyrene-II, $[\alpha]_D^{20}$ +95·5° (*c*, 1·28). (ii) β-Amyrenone (700 mg.) was added to sodium ethoxide, prepared from sodium (700 mg.) and absolute ethanol (15 c.c.), and 60% aqueous hydrazine hydrate (5 c.c.), and heated for 6 hours at 180—200° in a small autoclave. When cool, excess of water was added giving a precipitate which was filtered off and dried. This was dissolved in chloroform, the solution was filtered through activated charcoal, and methanol was added to the filtrate which deposited needles (455 mg.), m. p. 159—160°, when kept. The needles (120 mg.) were dissolved in pentane (10 c.c.) and chromatographed on alumina (20 g.; activity I). Elution with pentane (35 c.c.), after washing the column with the same eluent (25 c.c.), gave a fraction (120 mg.) which was crystallised from chloroform–methanol giving needles of β-amyrene-II, m. p. 162—163° undepressed on admixture with authentic β-amyrene-II, $[\alpha]_D^{20}$ +96·5° (*c*, 1·16).

*Action of Hydrochloric Acid–Acetic Acid on β-Amyrene-*II.—(*a*) β-Amyrene-II (47 mg.) was dissolved in acetic acid (20 c.c.), and concentrated hydrochloric acid (8 c.c.) was slowly added to the warm solution. The mixture was refluxed for 16 hours and, after it had cooled, excess of water was added. The product was isolated by benzene extraction, and was crystallised from chloroform–methanol, giving short needles (31 mg.), m. p. 185—188°, $[\alpha]_D^{20}$ −19° (*c*, 1·03). Three recrystallisations from the same solvent gave β-amyrene-III, m. p. 190—191° undepressed on admixture with authentic β-amyrene-III, $[\alpha]_D^{20}$ −33° (*c*, 0·46).

(*b*) β-Amyrene-II (50 mg.) was dissolved in warm acetic acid (20 c.c.), and concentrated hydrochloric acid (8 c.c.) was added. After the mixture had been heated under reflux for 15 minutes, excess of water was added and the product isolated by benzene extraction. Crystallisation from chloroform–methanol gave needles (15 mg.), m. p. 157—161°, $[\alpha]_D^{20}$ +38° (*c*, 0·503). The value of the specific rotation suggested that the needles were a mixture of β-amyrene-II (55%) and β-amyrene-III (45%). A synthetic mixture of β-amyrene-II (55%) and β-amyrene-III (45%) melted at 157—160·5°, after crystallisation from chloroform–methanol. Recrystallisation of the melt from the same solvent gave needles, m. p. 157—159°.

*α-Amyrene-*II.—(a) *Hydrogenation of α-amyradiene-*II. α-Amyradiene-II (210 mg.) (Winterstein and Stein, *loc. cit.*) was dissolved in acetic acid (30 c.c.)–ethyl acetate (10 c.c.) and hydrogenated for 30 minutes at 20°, Adams's platinum oxide being used as catalyst. The product was crystallised from acetone giving platelets of α-amyrene-II (96 mg.), m. p. 112·5—123° (112—113° capillary). Further crystallisations gave platelets melting partially at 115°, after which the melt crystallised in short needles, m. p. 123·5—124°, $[\alpha]_D^{20}$ +97° (*c*, 0·80).

(b) *Wolff–Kishner reduction of α-amyrenone.* α-Amyrenone (1 g.) was added to 60% aqueous hydrazine hydrate (5 c.c.) and sodium ethoxide, prepared from sodium (0·7 g.) dissolved in absolute ethanol (15 c.c.), and the mixture was heated at 200—230° for 6 hours in a small autoclave. Dilution with water, and benzene extraction gave a product (755 mg.) which was dissolved in pentane (10 c.c.) and chromatographed on a column of neutral alumina (40 g.; activity I). Elution with pentane gave an oil (440 mg.) which was crystallised from ethyl acetate–chloroform–methanol giving platelets, m. p. 116—118°. Three recrystallisations from acetone gave α-amyrene-II, m. p. 123—124° undepressed on admixture with an authentic specimen, $[\alpha]_D^{20}$ +95° (*c*, 1·13).

(c) *Clemmensen reduction of α-amyrenone.* α-Amyrenone (1 g.) was dissolved in acetic acid (50 c.c.) with warming, zinc amalgam (7 g.) and concentrated hydrochloric acid (20 c.c.) were added, and the mixture was refluxed for 16 hours. The product, isolated with benzene, was dissolved in pentane and chromatographed in a column of neutral alumina (30 g.; activity I). Elution with pentane gave

an oil, crystallisation of which from chloroform–ethyl acetate–methanol gave platelets (450 mg.), m. p. 110—111°. These were dissolved in pentane (10 c.c.) and rechromatographed on a column of alumina (20 g.; activity I). Elution with pentane gave a fraction (325 mg.) which, after two crystallisations from acetone, yielded α-amyrene-II, m. p. 123—124° undepressed on admixture with an authentic specimen, $[\alpha]_D^{20}$ +94° (*c*, 0·67).

The Action of Sulphuric Acid–Acetic Acid on α-Amyrenone.—α-Amyrenone (500 mg.) was dissolved in benzene (5 c.c.), and a mixture of acetic acid (40 c.c.) and sulphuric acid (8 c.c.; *d* 1·84) was added with shaking. The mixture was kept at 20° for 15 days and then diluted with water, and the product isolated by benzene extraction. The product was dissolved in light petroleum (15 c.c.; b. p. 40—60°) and chromatographed on a column of alumina (50 g.; activity I). Elution with benzene–light petroleum (b. p. 40—60°) (2 : 1) gave 430 mg. of crystalline material. Recrystallisation of this from chloroform–methanol gave unchanged α-amyrenone, m. p. 125—126° undepressed on admixture with an authentic specimen, $[\alpha]_D^{20}$ +109° (*c*, 1·3).

Attempted Isomerisation of α-Amyrenone by using Vigorous Conditions.—α-Amyrenone (520 mg.) was dissolved in benzene (5 c.c.), and a mixture of acetic acid (40 c.c.) and sulphuric acid (8 c.c.; *d* 1·84) was added with shaking. The mixture was kept at 80° for 17 hours. The cooled, deep magenta solution was diluted with water, and the product isolated by ethereal extraction. The product (520 mg.) was dissolved in *n*-pentane–benzene (3 : 2) and chromatographed on a column of alumina (40 g.; activity I) Several fractions were obtained by elution, successively, with pentane–benzene (3 : 2), pentane–benzene benzene, ether, and ether–ethanol (95 : 5). None of the fractions could be crystallised, all remaining as oils or resins.

One of the authors (G. S. D.) is indebted to the University of Manchester for a post-graduate scholarship.

THE UNIVERSITY, MANCHESTER, 13. [*Received, October 5th*, 1950.]