LXII.—*Mandelonitrile Glucosides. Prulaurasin.*

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HAVING obtained Fischer's mandelonitrile glucoside from amygdalin in the manner described in the preceding paper it appeared to be desirable to ascertain whether it should be regarded as the glucoside corresponding to amygdalin or as a mixture of stereoisomerides corresponding to the *iso*amygdalin into which amygdalin is converted by alkali (Dakin, Trans., 1904, 85, 1512) and which is also formed from it by the action of strong hydrochloric acid. It was found that the addition of a mere trace of baryta conditioned an immediate and rapid alteration of the rotatory power, the lævorotation becoming almost doubled without change of sign. There was no evidence of hydrolysis; but the glucoside could no longer be isolated in the crystalline condition, either by concentrating the solution or by extracting with ethyl acetate.

In his original description of mandelonitrile glucoside, Emil Fischer (*Ber.*, 1895, 28, 1508) states that he proposed to "attempt to isolate it from the obviously impure preparation which has been described under the name of 'amorphous amygdalin' or 'laurocerasin.'" Now laurocerasin has been obtained recently in the crystalline condition by Hérissé (Compt. rend., 1905, 141, 959; *J. Pharm. Chim.*, 1906, [vi], 24, 537), and renamed by him *Prulaurasin*; it has a higher rotatory power than Fischer's glucoside. Moreover, a third isomeric form of mandelonitrile glucoside (*Sambunigrin*) has been separated by Bourquelot and Danjou (Compt. rend., 1905, 141, 598) from the leaves of the common elder (*Sambucus niger*); this substance has the same melting point as Fischer's glucoside but higher rotatory power even than Hérissé's prulaurasin from laurel leaves.*

Amygdalin has been isolated from bitter almonds, peach kernels, cherry-laurel kernels, plum stones, and the fruit kernel of the bird cherry; it is noteworthy, however, that all attempts to obtain it from the leaves of these plants and from many other leaves which yield hydrogen cyanide on distillation with water have ended in the production of an uncrystallisable syrup only slightly soluble in ethyl acetate but giving with emulsin the same products as amygdalin. To this substance the name "amorphous amygalin" was applied by Winckler. Lehmann, who analysed such a substance, gave to it the formula $C_{80}H_{67}O_{60}N$ and proposed to call it "laurocerasin," supposing it to be a definite compound of amygdalin and amygdalinic acid. From results which he has recently obtained with material prepared carefully from the bark of *Prunus padus* and from cherry-laurel leaves, Jouck has deduced the formulæ $C_{42}H_{60}O_{21}N$ or $C_{42}H_{62}O_{21}N$. The work of Schoonbrodt, who in 1868 obtained a small proportion of bitter acicular crystals from amorphous amygdalin by the use of alcoholic ether, appears to have been generally overlooked; this substance was doubtless the same as that recently isolated by Hérissé with so much skill from the same source, namely, laurel leaves.

In the case of elder leaves, the glucoside is not accompanied by the enzyme necessary to effect its decomposition, so that the presence of hydrogen cyanide in this plant had been overlooked; as a matter of fact, the cyanogenetic glucoside "sambunigrin" was obtained without difficulty, when once its presence had been demonstrated, by Bourquelot and Danjou.

The properties of the three isomeric glucosides are set out in the following table:

* The production of hydrogen cyanide from a plant was long held to be an indication of the presence of amygdalin.

	$[\alpha]_D$.	M. p.	
Mandelonitrile glucoside (Fischer).....	-26.9	147—150°	Crystallises readily from hot ethyl acetate.
Prulaurasin	-52.7	120—122	Hygroscopic, obtained crystalline with difficulty.
Sambunigrin	-76.3	151—152	Crystallises readily from hot ethyl acetate.

Dunstan and Henry speak of them in their Report (York, 1906) to the British Association in the following terms :

“If it may be assumed that they are different—and the evidence on this point is not as conclusive as is desirable, having regard to the difficulty of isolating these glucosides in a pure state from plants—the differences between them probably lie in the nature of the sugar residue and it is desirable that the sugars produced from them on hydrolysis should be carefully examined.” They have since (*Bull. Imp. Inst.*, 1906, 4, 340) suggested that “possibly two or perhaps all of them may prove to be identical.”

There can be no doubt that they are definite isomeric substances. As they are readily attacked by emulsin, giving benzaldehyde, hydrogen cyanide and glucose, it is evident that they are all compounds of the β -glucoside type and that the isomerism is not of the order which obtains between the α - and β -methylglucosides.

Prulaurasin, in fact, is entirely analogous to *iso*amygdalin; it is a mixture of the two stereoisomeric *d*- and *l*-mandelonitrile β -glucosides. Sambunigrin must be the β -glucoside of dextromandelic acid. The “mixed” derivative has a lower melting point; moreover, its rotatory power, as Hérissé has pointed out, is the mean of the rotatory powers of the other two glucosides. In the case of the biose derivatives, the dextromandelic acid modification is at present unknown, but a comparison of the properties of amygdalin with those of *iso*amygdalin shows that strict parallelism exists between the latter and prulaurasin :

	$[\alpha]_D$.	M. p.	
Amygdalin..... (trihydrate)	-35.51	200°	May be crystallised from an aqueous solution.
<i>iso</i> Amygdalin (dihydrate)	-47.6	125—140°	Hygroscopic, will not crystallise from water.

Preparation of Prulaurasin.—When *l*ævomandelonitrile glucoside is dissolved in water and the solution is rendered very slightly alkaline with baryta or ammonia, the rotatory power falls rapidly from $[\alpha]_D - 26.0^\circ$ to $[\alpha]_D - 53.7^\circ$; the latter is approximately the rotatory power of prulaurasin given by Hérissé. The conversion takes place with the utmost readiness at 25°, following the unimolecular law :

Time in minutes.	α_D .	$\frac{10^5}{t} \log_{10} \frac{\alpha}{\alpha - x}$.
0	$-3^{\circ}53'$	—
9	4 11	(576)
35	4 35	660
65	4 53	678
80	4 57	681
110	5 8	688
∞	5 22	—

Five grams of Fischer's glucoside were dissolved in $N/500$ baryta; after six hours, when the rotatory power was constant at $[\alpha]_D - 53.7^{\circ}$, the solution was saturated with carbon dioxide and filtered. The liquid was then evaporated at 60° under reduced pressure and the residue was dried in a good vacuum at 101° . The powdered material dissolved with difficulty in boiling anhydrous ethyl acetate, from which it was precipitated as a syrup by dry ether. This syrup crystallised slowly during the cold weather. The white solid thus obtained was more readily soluble in dry ethyl acetate than the original substance; it was again precipitated by dry ether and allowed to crystallise. The recrystallised glucoside was washed with the mixture of solvents, then with dry ether and dried in a vacuum over sulphuric acid. When prepared in this way, prulaurasin softens at 120° and melts at 123 — 125° . We are greatly indebted to M. Hérissé for having placed at our disposal a small quantity of the glucoside obtained from *Prunus laurocerasus*, which has enabled us to satisfy ourselves that this material is indistinguishable from the product made in the manner described from amygdalin. On mixing M. Hérissé's sample—which softened at 115° and melted at 118 — 120° —with ours, a mixture was obtained which melted at 116 — 120° . In grinding together the two specimens for melting point determinations, it was found necessary to exclude moisture by covering the material with dry ether, which was afterwards evaporated off in a vacuum. We have also prepared prulaurasin from Fischer's glucoside by the use of ammonia instead of baryta.

It is evident that Hérissé's product was not quite free from water, the value he gives for the rotatory power being slightly lower than ours, as is also the melting point. The analyses given by Hérissé also point to the presence of a little water in the glucoside.

The glucosides derived from racemic mandelonitrile are also further distinguished from the lævomandelonitrile derivatives by the properties of their acetyl derivatives, which are readily obtained with the aid of acetic anhydride. Amygdalin and isoamygdalin give hepta-acetyl derivatives; lævomandelonitrile glucoside and prulaurasin give tetra-acetyl derivatives. The acetylated mixed product in each case has the greater solubility in alcohol and the lower melting point:

	M. p.	$[\alpha]_D^{25}$. (5 per cent. solution in ethyl acetate).	Character.
Hepta-acetylamygdalin.....	167°	- 34·8°	Orthorhombic needles sparingly soluble in cold alcohol.
Hepta-acetylisoamygdalin .	148	- 35·5	Orthorhombic, soft needles somewhat soluble in cold alcohol.
Tetra-acetyl- Fischer's glucoside	136	- 21·7	Orthorhombic, very fine, long needles, moderately soluble in cold alcohol.
Tetra-acetylprulaurasin ...	120—123°		Orthorhombic needles, extremely soluble in cold alcohol.

Hepta-acetylamygdalin.—This compound was prepared by Schiff (*Annalen*, 1870, **154**, 337), who omitted to state its melting point or its rotatory power. It is possible to effect complete acetylation of amygdalin by means of boiling acetic anhydride without the mandelonitrile radicle undergoing change; the product obtained from *iso*-amygdalin by the same process is quite a distinct substance. Ordinary hydrated amygdalin is completely acetylated by boiling it during two hours with ten times its weight of acetic anhydride. The oil which is precipitated on pouring the cooled liquid into water solidifies quickly and when dried is readily purified by crystallisation from hot ethyl alcohol (95 per cent.). It crystallises in rosettes of colourless needles, which show extinctions parallel to the long edges and hence are probably orthorhombic. It is readily soluble in ethyl acetate or chloroform but very sparingly so in cold alcohol. It is not acted on by emulsin :

0·2073 gave 0·4089 CO₂ and 0·1021 H₂O. C = 54·12; H = 5·47.

0·2082 „ 0·4151 CO₂ „ 0·1028 H₂O. C = 54·35; H = 5·49.

C₃₄H₄₁O₁₈N requires C = 54·33; H = 5·46 per cent.

Hepta-acetylisoamygdalin crystallises in small, soft rosettes melting at 148°, which show parallel extinctions and are therefore orthorhombic. It is readily soluble in chloroform or ethyl acetate, and sparingly so in cold alcohol. This substance has a specific rotatory power which is very near to that of hepta-acetylamygdalin itself, but it is more soluble in alcohol; a mixture of the two substances melted at 141—144°:

0·2086 gave 0·4163 CO₂ and 0·1036 H₂O. C = 54·42; H = 5·52.

0·2052 „ 0·4081 CO₂ „ 0·1012 H₂O. C = 54·24; H = 5·48.

C₃₄H₄₁O₁₈N requires C = 54·33; H = 5·46 per cent.

Tetra-acetyl-1-mandelonitrile glucoside, when recrystallised from

alcohol, forms a mass of very fine, soft needles, which show parallel extinctions and are therefore orthorhombic:

0.2171 gave 0.4506 CO_2 and 0.1046 H_2O . $\text{C} = 56.60$; $\text{H} = 5.36$.

0.2055 „ 0.4289 CO_2 „ 0.1000 H_2O . $\text{C} = 56.92$; $\text{H} = 5.41$.

$\text{C}_{22}\text{H}_{25}\text{O}_{10}\text{N}$ requires $\text{C} = 57.02$; $\text{H} = 5.40$ per cent.

Tetra-acetylprulaurasin.—To prepare this compound, the crude material obtained by evaporating down an aqueous solution of the glucoside in a vacuum was dissolved in twenty times its weight of boiling acetic anhydride; after boiling the liquid during three hours, it was poured into water; an oil separated which solidified only after several days at a low temperature. The solidified acetyl compound dissolved with great readiness in benzene, chloroform, ethyl acetate, methyl acetate, acetone, or alcohol, but not in light petroleum. It could only be obtained crystalline by cooling a strong solution in alcohol to about -5° ; very small needles showing a parallel extinction were then obtained:

0.1907 gave 0.3988 CO_2 and 0.0886 H_2O . $\text{C} = 57.03$; $\text{H} = 5.16$.

$\text{C}_{22}\text{H}_{25}\text{O}_{10}\text{N}$ requires $\text{C} = 57.02$; $\text{H} = 5.40$ per cent.

Inasmuch as sambunigrin is probably a single substance like Fischer's glucoside, the fact that it occurs alone in certain plants whilst a mixture of the two isomeric glucosides is met with in others raises interesting questions. Benzylidene cyanohydrol, formed by the coalescence of benzaldehyde and hydrogen cyanide, being a mixture of stereoisomerides, it is rather to be expected that the two glucosides should occur together; from this point of view, prulaurasin is a normal product and the appearance of sambunigrin alone is somewhat remarkable; the latter is also a remarkable substance as it does not correspond to amygdalin and because no corresponding bioside is known. Amygdalin is not known to occur in leaves but only in the fruits and kernels; it is not improbable that its isomeride may be met with in the fruits of plants the leaves of which contain sambunigrin; it should have a higher lævorotatory power, $[\alpha]_D - 60^\circ$, approximately.

Our best thanks are due to Professor H. E. Armstrong for most valuable criticism and advice.

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