589. Solanum *Alkaloids. Part V. Solasodine.*

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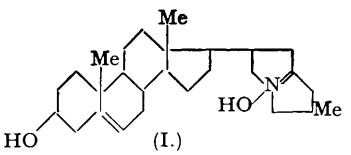
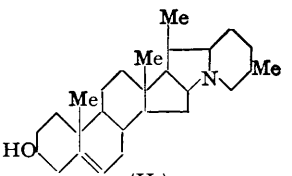
The formulation of solasodine as a carbinol-amine proposed in Part II (*J.*, 1942, 3) has been revised. It has now been shown that solasodine contains a secondary amino-group and an ether linkage, besides the hydroxyl group at $C_{(3)}$. The ether linkage is intimately associated with the nitrogen atom and evidence is adduced for the presence in solasodine of a novel *spiro*diheterocyclic system derived from a carbinol-amine. The new formula proposed for solasodine makes it the nitrogen analogue of diosgenin.

In Part II (*J.*, 1942, 3), formula (I) was suggested for solasodine, this being the ammonium hydroxide form of a carbinol-amine. The skeletal structure was based on two assumptions, first, that the carbon skeleton is the same as in cholesterol and, secondly, that the heterocyclic ring structure has only one point of attachment to the steroid ring system. There is still no exception to the fact that steroids of known structure containing 27 carbon atoms all have the same carbon skeleton as cholesterol and, presumably, this is still the case with solasodine. If



(I.)



(II.)

the second assumption is correct, there is no alternative structure for the heterocyclic ring system to that proposed. If, however, there is more than one point of attachment of the heterocyclic ring system to the steroid nucleus then a number of possibilities exist for solanidine, including (II), of which we regarded solasodine as the carbinol-amine derivative (McGillivray, Thesis, University of New Zealand, 1941). Craig and Jacobs (*J. Biol. Chem.*, 1941, **141**, 253) suggested that the same heterocyclic ring system was present in the *Veratrum* alkaloid, cevine, following their isolation of 2-ethyl-5-methylpyridine as one of the products of selenium dehydrogenation (*idem, ibid.*, 1937, **120**, 447). Later Prelog and Szpilfogel (*Helv. Chim. Acta*, 1942, **25**, 1306) and Craig and Jacobs (*Science*, 1943, **97**, 122) isolated the same base by dehydrogenation of solanidine. The former authors confirmed its structure by synthesis and proposed formula (II) for solanidine. This structure has since been elegantly confirmed by the partial synthesis of a solanidine derivative, *allo*solanidan-3β-ol, from sarsasapogenin by Uhle and Jacobs (*J. Biol. Chem.*, 1945, **160**, 243).

From the selenium dehydrogenation of solasodine, Rochelmeyer (*Arch. Pharm.*, 1937, **275**,

336) isolated a picrate, m. p. 140—142°, which agrees with that from 2-ethyl-5-methylpyridine. We have isolated the same base by dehydrogenation of a hydrolytic product of solmargine, a new alkaloid from *Solanum marginatum*, which we have proved to be a derivative of solasodine (forthcoming communication), and confirmed its identity by direct comparison of the picrate and styphnate with authentic specimens. Since methyl*cyclo*pentenophenanthrene was obtained from both solanidine (Soltys and Wallenfels, *Ber.*, 1936, **69**, 811) and solasodine (Rochelmeyer, *Arch. Pharm.*, 1936, **274**, 543) by selenium dehydrogenation, solanidine and solasodine are closely related—in our earlier view, as free base and carbinol-amine respectively, a relationship also suggested by Craig and Jacobs (*J. Biol. Chem.*, 1943, **149**, 451).

The constitution of solasodine as a carbinol-amine arose from two facts. Acetylation with acetic anhydride in pyridine afforded a monoacetyl derivative. This is regarded as an *O*-acetyl derivative since it is soluble in dilute acids and, more specifically, the 3-*O*-acetyl derivative, as, unlike solasodine itself, it fails to form a digitonide. Since primary and secondary amines are normally acetylated more readily than alcoholic groups we concluded that solasodine contained neither a primary nor a secondary amino-group. A second *C*-hydroxyl group was not present since vigorous dehydration did not give a triene but afforded only the 3 : 5-diene, arising from dehydration at the $C_{(3)}$-hydroxyl group in association with the $C_{(5)}$–$C_{(6)}$ double bond already present. To accommodate the additional fact that solasodine shows two active hydrogens by the Zerewitinoff estimation, the remaining oxygen was combined with the nitrogen as a carbinol-amine.

The second fact concerned the reaction of solasodine with nitrous acid. The product corresponded to condensation with nitrous acid with elimination of water. We reported that ammonia regenerated solasodine, thus eliminating a nitrosamine structure and supporting our view that it was an anhydro-salt, typical of carbinol-amines.

The reaction of solasodine with bromine in chloroform solution, the reaction with methyl iodide and its behaviour on hydrogenation also tended to support the carbinol-amine structure, although it failed to give a methyl or an ethyl ether when crystallised from methyl or ethyl alcohol (cf. Part II).

Attempts have now been made to provide a more rigid proof for the carbinol-amine structure and to convert solasodine into solanidine.

Some evidence was adduced in favour of the carbinol-amine structure. Solasodine, on hydrogenation in the presence of Adams's catalyst, forms dihydrosolasodanol * (tetrahydrosolasodine), which is explicable by saturation of the $C_{(3)}$–$C_{(5)}$ double bond and hydrogenation of the carbinol-amine by a type of Emde degradation. On the revised formula for solanidine (II), there are two alternative structures for solasodine with the carbinol group at either $C_{(16)}$ or $C_{(22)}$ (apart from the isomeric quaternary hydroxide form) (cf. Part II, *loc. cit.*). According to the first, dihydrosolasodanol may then be formulated as (III).

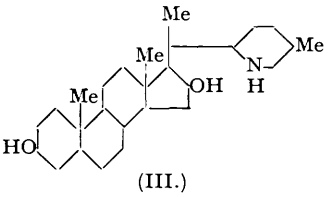
Dihydrosolasodanol contains three active hydrogen atoms by Zerewitinoff estimation, it forms a triacetyl derivative insoluble in dilute acids and a nitrosamine which is stable to ammonia but is hydrolysed back to dihydrosolasodanol with hydrochloric acid. The action of methyl iodide forms the hydriodide of dihydro-*N*-methylsolasodanol, converted by ammonia into the free base.

Dihydrosolasodanol is also obtained by hydrogenation of solasodanol in the presence of Adams's catalyst. The above properties of dihydrosolasodanol would agree with a formulation such as (III.)

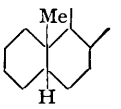
Other evidence, however, fails to support the carbinol-amine structure. Solasodine in its quaternary ammonium hydroxide form would be expected to undergo a Hofmann degradation by the action of heat alone. It was recovered unchanged after being heated for some time at its melting point. Its salts, such as the hydrochloride, would be derivatives of the quaternary ammonium hydroxide form, and could conceivably yield solanidine derivatives on hydrogenation (cf. the conversion of cotarnine into hydrocotarnine by Clayson, *J.*, 1949, 2016). Solasodine hydrochloride, in glacial acetic acid–alcohol solution, afforded only dihydrosolasodanol on hydrogenation over a platinum oxide catalyst. Acid or alkaline reducing agents could also conceivably reduce the carbinol-amine to a tertiary amine, solanidine in this case. Acid reducing agents complicate the issue in that solasodine undergoes dehydration with methyl-alcoholic hydrogen chloride and even with dilute aqueous hydrochloric acid during the hydrolysis of solasonine (cf. Rochelmeyer, *Arch. Pharm.*, 1937, **275**, 336, and Part II). For this reason,

* To avoid ambiguity with isomeric hydro-derivatives (cf. the succeeding paper) it is necessary to adhere as far as possible to a strict systematic nomenclature. We hope to present evidence later on the stereochemistry of solasodine and its derivatives.

solasodanol was chosen for the experiments. It was recovered unchanged, however, after attempted reduction with zinc and acetic acid, zinc and hydrochloric acid, and sodium amalgam.



(III.)



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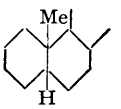
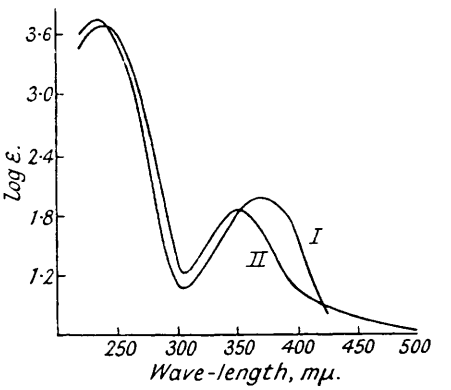


(V.)

Hydrogenation of solaso-3 : 5-diene with a palladium–charcoal catalyst reduces only the two double bonds with the formation of two isomeric compounds, whose isomerism results from the differing spatial configuration about $C_{(5)}$. From the difference in melting points of the isomers, the higher-melting formed is named " α "-solasodan, corresponding possibly to cholestane, and the lower-melting form " β "-solasodan, related to coprostane, with partial formulæ (IV) and (V) respectively. " α "-Solasodan is also unchanged on attempted reduction with zinc and hydrochloric acid.

As a carbinol-amine, solasodine should yield the corresponding $C_{(16)}$(or $C_{(22)}$)-cyano-compound by reaction with potassium cyanide. Hydrolysis of the cyano-compound followed by decarboxylation of the resulting carboxylic acid could then yield solanidine, although this route for the conversion of strychnine into ω-strychnine was unsuccessful owing to resistance of the cyanostrychnine to hydrolysis (Leuchs, Flammersfeld, and Villain, *Ber.*, 1943, **76**, 1065). Solasodine reacted with potassium cyanide in glacial acetic acid but the product was not the required cyanosolasodine since solasodine was regenerated from it by the action of ammonia.

Finally, solasodine failed to condense with nitromethane—another reaction typical of carbinol-amines (cf. Hope and Robinson, *J.*, 1911, **99**, 2114).



I, N-*Nitrososolasodine*.
II, *Dihydro*-N-*nitrososolasodanol*.

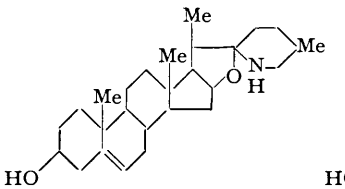
A reverse approach to the problem was then attempted through solanidine. Bailey and Robinson (*J.*, 1948, 703) have converted strychnine and brucine into the *pseudo*(or carbinol-amine)-derivatives by the action of potassium chromate on the corresponding *N*-oxides. After treatment of dihydrosolanidine *N*-oxide, prepared by the action of perbenzoic acid on dihydrosolanidine, with potassium chromate, dihydrosolanidine was the only product isolated. Reduction of the *N*-oxide with sulphur dioxide also regenerated dihydrosolanidine.

These failures led us to re-examine our original premises for the structure, with illuminating results. As stated previously, solasodine reacts with acetic anhydride–pyridine to form the *O*-acetyl derivative. In a hydroxyl determination, however, with a semi-micro-modification of Peterson, Hedberg, and Christensen's method (*Ind. Eng. Chem. Anal.*, 1943, **15**, 225), solasodine was shown to contain two acetylatable groups. We now find that solasodine reacts with acetic anhydride under varying conditions in different ways. Although we have not yet prepared a crystalline diacetyl derivative, we have obtained, by the action of acetic anhydride and sodium acetate, an amorphous product insoluble in dilute acids, with a 14·1% acetyl content (calculated for 2 acetyl groups, 18·2%).

When solasodine is treated in acetic acid solution with sodium nitrite, the product obtained corresponds to the condensation of nitrous acid with elimination of water. We reported in Part II that the action of ammonia on this compound regenerated solasodine, thus eliminating a nitrosamine structure and supporting the view that it was the anhydro-salt of nitrous acid in keeping with the carbinol-amine structure of solasodine. We have now found that this is incorrect and the the pure product is unchanged by the action of aqueous or alcoholic ammonia and could therefore be a nitrosamine. Liebermann's nitroso-reaction is not given by this compound and aqueous or alcoholic hydrochloric acid does not regenerate solasodine by hydrolysis as expected (cf. dihydro-*N*-nitrososolasodanol above) but forms an amorphous product, m. p. 108—114°, first described by Oddo (*Gazzetta*, 1911, **41**, i, 534), on which we shall report

later. The presence of a nitrosamine group, however, is indicated by the fact that Oddo and Caronna (*Ber.*, 1936, **69**, 283) obtained solasodine and ammonia on reduction of this derivative with zinc and acetic acid. The presence of a nitrosamine group is also shown by the ultraviolet absorption spectrum which shows two peaks, one of high intensity at 234·5 mμ. (log ε 3·78) and the other at 370 mμ. (log ε 1·98) (see figure). Di(*cyclo*hexylmethyl)-*N*-nitrosamine shows similar absorption peaks at 240 mμ. (log ε 3·9) and 355 mμ. (log ε 1·95), while 1-nitrosopiperidine has peaks at 235 mμ. (log ε 4·25) and 350 mμ. (log ε 2·0) (Goldberg and Kirchsteiner, *Helv. Chim. Acta*, 1943, **26**, 289).

The presence of both a hydroxyl and a secondary amino-group thus accounts for the two active hydrogens in the Zerewitinoff estimation. Since a carbonyl group is not present the remaining oxygen must be present as an ether. No methoxyl or ethoxyl group is present but there is evidence that the ether linkage is closely associated with the secondary amino-group. Solasodine is a considerably weaker base than solanidine and not a stronger base as expected on a carbinol-amine formulation. In contrast, dihydrosolasodanol is a much stronger base, stronger even than solanidine. Details of these measurements and other related compounds will be submitted later. This weakened basicity may explain the formation of an *O*-acetyl and not an *N*-acetyl derivative. The reaction of hydrochloric acid with nitrososolasodine is also apparently anomalous.



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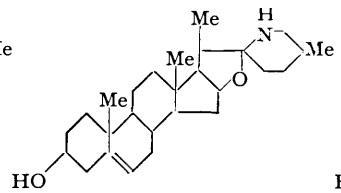

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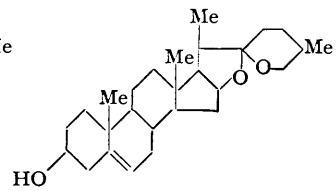
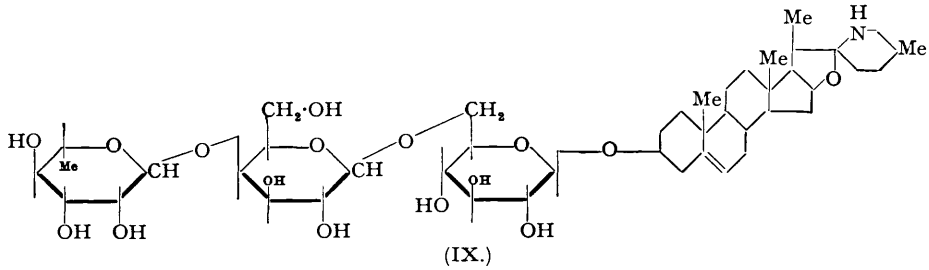


(VIII.)

The formation of dihydrosolasodanol by hydrogenation can now be explained by hydrogenolysis of the oxide ring. This ready fission, however, in contrast with the difficulty of opening a polymethylene oxide ring such as that of tetrahydrofuran (cf. Owen, *Ann. Rep.*, 1945, **42**, 171), again emphasises the association of the ether linkage with the nitrogen atom. For these reasons, we suggest that both the ether and the secondary amino-group are attached to the same carbon atom. To accommodate the formation of 2-ethyl-5-methylpyridine on selenium dehydrogenation we retain the six-membered heterocyclic ring of solanidine. On both stereochemical and phytochemical grounds the ether linkage can then best be placed between $C_{(16)}$ and $C_{(22)}$, leading to the formulation of solasodine as (VI) or (VII), which is thus the nitrogen analogue of diosgenin (VIII). Our revised formulation for solasonine (IX), including the above structure



(IX.)

for solasodine and the mode of linkages in the trisaccharide moiety (forthcoming communication) was submitted to Mr. J. Murray in December, 1949, and published by him in a review of plant products of New Zealand (*J. New Zealand Inst. Chem.*, 1950, **14**, 48).

On this new formulation, no modification of the structure of dihydrosolasodanol is necessary but its description as a *chano*-compound is now incorrect. The alternative name, dihydro*chano*-solasodanol should, therefore, be discontinued. The ready reductive fission of the oxide ring by catalytic hydrogenation and by lithium aluminium hydride (succeeding paper) is comparable with analogous reactions in the sapogenin series. Catalytic hydrogenation of sarsasapogenin or *iso*sarsasapogenin in an acidic medium with a platinum catalyst yields dihydrosarsasapogenin, whereas both oxide rings are simultaneously opened by Clemmensen reduction with the formation of tetrahydrosarsasapogenin (Marker and Rohrmann, *J. Amer. Chem. Soc.*, 1939, **61**, 943).

A similar *spiro*diheterocyclic system is included in one of several possible structures proposed by Jacobs and Huebner (*J. Biol. Chem.*, 1947, **170**, 635) for the *Veratrum* alkaloid, jervine. Little supporting evidence is given for the association of the ether linkage with the secondary amino-group, and Fieser and Fieser ("Natural Products Related to Phenanthrene," Reinhold Publ. Corp., 3rd Edn., p. 605) prefer a variant of that proposed by Jacobs and Huebner. Jervine, however, readily forms an *N*-acetyl derivative in marked contrast with the behaviour of solasodine.

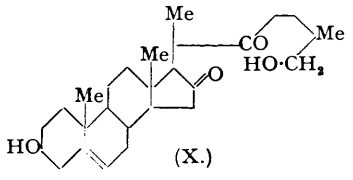
The different stereochemical configuration about $C_{(22)}$ leads to the isomers (VI) and (VII) similar to the normal and *iso*-members of the sapogenin series. We suggest now that solasodine may be represented by one of these, and that solauricidine, a very closely allied isomer (cf. Parts III and IV, *J.*, 1942, 12, 17), is represented by the other. In further attempts to obtain solauricidine from *Solanum auriculatum* we have been able to isolate only solasodine (cf. Part III), possibly owing to isomerisation of solauricidine to solasodine during the process. For this reason solauricidine is perhaps represented by (VII), corresponding to the normal members of the sapogenin series, and solasodine by (VI), corresponding to the *iso*-series of the sapogenins. In this case, the formula (IX) given for solasonine may be that of solauricine. This possibility is now being explored.

It is not yet possible to correlate the stereochemical configuration of solasodine with that of cholesterol by the method of molecular-rotation differences developed by Barton (*J.*, 1949, 2596, and earlier papers). At the moment, there are too many discrepancies in the reported rotations but we hope to report on this phase later.

It is possible that this *spiro*diheterocyclic system is also present in other alkaloids. Besides the *Veratrum* alkaloid jervine mentioned above, solanocapsine, peimine, and peiminine deserve consideration. Solanocapsine (Barger and Fraenkel-Conrat, *J.*, 1936, 1536), from *Solanum pseudocapsium*, contains both a secondary amino-group and an ether linkage, similarly to solasodine.

Peimine and peiminine from *Fritillaria roylei* (Chou, *Chinese J. Physiol.*, 1932, **6**, 265; Chi, Kao, and Chang, *J. Amer. Chem. Soc.*, 1936, **58**, 1306; 1940, **62**, 2896; Chou and Chu, *ibid.*, 1941, **63**, 2936; Wu, *ibid.*, 1944, **66**, 1778) are two steroid alkaloids shown by Chu and Chou (*ibid.*, 1947, **69**, 1257) to be interconvertible by oxidation and reduction respectively, owing to the presence in the respective bases of an alcoholic and a carbonyl group. Formulæ, $C_{26}H_{43}O_3N$ and $C_{26}H_{41}O_3N$, have been suggested for these bases but, on phytochemical grounds, these, as well as those of solanocapsine and solanocapsidine previously regarded as C_{26} alkaloids, are more probably C_{27} compounds. Peimine contains two alcoholic groups, leaving a nitrogen and an oxygen atom unaccounted for. On a $C_{27}H_{43}O_3N$ basis, peimine could therefore be a hydroxy-solasodine derivative.

A possible mode of phytosynthesis of solasodine could be through kryptogenin (X). When the $C_{(16)}$-carbonyl group is converted into a secondary alcohol, condensation to diosgenin (VIII) may occur under the influence of mineral or strong organic acids (Marker *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 2167; Kaufmann and Rosenkranz, *ibid.*, 1948, **70**, 3502). After replacement of the $C_{(26)}$-hydroxyl group by an amino-group and reduction of the $C_{(16)}$-carbonyl group as before, condensation could be similarly expected with the formation of solasodine. In this connection it is interesting to observe that tigogenin has been isolated from *Solanum dulcamara* (Marker *et al.*, *ibid.*, 1943, **65**, 1199).



(X.)

The pharmacological properties of compounds in this series will be reported elsewhere. It has already been shown (Krayer and Briggs, *Brit. J. Pharmacol.*, 1950, **5**, 118) that some members of this series have a selective antagonistic action to the cardioaccelerator effect of sympathomimetic amines.

Since this paper was written we have been informed by Dr. T. D. Fontaine, United States Department of Agriculture, that experiments in his laboratory show that tomatidine, the aglycone of tomatine extracted from tomato leaves, is probably identical with solasodanol and that, independently, they have proposed the same formula for solasodanol as that derived from our revised formula for solasodine.

Experimental.

Purification of Solasodine.—Crude solasonine, obtained as described in Part II, readily blackens on exposure to air, and a colourless product is then often difficult to obtain by normal methods. The precipitate which first forms on passage of ammonia into a solution of crude solasonine in 2% acetic acid

contains a greater quantity of the black material. If this is filtered off, the remainder of the solasonine can be obtained in a much purer form. A second method resulted from the fact that solasonine is more soluble in cold than in hot very dilute acetic acid. The alkaloid was dissolved in the minimum amount of cold 1% acetic acid and heated slowly. At about 50° a solid separated. By filtering off the product separating at each 10°-rise of temperature most of the colour could be removed in these fractions, and the bulk of the solasonine then recovered from the boiling solution in a greatly improved condition by passage of ammonia. The best method, however, is to proceed directly to the hydrolysis with 2—3% hydrochloric acid, the insoluble solasodine hydrochloride separating in a crystalline although still very dark condition. Hot alcohol will then remove most of the coloured impurity, and crystallisation of the hydrochloride from aqueous alcohol with charcoal readily gives a colourless product from which solasodine may be obtained as described.

Solasodine perchlorate, prepared in methyl alcoholic solution, crystallised from methyl alcohol in long, rectangular plates, m. p. 262—264° (decomp.).

Determination of Acetylatable Groups in Solasodine.—This was carried out by a semi-micro-modification of that described by Peterson, Hedberg, and Christensen (*Ind. Eng. Chem. Anal.*, 1943, **15**, 225). Solasodine (24·6 mg.) was allowed to react at room temperature for 60 hours in a sealed tube with acetic anhydride (66·5 mg.) and pyridine [Found : acetylatable groups (as OH) per mol., 2·08]. In a second experiment with solasodine (42·2 mg.) and acetic anhydride (73·3 mg.) the mixture was first allowed to react at room temperature for 60 hours and then heated for 2 hours at 100° [Found : acetylatable groups (as OH) per mol., 2·15]. In a control experiment, cholesterol (37·8 mg.) and acetic anhydride (42·3 mg.) were allowed to react as in the first case and gave 1·02 hydroxyl groups per mol.

Acetylation of Solasodine.—A mixture of solasodine (480 mg.), fused sodium acetate (800 mg.) and acetic anhydride (5 c.c.) was heated for 16 hours at 100° and finally to boiling. The cooled mixture was poured into 20% sodium acetate solution (30 c.c.) and the oil separating triturated with water until solid. Attempts to crystallise the *diacetate* were unsuccessful. After distillation at 0·02 mm. (bath-temp., 150—160°) it formed a glassy solid, m. p. 78—86°, insoluble in dilute acids (Found : Ac, 14·1. $C_{31}H_{47}O_4N$ requires 2Ac, 18·2%).

Action of Hydrogen Cyanide on Solasodine.—Potassium cyanide (480 mg., 6 mols.) in water (0·5 c.c.) was added to a solution of solasodine (500 mg.) in alcohol (5 c.c.) and glacial acetic acid (0·5 c.c.). A precipitate formed immediately, which dissolved when the mixture was heated. After the whole had been heated under reflux for 10 minutes crystalline material separated on cooling. Recrystallisation from 80% alcohol containing a little hydrocyanic acid, which appears to be essential, afforded hexagonal plates, m. p. 324° (decomp.) (Found : loss of wt. at 100°/high vacuum/P_2O_5, 6·6; C, 71·3, 69·7; H, 10·5, 10·0%. No satisfactory formula can yet be given to this substance). When an alcoholic solution of this substance is treated with concentrated aqueous ammonia at 100° for 1 hour, solasodine is regenerated, having m. p. and mixed m. p. 198—200·5° (picrate, m. p. and mixed m. p. 142°).

N-*Nitrososolasodine.*—The absorption spectrum of this compound was measured in alcoholic solution at different dilutions (*ca.* M/500—M/5000), using a Beckman spectrophotometer, model D.U., and is given in the figure.

Dihydrosolasodanol from Solasodanol.—Solasodanol (Part II) forms a picrate, crystallising from alcohol in fine yellow needles, m. p. 141·5—142° (decomp.), a *perchlorate*, crystallising from aqueous alcohol in needles, m. p. 141—142° (decomp.) Found : C, 62·2; H, 9·1. $C_{27}H_{45}O_2N,HClO_4$ requires C, 62·8; H, 9·0%). N-*Nitrososolasodanol* is formed from solasodanol (123 mg., 1 mol.) when sodium nitrite (135 mg., 7 mols.) in water (1 c.c.) is added to its ice-cold solution in alcohol (2 c.c.) and glacial acetic acid (0·19 c.c., 11 mols). It crystallises from methyl alcohol in needles, m. p. 272°, which, like *N*-nitrososolasodine, do not give a positive reaction in Liebermann's nitroso-reaction (Found : 73·3; H, 10·2. $C_{27}H_{44}O_3N_2$ requires C, 72·9; H, 10·0%).

A solution of solasodanol (200 mg.) in alcohol (150 c.c.) and glacial acetic acid (50 c.c.) was hydrogenated at 45 lbs. pressure in the presence of platinum oxide (200 mg.) for 24 hours. The filtered solution was concentrated in a vacuum, diluted with water, and made alkaline with ammonia. The precipitate (190 mg.), after repeated crystallisation from aqueous alcohol, had m. p. and mixed m. p. with dihydrosolasodanol, 289—291°. High dilution is apparently necessary for this preparation as in a similar experiment with only glacial acetic acid as solvent (300 mg. in 20 c.c.) hydrogenation was incomplete and a considerable amount of unchanged solasodanol was recovered.

Dihydrosolasodanol Derivatives.—In a determination of active hydrogen by the Zerewitinoff method in anisole–*iso*amyl ether solution, 77·65 mg. of dihydrosolasodanol, previously dried for one hour in a high vacuum at 100° over phosphoric oxide, evolved 13·15 c.c. of methane at 25°/770 mm., corresponding to 2·93 atoms of active hydrogen per mole.

Dihydrosolasodanol picrate, produced from the reactants in hot aqueous alcoholic solution, separated from its cold alcoholic solution on addition of water in fine, yellow needles, m. p. 140° (decomp.).

Triacetyldihydrosolasodanol. A solution of dihydrosolasodanol (133 mg.) in acetic anhydride (1·5 c.c.) containing 60% perchloric acid (1 drop) was kept overnight at room temperature. The oil, separating when the mixture was poured into water, solidified on trituration with aqueous acetone and, after repeated crystallisation from 80% alcohol, the *triacetyl* derivative formed rods, m. p. 153—154° (Found : C, 73·2; H, 9·8. $C_{33}H_{53}O_5N$ requires C, 72·9; H, 9·8%).

Dihydro-N-*nitrososolasodanol.* To an ice-cold solution of dihydrosolasodanol (200 mg.) in glacial acetic acid (10 c.c.) a strong aqueous solution of sodium nitrite was added until precipitation was complete. The *nitrosamine*, after repeated crystallisation from alcohol and aqueous alcohol, separated in colourless, short needles, m. p. 254—255° (decomp.) (Found : C, 72·3; H, 10·1; N, 6·4. $C_{27}H_{46}O_3N_2$ requires C, 72·6; H, 10·3; N, 6·3%). The absorption spectrum, measured in alcoholic solution at different dilutions

(*ca.* M/1000—M/3000) and illustrated in the figure, exhibits peaks at 238·2 mμ. (log ε 3·74) and 352·5 mμ. (log ε 1·87).

The nitroso-derivative was recovered unchanged after being heated with concentrated aqueous ammonia at 100° for 1 hour. It underwent hydrolysis, however, in acid solution. A solution of dihydronitrososolasodanol (20 mg.) in alcohol (10 c.c.) containing a few drops of concentrated hydrochloric acid was kept for 24 hours at room temperature. Excess of ammonia was then added and the mixture heated at 100° for ½ hour. The precipitated material, on crystallisation from aqueous alcohol, had m. p. and mixed m. p. with dihydrosolasodanol, 290—292°.

Dihydrosolasodanol hydriodide. A few drops of concentrated aqueous potassium iodide were added to a solution of dihydrosolasodanol (500 mg.) in glacial acetic acid (10 c.c.). A colourless precipitate formed immediately but rapidly darkened. After crystallisation from alcohol it formed short needles, m. p. 321—322° (slight decomp.). The iodine content was determined by Liepert's method (Pregl, " Quantitative Organic Microanalysis," 1937 Edn., p. 113) modified in this case simply for ionic halogen (Found : I, 23·2, 23·7. $C_{27}H_{47}O_2N$,HI requires I, 23·25%).

Dihydro-N-methylsolasodanol hydriodide. Dihydrosolasodanol (500 mg.), dissolved in dry anisole (10 c.c.), was heated with methyl iodide (1 c.c.) at 100° for 5 hours. The product (610 mg.) which separated on cooling, after repeated crystallisation from alcohol and 50% aqueous alcohol, formed colourless, small prisms, m. p. 285—286°. The iodine content was determined as before (Found : C, 59·8, 59·9; H, 8·5, 8·6; I, 22·7, 22·7. $C_{28}H_{49}O_2N$,HI requires C, 60·1; H, 9·0; I, 22·7%).

Dihydro-N-methylsolasodanol. The foregoing *hydriodide* (111 mg.), partly dissolved in methyl alcohol (1 c.c.), was treated for 1 hour at 100° with water (1 c.c.) and concentrated aqueous ammonia (1 c.c.). The product was repeatedly crystallised from methyl alcohol, forming long hair-like needles, m. p. 275° (Found : C, 78·3; H, 11·1. $C_{28}H_{49}O_2N$ requires C, 78·6; H, 11·1%).

" α "- *and* " β "-*Solasodan.*—Solasodiene (500 mg.), dissolved in glacial acetic acid (15 c.c.), was hydrogenated with a palladium–charcoal catalyst (500 mg.) at 43 lbs. pressure for 8 hours. After removal of the catalyst, the volume was reduced to *ca.* 4 c.c. by vacuum-distillation, and the final solution treated with excess of ammonia at 100° for 2 hours. The precipitate which formed could be separated by fractional crystallisation from alcohol into two products.

" α "-*Solasodan* crystallised from alcohol in hexagonal plates, m. p. 175—176°, $[\alpha]_D^{18}$ −81° ± 4° (*l*, 0·25; *c*, 1·136 in chloroform) (Found : C, 80·95, 81·1; H, 11·3, 11·3. $C_{27}H_{45}ON$ requires C, 81·1; H, 11·35%). The picrate, prepared in and crystallised from 80% alcohol, formed long, flat plates, m. p. 208° (decomp.).

" β "-*Solasodan*, obtained in smaller yield, crystallised from 80% alcohol in fine needles, m. p. 132—134° (Found : C, 80·35, 81·0; H, 11·6, 11·5. $C_{27}H_{45}ON$ requires C, 81·1; H, 11·35%). The picrate, prepared in and crystallised from 80% alcohol, formed very fine needles, m. p. 198—200° (decomp.).

" α "-Solasodan was recovered unchanged after treatment in 50% alcohol–hydrochloric acid (2N. with zinc dust at 100° for 9 hours.

Dihydrosolanidine N-Oxide.—A chloroform solution of perbenzoic acid (3·42 c.c., equiv. to 1·2 mols.) was added, with shaking, during 5 minutes to an ice-cooled solution of dihydrosolanidine (1 g.; Soltys, *Ber.*, 1933, **66**, 762) and the solution kept in the refrigerator for 17 hours. The solvent was removed at room temperature by passage of a rapid stream of air over the surface and finally in a desiccator. The residual white solid was shaken with dilute aqueous ammonia before filtration. The product could be separated by fractional crystallisation, first from acetone and then from 33% aqueous alcohol, into two compounds. The first, corresponding to the *N-oxide*, after repeated crystallisation from aqueous alcohol, separated in long colourless plates, m. p. 242—244° (decomp.) (162 mg.). In a further crystallisation it separated in slender needles (Found : C, 78·0; H, 11·0, N, 2·9. $C_{27}H_{45}O_2N$ requires C, 78·0; H, 10·9; N, 3·4%).

The second, corresponding to a *compound* of dihydrosolanidine with hydrogen peroxide, was repeatedly crystallised from aqueous alcohol and then formed slender, colourless needles, m. p. 178·5—179·5° (decomp.) (110 mg.) (Found : C, 74·6; H, 10·8; N, 3·6. $C_{27}H_{45}ON,H_2O_2$ requires C, 74·8; H, 10·85; N, 3·2%). The decomposition points of both products were erratic, giving inconsistent values on the same sample and varying considerably with the initial bath temperature.

After treatment of an aqueous alcoholic solution of the latter product (8 mg.) with concentrated aqueous ammonia at 100° for 1 hour and cooling, colourless needles separated, m. p. 204° (decomp.), but there was insufficient material for further examination.

The *N*-oxide (18 mg.) was dissolved in 50% alcohol (1 c.c.), and a slow stream of sulphur dioxide was passed into the solution for ½ hour. After removal of the sulphur dioxide and most of the alcohol on a water-bath, passage of ammonia precipitated a colourless solid which, after crystallisation from acetone, formed colourless needles, m. p. and mixed m. p. with dihydrosolanidine, 216·5—218·5°.

Similar reduction of the dihydrosolanidine–hydrogen peroxide compound also afforded dihydrosolanidine as needles, m. p. and mixed m. p. 217·5—220°.

Solasodine was recovered unchanged by similar treatment.

Attempted Rearrangement of the N-Oxide.—To a solution of dihydrosolanidine *N*-oxide (150 mg.) in hot 50% aqueous dioxan (6 c.c.) was added potassium chromate (50 mg.) dissolved in a few drops of water. The clear orange sclution rapidly became a turbid orange-brown and solid material separated. After 1 hour's heating, the solution was cooled and the resulting brown needles were filtered off. Careful crystallisation from acetone finally gave colourless needles, m. p. and mixed m. p. with dihydrosolanidine, 219·5—221·5°. In a blank experiment, the solution remained a clear yellow.

When the *N*-oxide was slowly heated at 0·01 mm., sublimation without melting occurred fairly rapidly at 245°. The colourless needles so formed had m. p. 239—240° (decomp.), undepressed by the original material.

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