

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XCVIII. Conversion of Isosarsasapogenin (Smilagenin) to Tigogenin

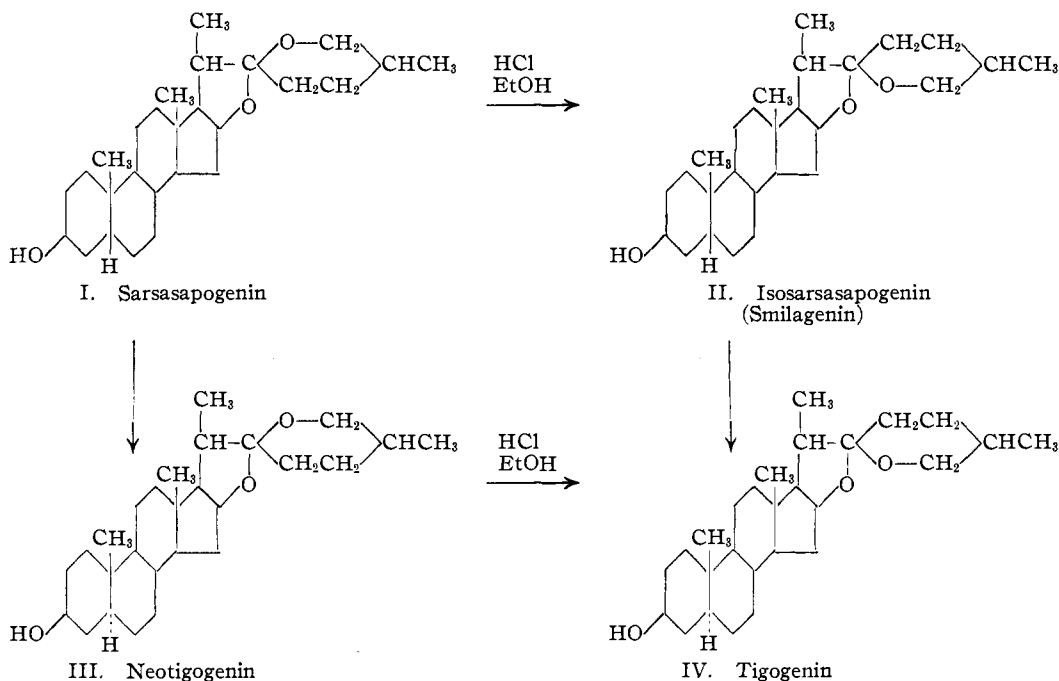
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There has been considerable evidence presented recently indicating that sarsasapogenin differs from tigogenin not only in its configuration at C-5 but also in the configuration of the side chain,¹ the most significant evidence in this connection being the conversion of sarsasapogenin (I) to neotigogenin (III).^{1,2} The fact that this transformation yielded neotigogenin rather than tigogenin suggested that the side chain of tigogenin possibly has the configuration of isosarsasapogenin^{3,4} rather than of sarsasapogenin.

As might be anticipated, neotigogenin upon treatment with aqueous ethanolic hydrochloric acid readily passes into tigogenin.

Experimental Part

Dibromo-isosarsasapogenone.—To a solution of 21 g. of isosarsasapogenone, m. p. 186–188°, in 1 liter of acetic acid containing 2 cc. of 48% hydrobromic acid was added 101.5 cc. of 1.05 *N* bromine in acetic acid over a period of fifteen minutes with stirring at 20°. Much hydrogen bromide came off and the solution turned a deep violet color. Water was added and the precipitate filtered,



We have now completely substantiated these predictions by effecting the conversion of isosarsasapogenin (II) to tigogenin (IV) by the procedure used for the conversion of sarsasapogenin to neotigogenin.¹ Isosarsasapogenone, prepared by the isomerization of sarsasapogenone with ethanolic hydrochloric acid, was converted to dibromo-isosarsasapogenone which upon treatment with pyridine yielded bromodehydro- $\Delta^{4,5}$ -isosarsasapogenone. Reduction of this product with sodium and ethanol yielded tigogenin.

dried and recrystallized from acetone containing 10% ethyl acetate to give white crystals, m. p. 184–188° dec.; yield 14 g.

Anal. Calcd. for $C_{27}H_{40}O_3Br_2$: C, 56.7; H, 7.1. Found: C, 57.1; H, 7.2.

Bromo-dehydro- $\Delta^{4,5}$ -isosarsasapogenone.—A solution of 14 g. of dibromo-isosarsasapogenone in 140 cc. of dry pyridine was refluxed for eight hours. The solution was cooled and the precipitated material collected, washed well with ether and water, and dried. It melted with decomposition at 245–246° and was probably a pyridinium salt.

Anal. Calcd. for $C_{32}H_{48}O_3NBr$: C, 59.0; H, 7.0. Found: C, 58.7; H, 6.5.

The filtrate from the above was dissolved in ether and the pyridine removed by shaking with dilute sulfuric acid.

- (1) Marker and Rohrmann, *THIS JOURNAL*, **62**, 647 (1940).
- (2) Goodson and Noller, *ibid.*, **61**, 2420 (1939).
- (3) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).
- (4) Marker and Rohrmann, *ibid.*, **62**, 898 (1940).

The ether solution was treated with Norit and the product crystallized from ether to give a product with m. p. 200–205°, dec.; yield 4.2 g.

Anal. Calcd. for $C_{27}H_{39}O_3Br$: C, 66.0; H, 8.0. Found: C, 65.8; H, 8.1.

Reduction of Bromo-dehydro- $\Delta^{4,5}$ -isosarsasapogenone with Sodium and Ethanol.—To a boiling solution of 4 g. of bromo-dehydro- $\Delta^{4,5}$ -isosarsasapogenone in 400 cc. of absolute ethanol was added 20 g. of sodium in small pieces over a period of one hour. Water was added and the precipitated solid taken up in ether, washed well with water and the ether evaporated. The residue was dissolved in a small amount of ethanol and to this was added a solution of 8 g. of digitonin in 400 cc. of 80% ethanol. After standing overnight the digitonide was collected, washed and dried; yield 6.2 g. This was decomposed with pyridine in the usual manner. The product was treated with Norit in methanol and crystallized from ether and methanol to give white crystals, m. p. 202–204°. A mixture with neotigogenin, m. p. 198–200°, melted at 174–185°. A mixture with sarsasapogenin, m. p. 199–201°, melted at 165–174°.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 77.8; H, 10.5.

With boiling acetic anhydride the product gave an acetate which crystallized from methanol as white plates, m. p. 202–204°. When mixed with tigogenin acetate, m. p. 203–204° it gave no depression in melting point.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 75.6; H, 9.9.

Isomerization of Neotigogenin into Tigogenin.—A solution of 100 mg. of neotigogenin in 20 cc. of ethanol and 2 cc. of concentrated hydrochloric acid was refluxed for eighty hours. Water was added and the product was crystallized from methanol-acetate, methanol and ethanol to give a product, m. p. 202–204°. When mixed with tigogenin, m. p. 204–206°, it melted at 203–206°. When mixed with neotigogenin of m. p. 199–201°, it melted at 180–186°.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 77.7; H, 10.6.

When refluxed with acetic anhydride it gave an acetate which when crystallized from methanol melted at 202–204°. When mixed with tigogenin acetate, m. p. 203–205°, it melted at 203–205°.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 75.8; H, 10.1.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Summary

Isosarsasapogenin has been converted to tigogenin, indicating that the tigogenin side chain is of the "iso-configuration."

Neotigogenin upon isomerization with hydrochloric acid is converted into tigogenin.

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Divalent Nitrogen. I. The Rate of Dissociation of Tetraphenylhydrazine¹

BY C. K. CAIN² AND F. Y. WISELOGLE

The successive substitution of the hydrogen atoms of ethane by phenyl groups weakens the ethane carbon-carbon linkage to such an extent that hexaphenylethane in solution undergoes rapid dissociation into free radicals at 0°. This marked decrease in the bond strength has been attributed in part to stabilization of the resulting triphenylmethyl radicals through resonance of the odd electrons in the aromatic nuclei, resonance which is not possible in hexaphenylethane.³

If stabilization of triarylmethyl radicals through increased resonance is responsible for dissociation in hexaarylethanes,⁴ then it seems reasonable to

predict that substitution by aryl groups of the hydrogen atoms of any simple dimeric molecule would weaken the central bond of the compound. An accumulation of aryl groups could lead to compounds which would dissociate at moderate temperatures to give relatively stable radicals. Indeed Wieland has attributed many of the reactions of tetraarylhydrazines, R_2N-NR_2 , to preliminary dissociation into free radicals, $R_2N\cdot$, in which the nitrogen atom is divalent.⁵ We have now undertaken a study of substituted hydrazines in order to determine the energetics of this dissociation process and thereby to determine the effect on the strength of the N-N bond of substituting various groups for hydrogen atoms. In this paper we report measurements of the rate of dissociation of tetraphenylhydrazine and from these data a calculation of the activation energy for the formation of diphenylnitrogen radicals.

(5) Wieland, "Die Hydrazine," Ferdinand Enke, Stuttgart, 1913, pp. 71–78.

(1) From a dissertation submitted by C. K. Cain in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Johns Hopkins University.

(2) E. I. du Pont de Nemours and Co. Fellow, 1938–1939.

(3) Pauling and Wheland, *J. Chem. Phys.*, **1**, 367 (1933).

(4) Recently the importance of resonance as a factor in promoting dissociation of polyarylethanes has been questioned. See, for example, Marvel, Mueller and Ginsberg, *THIS JOURNAL*, **61**, 2008 (1939). That resonance plays some part in stabilizing the radicals, however, is not disputed.