

## On Glucosyl Thioureides. Part—IV. Synthesis of 3-Aryl-2,6-diphenylimino-4-*S* tetra-*O*-acetyl-*D*-glucopyranosyl-5,6-dihydro-1,3,5-thiadiazine (Hydrochlorides)

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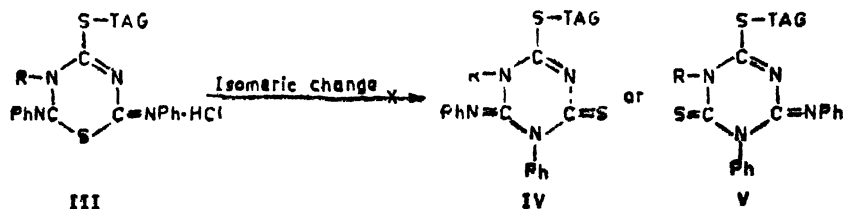
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Certain 3-aryl-2,6-diphenylimino-4-*S*-tetra-*O*-acetyl-*D*-glucopyranosyl-5,6-dihydro-1,3,5-thiadiazines (hydrochlorides) have been prepared by the interaction of phenylisocyanodichloride and 2-*S*-tetra-*O*-acetyl-*D*-glucopyranosyl-1-aryl-5-phenyl-2,4-isodithiobiurets. The identities of these products have been established on the basis of usual chemical transformations, Ir, and polarimetry. All the attempts to isomerize these products into the related 1,3,5-triazines (IV or V) have been unfruitful.

RECENTLY, we have reported a procedure for the synthesis of 4-aryl-5-phenylimino-3-*S*-tetra-*O*-acetyl-*D*-glucopyranosyl-1,2,4-thiadiazolines<sup>1</sup>. In view of the importance of thioglucosides in medicinal chemistry, it appeared interesting to synthesize certain 1,3,5-triazines having tetra-*O*-acetyl-*D*-glucopyranosyl group. Therefore, interaction of 2-*S*-tetra-*O*-acetyl-*D*-glucopyranosyl-1-aryl-5-phenyl-2,4-isodithiobiurets and phenylisocyanodichloride have been undertaken with a view to synthesize 1,3,5-triazine derivatives.

chloride was noticed. After reaction, benzene was distilled off. The residue when triturated several times with petroleum ether, was converted into a pale yellow solid. It was purified by precipitating it from its benzene solution with petroleum ether, m.p. 105°(d).

The product was acidic to litmus and gave effervescence with aqueous sodium bicarbonate. It was found non-desulphurisable when boiled with alkaline plumbite solution. It charred when heated with



When the interaction of phenylisocyanodichloride has been carried out with 2-*S*-tetra-*O*-acetyl-*D*-glucopyranosyl-1,5-diphenyl-2,4-isodithiobiuret in boiling benzene medium for 3 h, evolution of hydrogen

sulphuric acid. It afforded a picrate, m.p. 146°, when its ethanolic solution was treated with ethanolic picric acid. The product was found to have  $[\alpha]_D^{25} +13.78^\circ$  (c 1.6408 in chloroform)<sup>2</sup>;  $\nu_{\max}$  1595,

TABLE I—SYNTHESIS OF 3-ARYL-2,6-DIPHENYLIMINO-4-*S*-TETRA-*O*-ACETYL-*D*-GLUCOPYRANOSYL-5,6-DIHYDRO-1,3,5-THIADIAZINES (HYDROCHLORIDES)

Sl. no.	2- <i>S</i> -Tetra- <i>O</i> -acetyl- <i>D</i> -glucopyranosyl-1-aryl-5-phenyl-2,4-isodithiobiurets (g)	3-Aryl-2,6-diphenylimino-4- <i>S</i> -tetra- <i>O</i> -acetyl- <i>D</i> -glucopyranosyl-5,6-dihydro-1,3,5-thiadiazines (hydrochloride) III m.p. (°C), yield (g)	Analysis % ; Found/(Calcd.) N S		$[\alpha]_D^{25}$ in chloroform (c)	Picrate m.p. °C	N% : Found/ (Calcd.)
1.	-1-phenyl-, (6.1)	-3-phenyl-, IIIa 105 (d), 3.0	7.62 (7.42)	7.84 (8.48)	+ 13.78° (1.6408)	146	9.73 (10.85)
2.	-1- <i>o</i> -tolyl-, (6.3)	-3- <i>o</i> -tolyl-, IIIb 135 (d), 3.5	7.16 (7.28)	8.10 (8.32)	- 7.226° (1.855)	140	10.97 (10.20)
3.	-1- <i>m</i> -tolyl-, (6.3)	-3- <i>m</i> -tolyl-, IIIc 128 (d), 4.0	6.76 (7.28)	7.68 (8.32)	+ 35.83° (0.9708)	180	11.00 (10.20)
4.	-1- <i>p</i> -tolyl-, (6.3)	-3- <i>p</i> -tolyl-, IIId 125 (d), 3.8	6.89 (7.28)	7.93 (8.32)	+ 312.1°	136	9.68 (10.20)
5.	-1- <i>o</i> -Cl-phenyl-, (6.5)	Not isolated	—	—	—	—	—
6.	-1- <i>m</i> -Cl-phenyl-, (6.5)	-3- <i>m</i> -Cl-phenyl-, IIIe 115 (d), 4.2	6.68 (7.09)	7.32 (8.11)	+ 3.161° (1.07)	138	10.60 (9.98)

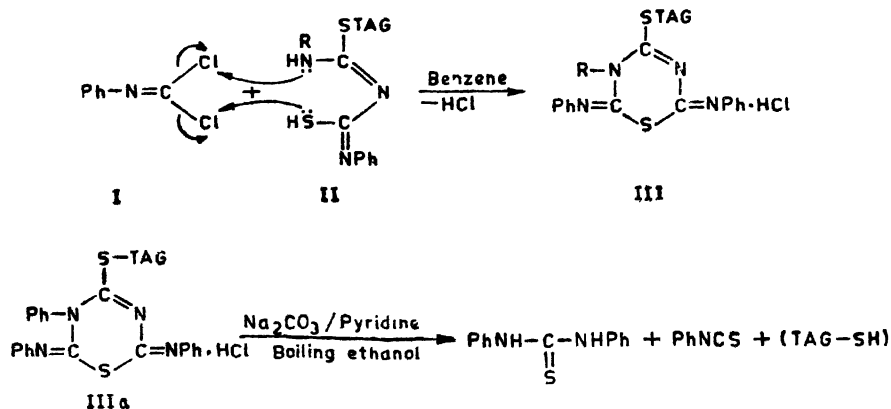
(N-C=N), 1625 (S-C=N), 685 (C-S-C) and 1750  $\text{cm}^{-1}$  (C=O) (present as acetyl group in glucose residue)<sup>3,4</sup>.

On the basis of the above facts it was quite evident that the reaction product with m.p. 105°(d) was a 1,3,5-thiadiazine (hydrochloride) for which structure 3-phenyl-2,6-diphenylimino-4-S-tetra-O-acetyl-D-glucopyranosyl-5,6-dihydro-1,3,5-thiadiazine (hydrochloride) (IIIa) has been assigned.

Attempts have been made also towards isomerization of the product with m.p. 105° (d), into the related 1,3,5-triazine (IVa or Va) by reacting it with (i) boiling ethanolic sodium carbonate and (ii) with ethanolic pyridine solutions. In both the cases product decomposed and 1,3-diphenylthiocarbamide, m.p. 154°, phenylisothiocyanate and thioglucoside have been detected from the decomposition products.

The interaction of phenylisocyanodichloride was also capable of extension to several other 2-S-tetra-O-acetyl-D-glucopyranosyl-1-aryl-5-phenyl-2,4-isodithiobiuretes (IIb-IIl). In all these cases the corresponding 1,3,5-thiadiazines (hydrochlorides) (IIIb-IIIl) only have been obtained (Table I).

The mechanism of formation of III may be depicted as follows :



where, R=(a) phenyl, (b) *o*-tolyl, (c) *m*-tolyl, (d) *p*-tolyl, (e) *o*-Cl-phenyl and (f) *m*-Cl-phenyl, TAG = Tetra-O-acetyl-D-glucopyranosyl.

### Experimental

The required 2-S-tetra-O-acetyl-D-glucopyranosyl-1-aryl-5-phenyl-2,4-isodithiobiuretes have been prepared as usual<sup>6</sup>. The phenylisocyanodichloride has been prepared by passing excess of chlorine gas into the chloroform solution of phenyl isothiocyanate<sup>6</sup>.

3-Aryl-2,6-diphenylimino-4-S-tetra-O-acetyl-D-glucopyranosyl-5,6-dihydro-1,3,5-thiadiazines (hydrochlorides) (III) :

Details of a typical experiment (where, aryl = phenyl) are as follows: A benzene solution of phenylisocyanodichloride (I) (0.01 M, 1.74 g in 20 ml) was mixed with a benzene suspension of 2-S-

tetra-O-acetyl-D-glucopyranosyl-1,5-diphenyl-2,4-isodithiobiuret (II) (0.01 M, 6.17 g in 40 ml). The mixture after shaking was refluxed over a boiling water bath for 3 h. During the reaction evolution of hydrogen chloride was noticed. Then benzene was distilled off. The resultant viscous residue was then triturated several times with petroleum ether, a pale yellow solid (IIIa) (3 g) was isolated. It was purified by precipitating it from its benzene solution with petroleum ether, m.p. 105° (d) (Found: C, 55.24, H, 4.52, N, 7.62, S, 7.84.  $\text{C}_{26}\text{H}_{24}\text{O}_9\text{N}_4\text{S}_2$ , HCl requires C, 55.65, H, 4.77, N, 7.42, S, 8.48%).

The other 3-aryl-2,6-diphenylimino-4-S-tetra-O-acetyl-D-glucopyranosyl-5,6-dihydro-1,3,5-thiadiazines (hydrochlorides) (IIIb-IIIl) have been prepared by the extension of reaction of phenylisocyanodichloride (I) to other 2-S-tetra-O-acetyl-D-glucopyranosyl-1-aryl-5-phenyl-2,4-isodithiobiuretes (IIb-IIl) (Table I).

Attempts towards the isomerization of IIIa to IVa/Va : (a) Reaction with ethanolic sodium carbonate :

The product (5 g) was mixed with 5% aqueous ethanolic solution of sodium carbonate (30 ml) and the resultant clear solution was refluxed over a boiling water bath for 4 h. During heating, gradually,

solution turned from yellow to dark brown in colour. The solvent ethanol was then distilled off and a viscous brown liquid was isolated. It had the characteristic odour of phenylisothiocyanate, which is confirmed by extracting it with petroleum ether followed by reaction with aniline, when 1,3-diphenylthiocarbamide<sup>7</sup>, m.p. 152° was isolated.

The petroleum ether insoluble semi-solid mass, when treated with little ethanol afforded a solid, crystallised from aqueous ethanol, m.p. 152. It was identified as 1,3-diphenylthiocarbamide on the basis of undepressed m.m.p. with authentic sample<sup>7</sup>. The ethanol solution responded to Molisch test indicating glucosyl compound.

(b) *Reaction with ethanolic pyridine :*

The product (5 g) was mixed with 5% ethanolic pyridine solution (50 ml) and the resultant clear solution was refluxed over a boiling water bath for 5 h. The solution gradually turned into a blackish brown in colour. After heating the solvent ethanol was distilled off. The viscous oily liquid was then washed with 5% aqueous hydrochloric acid to remove pyridine. The acid washed semi-solid had the odour of phenylisothiocyanate which was confirmed by extracting it with the help of petroleum ether and reacting the extract with aniline, when 1,3-diphenylthiocarbamide<sup>7</sup>, m.p. 151° was isolated.

The petroleum ether insoluble semi-solid when treated with a little ethanol afforded shining plates, crystallised from aqueous ethanol, m.p. 152°. It was identified as 1,3-diphenylthiocarbamide on the basis of undepressed m.m.p. with the authentic sample<sup>7</sup>. The ethanol soluble portion responded to positive Molisch test indicating the presence of glucosyl compound.

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