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Simple And Eco-Friendly Of Some Glycosides Bearing Triazolo[3,4-B][1,3,4]Thiadiazole Moiety Linked Through O Atoms

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Abstract: ***There is a vast variety of naturally occurring o-glycosides which have marked pharmacological properties and they have distinct physiological functions according to structure of their genin. The genin may contain widely diverse functional groups which markedly influence the chemical, physical and pharmacological proeprties of the corresponding glycosides. The 3-substituted-5,6-dihydro-6-[(3'-methoxy,4'-o-2,3,4,6,tetra-o-acetyl-β-o-glucopranosyl)phenyl]-s-triazolo [3,4-b][1,3,4]-thiadiazoles were prepared in microwave oven in 3-5 minutes at a cook level of 7 in a good yield.***

Keywords: ***antiviral, antileishmannial, thiocarbohydrazides, 2,3,4,6-tetra-o-acetyl-α-D-glucopyranosyl bromide, triazoles.***

I. INTRODUCTION

A triazole nuclear appears to be very important as regards pesticidal potency is concerned. Likewise a 1,3,4-thiadiazole ring is associated with diverse biological activities probably by virtue of incorporating a toxophoric-N=C-S-Linkage, the importance of which has been well stressed in many pesticides. Therefore the molecule which combines these two biolabile rings together to give a compact and planar system with a hope to obtain compounds of better biocidal activities. Further s-triazole and 1,3,4-thiadiazoles which exhibit diverse biological activities such as antimicrobial, bacteriocidal, antiinflammatry, antiviral, antihypertensive, antihelmintic and analgeric.

The glycosides are found in wide variety of natural products. The carbohydrate moiety in these glycoside is generally mono disaccharide or less frequent by a higher oligosaccharide. Numereous glycosides are used as drugs and have a wider therapeutic applications.

II. RESULT AND DISCUSSION

The general scheme involves the glucosidation of 3,6-disubstituted-s-triazolo[3,4-b][1,3,4]-thiadiazoles with 2,3,4,6-tetra-o-acetyl-α-D-glucopyranosyl bromide having o-glucosidic linkage.

p-Methoxy benzoic acid and p-nitro benzoic acid were esterified with $MeOH/H_2SO_4$ to get corresponding benzoates. Treatment with hydrazine hydrate (80%) gave corresponding benzoyl hydrazides. Further treatment with KOH/CS_2 gave their potassium salts. On heating these potassium salts on an oil bath with hydrazine hydrate (80%) gave corresponding 3-aryl-4-amino-5-mercapto-s-triazoles.

3-Methoxy-4-hydroxy benazldehyde was glucosidated with 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide and then condensed with different aliphatic as well as bromide and then condensed with different aliphatic as well as aromatic-s-triazoles in a microwave oven at a cook level of 7 in presence of DMF/TsOH to give the various substituted o-glucosidated-s-triazolo[3,4-b] [1,3,4]-thiadiazoles as fine solids. Their m.pts range between 130-225 °C.

Their IR sepctra recorded in KBr gave the absorption bands as KBr υ_{max} cm^{-1}: 3500-3400(-NH stretch), 1745-1720 (stretch), 1605-1585 (>C=N stretch), 1390-1290 (-C-N Aromatic stretch), 1260-1200 (-C-O-C Asymmetric stretch), 690-646(C-S stretch).

Their PMR spectra recorded in $CDCl_3$ showed the following signals:

δ 1.50-2.10(m, 12H, 4 x $-COCH_3$), 3.50-3.96(s, 3H, $-OCH_3$), 3.73-4.50 (m, 5H, $-OCH_2$, 3', 4' and 5'-H), 4.53-53-

5.40(m, 6H, 1', 2'-H), 5.65-5.95(s, 1H, 6-H), 5.90-5.95(s, 1H, NH), 6.90-8.53(m, 3H, Ar-H).

III. EXPERIMENTAL

4-(O-2,3,4,6-TETRA-O-ACETYL-B-D-GLUCOPYRANOSYL)-3-METHOXYBENZALDEHYDE (I)

A solution of 2,3,4,6-tetra-o-acetyl-α-D-glucopyranosyl bromide (20.0g, 48 m mol) in chloroform (200 ml) was stirred vigorously under reflux with a solution of 4-hydroxy-3-methoxy benzaldehyde (9.7g, 64 m mol) and tetrabutylammonium bromide (10.2 g, 32 m mol) as PTC in 5% aqueous NaOH solution (1.00 ml, 125 m mol). After 3 hours the mixture was cooled and diluted with water. The two phases were then separated. The organic layer was washed with 5% aqueous NaOH (2x50 ml), dried over anhydrous Na_2SO_4. Filtered and colourless solid (14.5g) m.pt 130 °C.

METHYL P-METHOXY BENZOATE (IIA)

In a 500 c.c round bottom round bottom flask placed a mixture of 37.39g (0.246 mol) of p-methoxy benzoic acid. 80g (2.5 mol) of absolute MeOH and 5g (2.7 mol) or conc. H_2SO_4. Added few small chips of porous porcelain, heated under reflux gently for 4 hours, distilled off excess alcohol, cooled and poured the residue into 250 ml of H_2O. Separated the payer and washed it with a solution of $NaHCO_3$, until all the free acid was removed, washed with water. Recrystallised from ethanol as colourless flakes (20.5 g) m.pt 47 °C [lit.[28] m.pt. 48 °C].

P-METHOXY-BENZOYL HYDRAZINE (IIB)

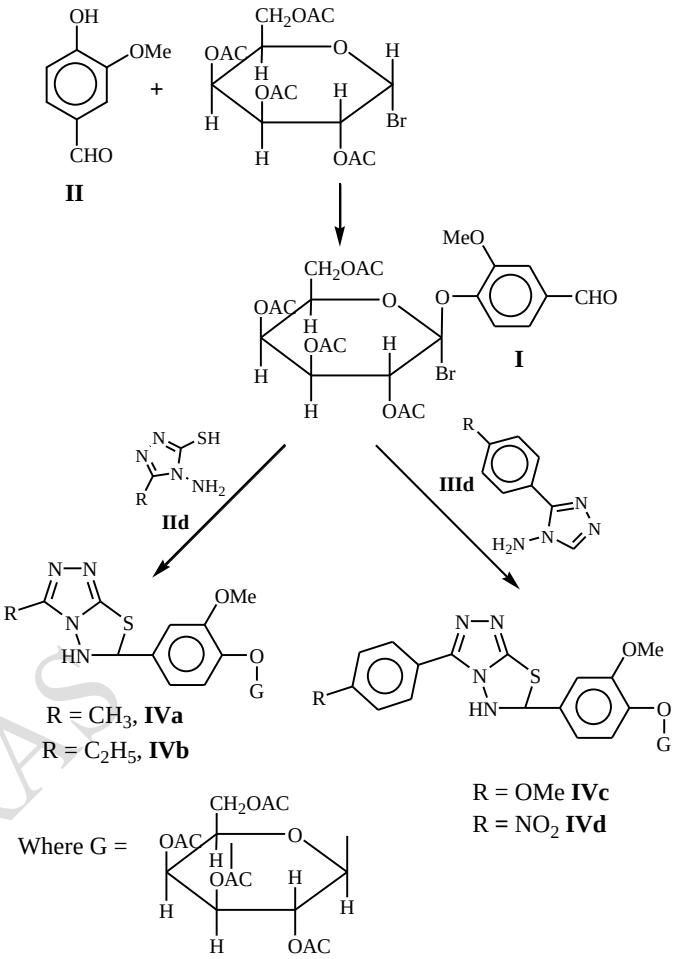
Ester (IIa; 16.6g, 0.1 mol) was refluxed with (80%) hydrazine hydrate (7.5g, 0.1 mol) in 25 ml of a absolute EtOH for 8 hours. On distilling excess EtOH, the hydrazide separates out which was filtered. Recrystallised from ethanol as shinning white needles (10.5g), m.pt 135 °C.

POTASSIUM SALT OF P-METHOXY BENZOYL HYDRAZINE (IIC)

Prepared by stirring at room temperature a solution of hydrazide (IIb; 16.6g, 0.1 mol), KOH (8.41g, 0.15 mol) and CS_2 (11.41g, 0.15 mol) in anhydrous EtOH (100 ml) for 10 hours. The mixture was then diluted with dry ether (200 ml) and the precipitated solid filtered. Dried in vaccum at 65 °C to give the required potassium salt in nearly quantitative yield, m.pt 263-265 °C.

3-[(4′-METHOXY)PHENYL]-4-AMINO-5-MERCAPTO-1,2,4 TRIAZOLE [IID]

A mixture of potassium salt (IIc; 28.0g, 0.1 mol) and (80%) hydrazine hydrate (12.5g, 0.25 mol) was heated on an oil bath at 140-160 °C for 4-5hours. Colour of the reaction mixture was changed to green with evolution of H_2S gas. The reaction mixture was then cooled and poured in cold water (850 ml). Acidified with conc. HCl, filtered, washed with cold water (2 x 50 ml) and recrystallised from ethanol as light yellow solid (19.5g) m.pt 204 °C (lit.[29] m.pt 205 °C).



METHYL P-NITRO BENZOATE (IIIA)

Prepared by refluxing a mixture of 41.08g (0.246 mol) of p-nitro benzoic acid, 80g (2.5 mol) of absolute MeOH and 5g (2.7 mol) of conc. H_2SO_4 with the procedure same as for IIa. Recrystallised from ethanol (13.8g) m.pt 94°C. (lit.[30] M.pt. 96 °C).

P-NITRO BENZOYL HYDRAZINE (IIIB)

Prepared for a mixture of ester (IIIa; 18.3g, 0.1 mol), 80% hydrazine hydrate (7.5g, 0.15 mol) in 25 ml of absolute EtOH with the procedure same as for IIb. Recrystallised from ethanol (11.5g) m.pt. 70 °C (lit.[31] m.pt 71-72 °C).

POTASSIUM SALT OF P-NITRO BENZOYL HYDRAZINE (IIIC)

Prepared by stirring at room temperature a mixture of hydrazine (IIIb; 18.1g, 0.1 mol), KOH (8.41g, 0.15 mol) and CS_2 (11.41g, 0.15 mol) in anhydrous EtOH, with the procedure same as for II_c in nearly quantitative yield m.pt above 300 °C.

3-[(4′-NITRO)PHENYL]-4-AMINO-5-MERCAPTO-1,2,4-TRIAZOLE (IIID)

Prepared by heating a mixture o potassium salt (IIIc; 29.5g, 0.1 mol), 80% hydrazine hydrate (12.5g, 0.25 mol) on an oil bath with the procedure same as for IIc. Recrystallised from ethanol as pale yellow solid (20g) m.pt 271 °C.

3-METHYL-5,6-DIHYDRO-6-[(3′-METHOXY-4′-O-2,3,4,6-TETRA-O-ACETYL-B-D-GLUCOPYRANOSY)PHENYL]-S-TRIAZOLO[3,4-B][1,3,4]-THIADIAZOLE (IVA)

An equimolar mixture of methyl mercapto amino-s-triazole IIa, (1.30g, 0.01 mol) and glucosidated vanillin (1; 4.28g, 0.01 mol) were dissolved in about 25 ml of DMF taken in a 100 ml beaker. A small amount (20 mg) of p-toluene sulphonic acid was added as a catalyst and the reaction mixture was heated in a microwave oven at a cook level of 7 for 3 minutes. Monitored the spot on TLC and then added about 50 ml of water. White solid precipitated filtered and crystallized from ethyl acetate and petroleum ether as light yellow solid (3.0g) m.pt 225 °C.

IR(KBr): 3430 (-NH-stretch), 1745, ( stretch), 1605- 1592 (>C = N stretch), 1380-1285 (-C-N

Aromatic stretch), 1260-1200 (-C-O-C Asymmetric stretch), 690-650 (-C-S-stretch).

PMR($CDCl_3$): 1.50(m, 12H, 4 x -$COCH_3$), 1.83(s, 3H, -CH_3), 3.50(s, 3H, -OCH_3), 3.73-4.40(m, 5H, -OCH_2), 3′, 4′ and 5′ - H), 4.53-4.66 (m, 6H, 1′, 2′-H), 5.66(s, 1H, 6-H), 5.95(s, 1H, -NH), 7.30-7.65(m, 3H, Ar-H).

Found: C, 49.02; H, 4.87; N, 9.36. $C_{25}H_{30}N_4O_{11}S$ requires C, 50.5; H, 5.05; N, 9.42%.

3-ETHYL-5,6-DIHYDRO-6-[(3′-METHOXY-4′-O-2,3,4,6-TETRA-O-ACETYL-B-D-GLUCOPYRANSOYL)PHENYL-S-TRIAZOLO[3,4-B][1,3,4]-THIADIAZOLE (IVB)

Prepared from IIb, (1.44g, 0.01 mol), glucosidated vanillin (1; 4.82g, 0.01 mol) and TsOH (20 mg) with the procedure same as for IVa. Recrystallised from ethyl acetate and petroleum ether as light yellow solid (3.2g) m.pt. 151 °C.

IR(KBr): 3500(-NH-stretch), 1750-1740 ( stretch). 1600-1595 (>C=N stretch), 1385-1209(-C-N-Aromatic stretch), 1250-1205(C-O-C-Asymmetric stretch) and 685-670 (C-S stretch).

PMR($CDCl_3$): 1.96-2.00(m, 12H, 4 x –$COCH_3$), 3.96(3H, -OCH_3), 3.85-4.40(m, 5H, -OCH_2, 3′, 4′ and 5′ -H), 4.96-5.36(m, 6H, 1′, 2′, -H), 5.90(m, 6H-NH) and 6.9-7.6(m, 3H, Ar-H).

Found: C, 51.09; H, 5.15; N, 9.12, $C_{26}H_{32}N_4O_{11}S$ requires C, 51.31; H, 5.26 and N, 9.21%.

3-[(4′-METHOXY)PHENYL]-5,6-DIHYDRO-6[(3′-METHOXY-4′,O-2,3,4,6-TETRA-O-ACETYL-B-D-GLUCOPYRANOSYL) PHENYL]-S-TRIAZOLO[3,4-B][1,3,4]-THIADIAZOLE (IVC).

Prepared from (IId; 2.22g, 0.01 mol), glucosidated vanillin (1; 4.82g, 0.01 mol) and TsOH (20 mg) with the procedure same as for IVa. Recrystallised from ethyl acetate and petroleum ether as yellow solid (3.5 g) m.pt (202-205 °C).

IR(KBr): 3450(-NH-stretch), 1750-1745 ( stretch), 1605-1590(>C=N stretch), 1390-1300(-C-N Aromatic stretch), 1255-1205(C-O-C-Asymmetric stretch) and 689-655(C-S stretch).

PMR($CDCl_3$): 1.96-2.10(m,12H, 4 x -OCH_3), 3.90(s, 6H, 2 x –OCH_3), 3.96-4.50(m, 5H, -OCH_2, 3′, 4′ and 5′-H), 4.90-5.40(m, 6H, 1′, 2′-H), 5.65(s, 1H, 6-H), 5.90(s, 1H, -NH), 7.83-8.53(m, 7H, Ar-H).

Found: C, 54.05; H, 4.20; N, 8.7. $C_{31}H_{34}O_{12}S$ requires C, 54.22; H, 4.95 and N, 8.16%.

3-[(4′-NITRO)PHENYL]-5,6-DIHYDRO-6[(3′-METHOXY-4′-O-2,3,4,6-TETRA-O-ACETYL-B-D-GLUCOPYRANOSYL)PHENYL-S-TRIAZOLO[3,4-B][1,3,4]-THIADIAZOLE (IVD)

Prepared from (IIId; 2.37g, 0.01 mol), glucosidated vanillin (1; 4.82g, 0.01 mol) and TsOH (20 mg) with the procedure same as for IVa. Recrystallised from ethyl acetate and petroleum ether as light yellow solid (3.6g) m.pt 130 °C.

IR(KBr): 3420 (-NH- stretch), 1730-1720 ( stretch), 1600-1585(>C=N stretch), 1380-1290(-C-N-Aromatic stretch), 1250-1200(C-O-C-Asymmetric stretch) and 680-646(C-S stretch).

PMR($CDCl_3$): 2.00-2.20(m, 12H, 4x –OCH_3), 3.72(s, 3H, -OCH_3), 3.85-4.35(m, 5H, -OCH_2, 3′, 4′ and 5′ - H), 4.95 – 5.36(m, 6H, 1′, 2′-H), 5.73(s, 1H, 6-H), 5.95(s, 1H, -NH), 7.55-8.40(m, 7H, Ar-H).

Found: C, 51.13; H, 4.24; N, 9.02. $C_{30}H_{31}N_5O_{13}S$ requires C, 51.35; H, 4.42 and N, 9.98%.

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