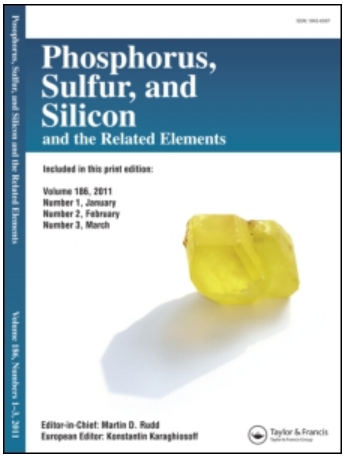

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Regioselective Synthesis of C-Nucleosides Via Condensation of 2-Hydrazino-thia-diaza-benzo[a]-azulen-4-one

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To cite this Article El-Gazzar, A. B. A.(2005) 'Regioselective Synthesis of C-Nucleosides Via Condensation of 2-Hydrazino-thia-diaza-benzo[a]-azulen-4-one', Phosphorus, Sulfur, and Silicon and the Related Elements, 180: 1, 283 — 293
To link to this Article: DOI: 10.1080/104265090509108
URL: http://dx.doi.org/10.1080/104265090509108

Phosphorus, Sulfur, and Silicon, 180:283–293, 2005

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/104265090509108

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Regioselective Synthesis of C-Nucleosides Via Condensation of 2-Hydrazino-thia-diaza-benzo[a]-azulen-4-one

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Keywords 2-Hydrazino-10-thia-1,3-diaza-benzo[a]azulen-4-one; ^{1}H; ^{13}C.NMR spectroscopy; cyclo-condensation; mono-saccharaides

INTRODUCTION

In connection with my program dealing with the discovery of C-nucleosides[1–6] and acyclic-C-nucleosides[1,5] as well as the rapid growth in the literature dealing with their biological activity in the last 50 years, prompted me to become involved in a program to synthesize some acyclic-C-nucleosides. Depending on whether the above synthesized 2-hydrazino derivative reacts smoothly with aromatic aldehydes to give the corresponding hydrazone derivatives, experiments are made to react this hydrazine derivative with some mono-saccharaides. The produced hydrazones are cyclized to give acyclic-C-nucleosides which may show biological activities.

The biological,[8] bactericidal,[9] and medicinal activities[10] of pyrimidine and fused pyrimidine derivatives, prompted me to study the reactivity of the 2-hydrazine-10-thia-1,3-diaza-benzo[a]azulen-4-one (**4**) toward the mono-saccharaides to synthesize new C-nucleosides derived from thieno[2,3-*d*]pyrimidine (**3**). Thus, seberone reacted with ethyl cyanoacetate and sulfur metal in presence of absolute ethanol and diethylamine to give 2-amino-thiophene-3-ethyl ester[11] derivative (**1**). The latter compound reacts with potassium thiocyanate[12] in dioxane/hydrochloric acid (gas) to give the thieno[2,3-d]pyrimidine derivative (**2**), which gives 2-methylthio derivative (**3**) when treated with one mole of methyliodide in ethanolic sodium hydroxide solution.[13]

Received March 5, 2004; accepted June 22, 2004.
Dedicated to Professor Ahmed Saleh Aly on the occasion of his 62nd birthday.
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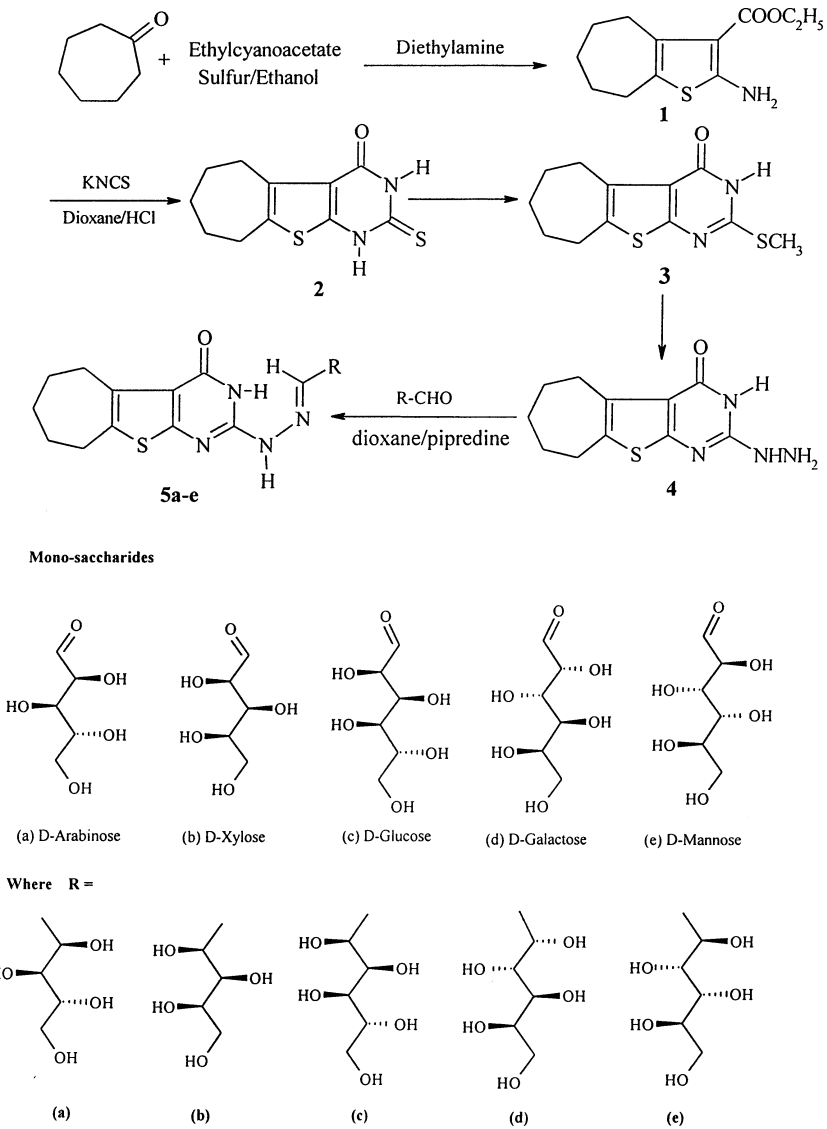
Action of hydrazine hydrate on the 2-methylthio derivative,[4] afforded the starting material 2-hydrazine-3,5,6,7,8,9-hexahydro-10-thia-1,3-diaza-benzo[a]azulen-4-one (**4**).

According to El-gazzar and Shisho[13,14] synthesis of pyrimidine derivatives the reaction of 2-hydrazino-10-thia-1,3-diaza-benzo[a]azulen-4-one (**4**) with some penta mono-saccharides, namely, D-arabinose and D-xylose in dry dioxane in the presence of catalytic amounts of piperidine yielded the corresponding hydrazones **5a**,**b**. The spectral data beside the correct values in elemental analyses support the open chain nature of the sugar residue in **5a**,**b**. Moreover, the IR (KBr) spectrum for **5a** displayed absorption bands at 3419 cm^{-1} (broad, OH), 3241 (NH), 1685 (C=O). The NMR spectrum of compound **5b**, as an example, showed signals at δ 1.61 (m, 4H, $2CH_2$), 1.83 (m, 2H, CH_2), 2.65 (m, 2H, CH_2), 3.27 (m, 2H, CH_2), 3.51 (m, 4OH, D_2O exchangeable, OH-2′, OH-5′), 4.23 (q, 1H, J = 6 Hz, H-4′), 4.42 (m, 2H, H-5′′), 4.63 (d, 1H, J = 5 Hz, H-3′), 5.79 (dd, 1H, J = 7 Hz, H-2′), 7.39 (d, 1H, J = 4 Hz, H-1′), and 10.20–10.65 (brs, NH, D_2O exchangeable), (Experimental, Scheme 1). The hydrazone derivatives **5a**,**b** were stirred at room temperature in acetic anhydride-pyridine (1:1) mixture to afford the corresponding 3-(2′,3′,4′,5′-O-tetraacetyl-glycosyl)-6,7,8,9,10-pentahydro-cycloheptathieno[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one (**7a**,**b**) (Scheme 2). The spectral data beside the correct values in elemental analyses support the structure. Moreover, it is reported in literature that N-3 nitrogen atom and not N-1 nitrogen atom involved in the cyclization in pyrimidine ring.[7] Also, there is no signal for the methylene proton of the triazole, which supports the structure **7a–e** not **6a–e**. The NMR spectrum of compound **5a**, as an example, showed signals at δ 1.59 (m, 4H, $2CH_2$), 1.78 (m, 2H, CH_2), 1.93 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.19 (s, 3H, CH_3) 2.61 (m, 2H, CH_2), 3.21 (m, 2H, CH_2), 4.69 (m, 1H, H-3′), 5.21 (m, 2H, H-4′), 5.43 (m, 1H, H-2′), 5.79 (m, 1H, H-1′), 10.11 (brs, NH, D_2O exchangeable).

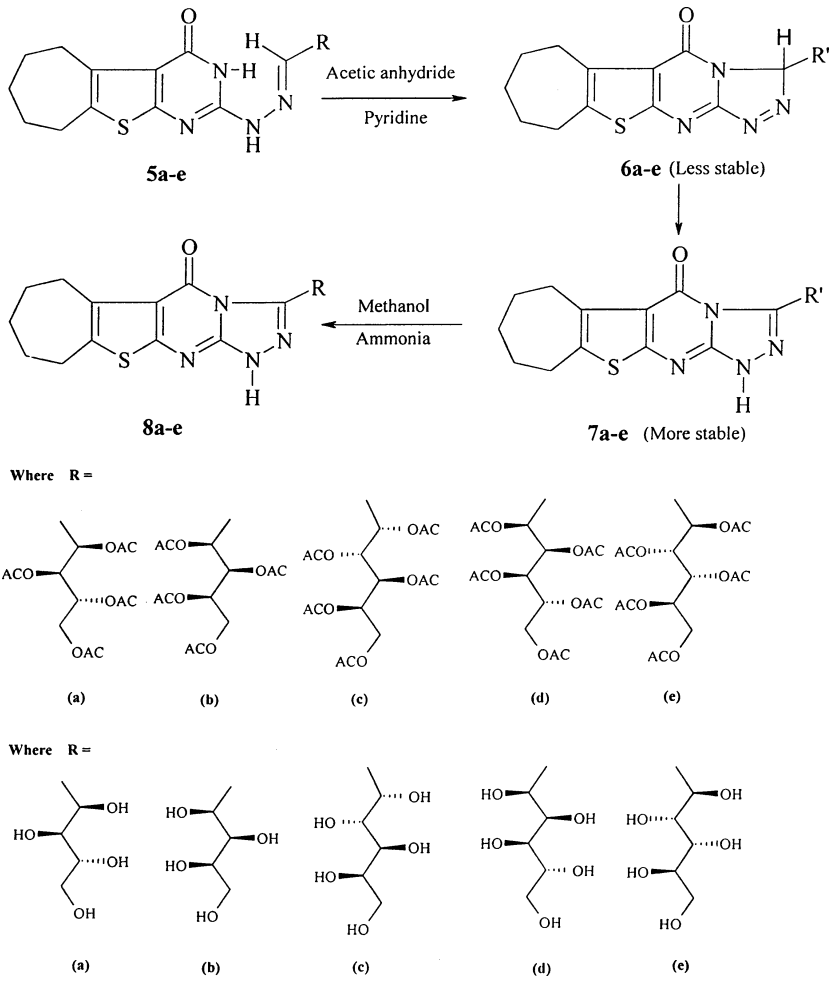
De-protection of the protected acyclic-C-nucleosides **7a**,**b** could be achieved by treatment with methanolic ammonia solution (25%) at room temperature for 24 hours. The de-protected acyclic-C-nucleosides, mainly, 3-glycosyl-6,7,8,9,10-pentahydro-cyclohepta-thieno[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one (**8a**,**b**), were obtained (Scheme 2). The ^{13}C-NMR for **8b**, as an example showed six lines at δ 23.5, 25.2, 27.3, 28.2, 30.4, and 31.65 ppm for the sp^3 carbon atoms CH_2. It also, showed three signals at δ 61.3, 67.4, and 71.3 ppm for the sp^3 carbon atoms of the C-1′–C-3′ (CH of the sugar moity). The thienopyrimidine and triazole carbons at δ 113.1, 128.0, 130.6, 139.1, 147.8,



SCHEME 1

and 151.6 ppm. And the only carbonyl group of the pyrimidone ring resonates at δ 159.7 ppm (see experimental).

Likewise, heating under reflux 2-hydrazino (4) with some aldohexoses namely D-glucose, D-galactose, and D-mannose in boiling dioxane in presence of catalytic amounts of piperidine yielded the



SCHEME 2

acyclic-C-nucleosides **5c–e**. The structure was confirmed by elemental analysis, and spectral data (Scheme 1, Experimental). The ^{1}H-NMR spectrum of compound **5a**, as an example, showed signals at δ 1.64 (m, 4H, $2CH_2$), 1.80 (m, 2H, CH_2), 2.62 (m, 2H, CH_2), 3.24 (m, 2H, CH_2), 3.53 (m, 5OH, D_2O exchangeable), 3.68 (m, 1H, H-5′), 4.27 (m, 2H, H-6′, H-6″), 4.42 (m, 1H, H-4′), 4.63 (m, 1H, H-3′), 5.54 (m, 1H, H-2′), 7.43 (m, 1H, H-1′), and 10.09–10.25 (brs, NH, D_2O exchangeable). On the other hand, acetylating of compounds **5c–e** with acetic anhydride-pyridine, at room temperature, afforded the protected penta-O-acetyl derivatives **7c–e**. The spectral data beside the

correct values in elemental analyses support the cyclic C-nucleosides. Mainly, 3-(1′,2′,3′,4′,5′-O-pentaacetyl-glucosyl)–6,7,8,9,10-pentahydro-cycloheptathieno[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one (**7c**). Its ^{1}H-NMR spectrum showed signals at δ 1.61 (m, 4H, $2CH_2$), 1.78 (m, 2H, CH_2), 1.82 (s, 3H, CH_3), 1.93 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 2.63 (m, 2H, CH_2), 3.23 (m, 2H, CH_2), 4.68 (m, 1H, H-4′), 5.27 (d, 1H, J = 10.6 Hz, H-3′), 5.42 (m, 2H, H2′,5′), 5.63 (s, 1H, H-2′), 5.71 (s, 1H, H-1′), 8.65 (brs, NH, D_2O exchangeable).

Finally, the de-protection of the protected acyclic-C-nucleosides of **7c–e** could be achieved when they were stirred in methanolic ammonia solution at room temperature to give the acyclic-C-nucleosides **8c–e**. Mainly, 3-glucosyl-6,7,8,9,10-pentahydro-cyclohepta-thieno[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one (**8c**). Its IR (KBr) for compound **8c**, as an example, displayed absorption bands around 3440, 3460 (hydroxyl groups) and 3265 (NH) cm^{-1} and revealed the absence of any absorption in the carbonyl region except that of the carbonyl pyrimidone. Also, its NMR spectrum showed at showed signals at δ 1.63 (m, 4H, $2CH_2$), 1.79 (m, 2H, CH_2), 2.61 (m, 2H, CH_2), 3.12 (m, 5H, 5OH, D_2O exchangeable), 3.23 (m, 2H, CH_2), 3.38 (m, 1H, H-3′), 3.67 (m, 2H, H-5′, H-5″), 4.28 (m, 1H, H-2′), 4.63 (m, 1H, H-1′), 9.25 (brs, NH, D_2O exchangeable).

CONCLUSION

The prepared nucleosides seem to be interesting for biological activity studies. Furthermore, the present investigation offers rapid and effective new procedures for the synthesis of C-nucleosides systems.

EXPERIMENTAL

Melting points are uncorrected; IR spectra (KBr): Pye Unicam SP-1000 cm^{-1}; ^{1}H-nmr/^{13}C-nmr spectra (DMSO-d_6), ($CDCl_3$): Varian Gemini 200 MHz Spectrometer, TMS as internal standard, chemical shifts in δ (ppm). Micro-analytical data were preformed by the Micro-analytical Center at Cairo University and National Research Centre (Egypt). Elemental analyses (C, H and N) are in accordance with the calculated values (Table I).

2-(Glycosyl-hydrazon)-3,5,6,7,8,9-hexahydro-10-thia-1,3-diaza-benzo[a]azulen-4-one (5a–e)

General procedure. A solution of compounds **4** (10 mmol) and aldopentoses or aldohexoses (10 mmol) in dry dioxane in presence of catalytic amounts of pipridine, The mixture was refluxed for 3–5 h in a mixture of acetic anhydride-pyridine (20 ml: 20 ml) was stirred at room

TABLE I Physical Data for the Products 5, 7, 8

Comp. no.	m.p. °C	Yield %	M.F. (M. wt.)	Elemental analyses calcd./found C	H	N
5a	213–215	65	$C_{16}H_{22}N_4O_5S$	50.25	5.80	14.65
	melted		382.4	50.31	5.74	14.38
5b	221–223	63	$C_{16}H_{22}N_4O_5S$	50.25	5.80	14.65
	melted		382.4	50.19	5.72	14.47
5c	189–192	65	$C_{17}H_{24}N_4O_6S$	49.50	5.87	13.58
	melted		412.5	49.63	5.82	13.43
5d	201–203	66	$C_{17}H_{24}N_4O_6S$	49.50	5.87	13.58
	melted		412.5	49.45	5.68	13.39
5e	195–197	68	$C_{17}H_{24}N_4O_6S$	49.50	5.87	13.58
	melted		412.5	49.61	5.74	13.45
7a	207–209	59	$C_{24}H_{28}N_4O_9S$	52.55	5.14	10.21
	melted		548.6	52.46	5.08	10.13
7b	186–188	61	$C_{24}H_{28}N_4O_9S$	52.55	5.14	10.21
	melted		548.6	52.43	5.11	10.09
7c	167–169	53	$C_{27}H_{32}N_4O_{11}S$	52.25	5.20	9.03
	melted		620.6	52.19	5.13	8.97
7d	179–181	60	$C_{27}H_{32}N_4O_{11}S$	52.25	5.20	9.03
	melted		620.6	52.16	5.16	8.93
7e	191–193	52	$C_{27}H_{32}N_4O_{11}S$	52.25	5.20	9.03
	melted		620.6	52.20	5.10	9.14
8a	153–155	51	$C_{16}H_{20}N_4O_5S$	50.52	5.30	14.73
	melted		380.4	50.47	5.23	14.56
8b	161–163	53	$C_{16}H_{20}N_4O_5S$	50.52	5.30	14.73
	melted		380.4	50.43	5.19	14.66
8c	141–143	57	$C_{17}H_{22}N_4O_6S$	49.75	5.40	13.65
	melted		410.4	49.67	5.26	13.53
8d	130–133	55	$C_{17}H_{22}N_4O_6S$	49.75	5.40	13.65
	melted		410.4	49.61	5.42	13.49
8e	147–150	57	$C_{17}H_{22}N_4O_6S$	49.75	5.40	13.65
	melted		410.4	49.58	5.37	13.57

temperature for 24 h, poured into water (100 ml), neutralized with hydrochloric acid solution. The solid that separated was filtered, washed with ethanol, dried, and crystallized from the proper solvent to produce **5a–e**, in good yields.

2-(Arabinosylhydrazon)-3,5,6,7,8,9-hexahydro-10-thia-1,3-diaza-benzo[a]azulen-4-one (5a)

From compound **4** (2.50 g, 10 mmol), D-arabinose (1.50 g, 10 mmol). The compound was obtained as a white powder, crystallized from dioxane. IR (KBr) cm^{-1}: 3419 (broad, OH), 3241 (NH), 1685 (C=O). ^{1}H-NMR (DMSO-d_6) ppm: δ 1.59 (m, 4H, $2CH_2$), 1.78 (m, 2H, CH_2), 2.63 (m,

2H, CH_2), 3.24 (m, 2H, CH_2), 3.37 (m, 4OH, D_2O exchangeable, OH-2′, OH-5′), 4.21 (q, 1H, J = 5.8 Hz, H-4′), 4.39 (m, 2H, H-5″), 4.59 (d, 1H, J = 5.2 Hz, H-3′), 5.73 (dd, 1H, J = 6.7 Hz, H-2′), 7.37 (d, 1H, CH methylene) and 10.08–10.45 (brs, NH, D_2O exchangeable).

2-(Xylosylhydrazon)-3,5,6,7,8,9-hexahydro-10-thia-1,3-diaza-benzo[a]azulen-4-one (5b)

From compound **4** (2.50 g, 10 mmol), D-xylose (1.50 g, 10 mmol). The compound was obtained as a white powder, crystallized from dioxane. IR (KBr) cm^{-1}: 3412 (broad, OH), 3219 (NH), 1689 (C=O). ^{1}H-NMR (DMSO-d_6) ppm: δ 1.61 (m, 4H, $2CH_2$), 1.83 (m, 2H, CH_2), 2.65 (m, 2H, CH_2), 3.27 (m, 2H, CH_2), 3.51 (m, 4OH, D_2O exchangeable, OH-2′, OH-5′), 4.23 (q, 1H, J = 6 Hz, H-4′), 4.42 (m, 2H, H-5″), 4.63 (d, 1H, J = 5 Hz, H-3′), 5.79 (dd, 1H, J = 7 Hz, H-2′), 7.39 (d, 1H, CH methylene) and 10.20–10.65 (brs, NH, D_2O exchangeable).

2-(Glucosylhydrazon)-3,5,6,7,8,9-hexahydro-10-thia-1,3-diaza-benzo[a]azulen-4-one (5c)

From compound **4** (2.50, 10 mmol), D-glucose (1.80, 10 mmol). The compound was obtained as a white powder, crystallized from dioxane. IR (KBr) cm^{-1}: 3429 (broad, OH), 3217 (NH), 1686 (C=O). ^{1}H-NMR (DMSO-d_6) ppm: δ 1.60 (m, 4H, $2CH_2$), 1.76 (m, 2H, CH_2), 2.63 (m, 2H, CH_2), 3.23 (m, 2H, CH_2), 3.60 (m, 5H, 5OH, D_2O exchangeable OH-2′-OH-6′), 4.25 (m, 1H, CH, H-3′), 4.35 (m, 2H, CH_2, H2–6′), 4.50 (m, 2H, 2CH, H-3′ and H-4′), 5.20 (dd, 1H, CH, J = 7.5 Hz, H-2′), 7.65 (d, 1H, J = 7.5, H-1′), 11.30 (brs, 1H, NH, D_2O exchangeable) and 11.45 (brs, 1H, NH, D_2O exchangeable).

2-(Galactosylhydrazon)-3,5,6,7,8,9-hexahydro-10-thia-1,3-diaza-benzo[a]azulen-4-one (5d)

From compound **4** (2.50 g, 10 mmol), D-galactose (1.80 g, 10 mmol). The compound was obtained as a white powder, crystallized from dioxane. IR (KBr) cm^{-1}: 3400 (broad, OH), 3249 (NH), 1687 (C=O). ^{1}H-NMR (DMSO-d_6) ppm: δ 1.63 (m, 4H, $2CH_2$), 1.77 (m, 2H, CH_2), 2.62 (m, 2H, CH_2), 3.20 (m, 2H, CH_2), 3.57 (m, 5H, 5OH, D_2O exchangeable OH-2′-OH-6′), 4.23 (m, 1H, CH, H-3′), 4.31 (m, 2H, CH_2, H2–6′), 4.53 (m, 2H, 2CH, H-3′ and H-4′), 5.23 (dd, 1H, CH, J = 7.5 Hz, H-2′), 7.70 (d, 1H, J = 7.5, H-1′), 11.21 (brs, 1H, NH, D_2O exchangeable) and 11.38 (brs, 1H, NH, D_2O exchangeable).

2-(Manosylhydrazon)-3,5,6,7,8,9-hexahydro-10-thia-1,3-diaza-benzo[a]azulen-4-one (5e)

From compound **4** (2.50 g, 10 mmol), D-mannose (1.80 g, 10 mmol). The compound was obtained as a white powder, crystallized from

dioxane. IR (KBr) cm^{-1}: 3406 (broad, OH), 3256 (NH), 1684 (C=O). ^{1}H-NMR (DMSO-d_6) ppm: δ 1.64 (m, 4H, $2CH_2$), 1.79 (m, 2H, CH_2), 2.59 (m, 2H, CH_2), 3.19 (m, 2H, CH_2), 3.49 (m, 5H, 5OH, D_2O exchangeable OH-2′-OH-6′), 4.25 (m, 1H, CH, H-3′), 4.29 (m, 2H, CH_2, H2–6′), 4.50 (m, 2H, 2CH, H-3′ and H-4′), 5.26 (dd, 1H, CH, J = 7.4 Hz, H-2′), 7.67 (d, 1H, J = 7.4, H-1′), 11.23 (brs, 1H, NH, D_2O exchangeable) and 11.41 (brs, 1H, NH, D_2O exchangeable).

3-(O-Acetylglycosyl)-6,7,8,9,10-pentahydro-cyclohepta-thieno[2,3-d][1,2,4]-triazolo[4,3-a]pyrimidin-5-one (7a–e)

General procedure. A solution of compounds **5a–e** (10 mmol) in a mixture of acetic anhydridepyridine (20 ml: 20 ml) was stirred at room temperature for 24 h, poured into water (100 ml). The reaction mixture was then extracted with chloroform several times and after the removel of chloroform under reduced pressure, the formed crystals was recrystallized from the proper solvent to produces **7a–e**, in good yields.

3-(2′,3′,4′,5′-O-tetraacetyl-arabinosyl)-6,7,8,9,10-pentahydro-cyclohepta-thieno[2,3-d][1,2,4]-triazolo-[4,3-a]pyrimidin-5-one (7a)

From compound **5a** (3.82 g, 10 mmol). The compound was obtained as a white powder, crystallized from ethanol. IR (KBr) cm^{-1}: 3231 (NH), 1756–1734 (4 C=O, acetyl) 1687 (C=O, pyrimidone). ^{1}H-NMR ($CDCl_3$) ppm: δ 1.63 (m, 4H, $2CH_2$), 1.79 (m, 2H, $-CH_2$), 1.92 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 2.61 (m, 2H, CH_2), 3.20 (m, 2H, CH_2), 4.40 (m, 2H, H2-4′), 5.20 (m, 1H, H-3′), 5.45 (m, 1H, H-2′), 5.52 (m, 1H, H-1′), 8.75 (brs, NH, D_2O exchangeable).

3-(2′,3′,4′,5′-O-Tetraacetyl-xylosyl)-6,7,8,9,10-pentahydro-cyclohepta-thieno[2,3-d]-[1,2,4]-triazolo[4,3-a]pyrimidin-5-one (7b)

From compound **5b** (3.82 g, 10 mmol). The compound was obtained as a white crystals, crystallized from ethanol. IR (KBr) cm^{-1}: 3220 (NH), 1751–1729 (4 C=O, acetyl) 1681 (C=O, pyrimidone). ^{1}H-NMR ($CDCl_3$) ppm: δ 1.61 (m, 4H, $2CH_2$), 1.76 (m, 2H, $-CH_2$), 1.91 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 2.62 (m, 2H, CH_2), 3.22 (m, 2H, CH_2), 4.41 (m, 2H, H2-4′), 5.23 (m, 1H, H-3′), 5.47 (m, 1H, H-2′), 5.58 (m, 1H, H-1′), 8.92 (brs, NH, D_2O exchangeable).

3-(1′,2′,3′,4′,5′-O-Pentaacetyl-glucosyl)-6,7,8,9,10-pentahydro-cyclohepta-thieno[2,3-d][1,2,4]-triazolo[4,3-a]pyrimidin-5-one (7c)

From compound **5c** (4.12 g, 10 mmol). The compound was obtained as a white powder, crystallized from ethanol. IR (KBr) cm^{-1}: 3208 (NH),

1749–1726 (5 C=O, acetyl) 1689 (C=O, pyrimidone). ^{1}H-NMR ($CDCl_3$) ppm: δ 1.61 (m, 4H, $2CH_2$), 1.78 (m, 2H, CH_2), 1.82 (s, 3H, CH_3), 1.93 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 2.63 (m, 2H, CH_2), 3.23 (m, 2H, CH_2), 4.68 (m, 1H, H-4′), 5.27 (d, 1H, J = 10.6 Hz, H-3′), 5.42 (m, 2H, H2′,5′), 5.63 (s, 1H, H-2′), 5.71 (s, 1H, H-1′), 8.65 (brs, NH, D_2O exchangeable).

3-(1′,2′,3′,4′,5′-O-Pentaacetyl-Galactosyl)-6,7,8,9,10-pentahydro-cyclohepta-thieno[2,3,-d][1,2,4]-triazolo [4,3-a]pyrimidin-5-one (7d)

From compound **5d** (4.12 g, 10 mmol). The compound was obtained as a white powder, crystallized from ethanol. IR (KBr) cm^{-1}: 3225 (NH), 1743–1720 (5 C=O, acetyl) 1683 (C=O, pyrimidone). ^{1}H-NMR ($CDCl_3$) ppm: δ 1.58 (m, 4H, $2CH_2$), 1.76 (m, 2H, CH_2), 1.79 (s, 3H, CH_3), 1.89 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.60 (m, 2H, CH_2), 3.19 (m, 2H, CH_2), 4.64 (m, 1H, H-4′), 5.29 (d, 1H, J = 10.7 Hz, H-3′), 5.45 (m, 2H, H2′,5′), 5.66 (s, 1H, H-2′), 5.73 (s, 1H, H-1′), 8.98 (brs, NH, D_2O exchangeable).

3-(1′,2′,3′,4′,5′-O-Pentaacetyl-manosyl)-6,7,8,9,10-pentahydro-cyclohepta-thieno[2,3-d][1,2,4]-triazolo [4,3-a]pyrimidin-5-one (7e)

From compound **5e** (4.12 g, 10 mmol). The compound was obtained as a white powder, crystallized from ethanol. IR (KBr) cm^{-1}: 3218 (NH), 1747–1723 (5 C=O, acetyl) 1688 (C=O, pyrimidone). ^{1}H-NMR ($CDCl_3$) ppm: δ 1.62 (m, 4H, $2CH_2$), 1.73 (m, 2H, CH_2), 1.80 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 2.61 (m, 2H, CH_2), 3.21 (m, 2H, CH_2), 4.70 (m, 1H, H-4′), 5.31 (d, 1H, J = 10.4 Hz, H-3′), 5.43 (m, 2H, H2′,5′), 5.65 (s, 1H, H-2′), 5.71 (s, 1H, H-1′), 9.51 (brs, NH, D_2O exchangeable).

3-(Glycosyl)-6,7,8,9,10-pentahydro-cycloheptathieno-[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one (8a–e)

General procedure. A solution of compounds **7a–e** (10 mmol) in methanolic ammonia solution (25%, 50 ml), was stirred at room temperature for 24 h, then neutralized with hydrochloric acid solution (under pH control). The excess of methanol was removed under reduced pressure, whereby a solid was precipitated. The precipitate so-formed was filtered off, was with cold water dried and recrystallized from the proper solvent to produces the compounds **8a–e**, in good yield.

3-Arabinosyl-6,7,8,9,10-pentahydro-cycloheptathieno-[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one (8a)

From compound **7a** (2.74 g, 5 mmol). The compound was obtained as a white powder, crystallized from ethanol. IR (KBr) cm^{-1}: 3445–3465

(broads band OH), 3229 (NH), 1684 (C=O, pyrimidone). ^{1}H-NMR ($CDCl_3$) ppm: δ 1.62 (m, 4H, $2CH_2$), 1.76 (m, 2H, CH_2), 2.64 (m, 2H, CH_2), 4.45 (m, 4H, 4OH, D_2O exchangeable, OH-1′, OH-4′), 4.65 (m, 1H, H-3′), 4.90 (m, 2H, H2-4′), 5.10 (m, 1H, H-2′) and 9.32 (brs, NH, D_2O exchangeable).

3-Xylosy-6,7,8,9,10-Pentahydro-cyclohepta-thieno-[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one (8b)

From compound **7b** (2.74 g, 5 mmol). The compound was obtained as a white powder, crystallized from ethanol. IR (KBr) cm^{-1}: 3436–3468 (broads band OH), 3203 (NH), 1685 (C=O, pyrimidone). ^{1}H-NMR ($CDCl_3$) ppm: δ 1.63 (m, 4H, $2CH_2$), 1.75 (m, 2H, CH_2), 2.65 (m, 2H, CH_2), 4.43 (m, 4H, 4OH, D_2O exchangeable, OH-1′, OH-4′), 4.67 (m, 1H, H-3′), 4.88 (m, 2H, H2–4′), 5.12 (m, 1H, H-2′) and 9.20 (brs, NH, D_2O exchangeable); ^{13}C-NMR ($CDCl_3$) ppm: δ 23.5, 25.2, 27.3, 28.2, 30.4, and 31.65 (6C, $6CH_2$), 61.3, 67.4 and 71.3 (3C, 3CHOH), 113.1, 128.0, 130.6, 139.1, 147.8, and 151.6 (6C, thienopyrimidine and triazole carbons) and 159.7 (C=O, pyrimidone).

3-Glucosyl-6,7,8,9,10-pentahydro-cycloheptathieno-[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one (8c)

From compoud **7c** (3.10 g, 5 mmol). The compound was obtained as a white crystals, crystallized from ethanol. IR (KBr) cm^{-1}: 3440–3460 (broads band OH), 3265 (NH), 1689 (C=O, pyrimidone). ^{1}H-NMR ($CDCl_3$) ppm: δ 1.63 (m, 4H, $2CH_2$), 1.79 (m, 2H, CH_2), 2.61 (m, 2H, CH_2), 3.12 (m, 5H, 5OH, D_2O exchangeable), 3.23 (m, 2H, CH_2), 3.38 (m, 1H, H-3′), 3.67 (m, 2H, H-5′, H-5″), 4.28 (m, 1H, H-2′), 4.63 (m, 1H, H-1′), 9.25 (brs, NH, D_2O exchangeable).

3-Galactosyl-6,7,8,9,10-pentahydro-cycloheptathieno-[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one (8d)

From compound **7d** (3.10 g, 5 mmol). The compound was obtained as a white powder, crystallized from ethanol. IR (KBr) cm^{-1}: 3435–3456 (broads band OH), 3260 (NH), 1686 (C=O, pyrimidone). ^{1}H-NMR ($CDCl_3$) ppm: δ 1.58 (m, 4H, $2CH_2$), 1.74 (m, 2H, CH_2), 2.59 (m, 2H, CH_2), 3.11 (m, 5H, 5OH, D_2O exchangeable), 3.25 (m, 2H, CH_2), 3.40 (m, 1H, H-3′), 3.71 (m, 2H, H-5′, H-5″), 4.31 (m, 1H, H-2′), 4.62 (m, 1H, H-1′), 9.51 (brs, NH, D_2O exchangeable).

3-Manosyl-6,7,8,9,10-pentahydro-cycloheptathieno-[2,3-d][1,2,4]triazolo[4,3-a]pyrimidin-5-one (8e)

From compound **7e** (3.10 g, 5 mmol). The compound was obtained as a white powder, crystallized from ethanol. IR (KBr) cm^{-1}: 3429–3456

(broads band OH), 3239 (NH), 1682 (C=O, pyrimidone). ^{1}H-NMR ($CDCl_3$) ppm: δ 1.60 (m, 4H, $2CH_2$), 1.77 (m, 2H, CH_2), 2.62 (m, 2H, CH_2), 3.13 (m, 5H, 5OH, D_2O exchangeable), 3.27 (m, 2H, CH_2), 3.42 (m, 1H, H-3′), 3.76 (m, 2H, H-5′, H-5′′), 4.31 (m, 1H, H-2′), 4.67 (m, 1H, H-1′), 9.37 (brs, NH, D_2O exchangeable).

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