A new direct synthetic access to 4-amino-2-*N*-(glycosyl/propyl)-1,2,4-triazole-3-thiones *via* hydrazinolysis of 3-*N*-((acylated glycosyl)/allyl)-1,3,4-oxadiazole-2-thiones

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Abstract

Hydrazinolysis of 3-*N*-alkyl-1,3,4-oxadiazole-2-thiones yielded 2-*N*-alkyl-4-amino-1,2,4-triazole-2-thiones in a straightforward new direct procedure. Whereas, hydrazinolysis of alkylsulfanyl-1,3,4-oxadiazole derivatives resulted in the opening of the oxadiazole ring and loss of the alkyl moiety, instead of a nucleophilic substitution at the electrophilic carbon or triazole formation. Thio-aza-Claisen rearrangement of the allyl moiety in 4-amino-1,2,4-triazole was successfully achieved by fusion at atmospheric pressure in the absence of solvents and catalysts.

Keywords: Hydrazinolysis, 1,3,4-oxadiazole-2-thione, 1,2,4-triazolethione, thio-aza-Claisen rearrangement

Introduction

4-Amino-1,2,4-triazole-3-thiones and their derivatives display a wide spectrum of biological activities. They show antimicrobial,[1-7] antiproliferative,[8] antituberculosis,[9-11] anticonvulsant,[12] analgesic,[13] anti-inflammatory,[14] antitumor[15] and antidepressant[16] activities in addition to their inhibitory activity of *trans*-cinnamate 4-hydroxylase[17] and urease[18] enzymes. On this basis, searching for the synthesis of new 4-amino-1,2,4-triazole-thione derivatives is justified.

It is well known that reaction of hydrazine hydrate with 1,3,4-oxadiazolethione **IV** in ethanol gives 4-amino-1,2,4-triazole-thione **I**.[1-13] We wondered what would happen in its reaction with *S*-alkylated 1,3,4-oxadiazoles **V** and *N*-alkylated 1,3,4-oxadiazole-thiones **VI**. We doubted the report[19] that reaction of **V** with hydrazine hydrate leads to replacement of *S*-alkyl with a hydrazino group without breakdown of the oxadiazole moiety. Others suggested that it will lead to formation of 4-amino-1,2,4-triazole **II**.[20] To the best of our knowledge, reaction of *N*-alkylated 1,3,4-oxadiazole-thiones **VI** with hydrazine hydrate to form **III** has not been discussed previously (**Figure 1**).

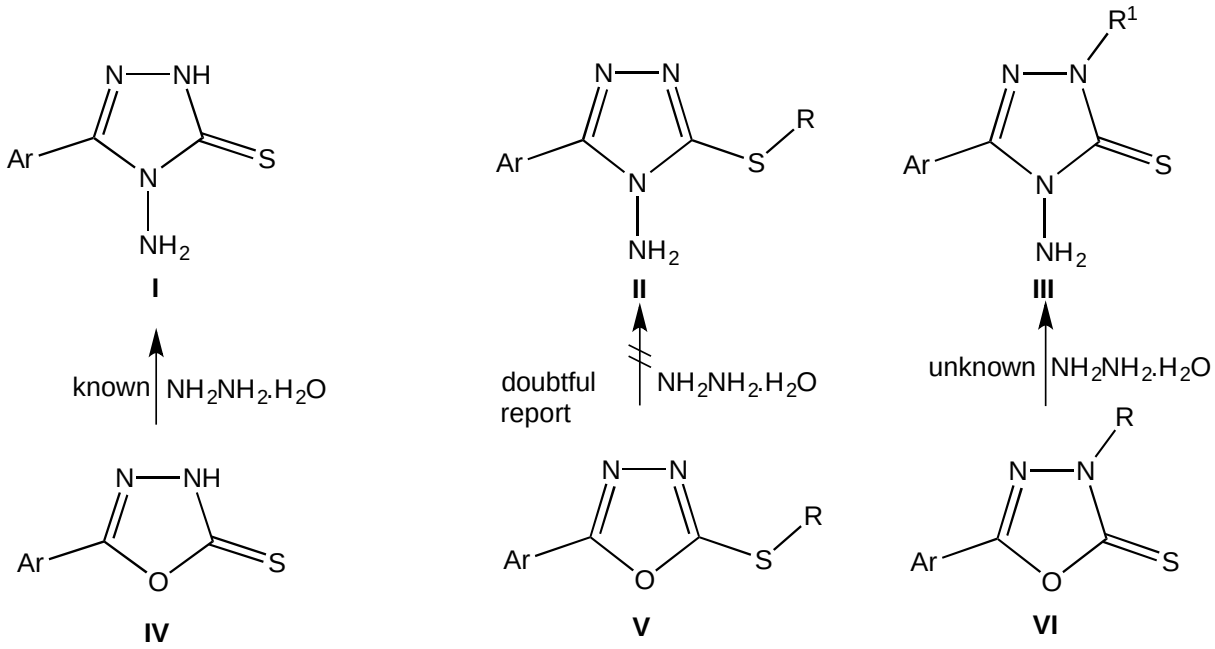


Figure 1. Formation of 4-Amino-1,2,4-triazoles from 1,3,4-oxadiazoles.

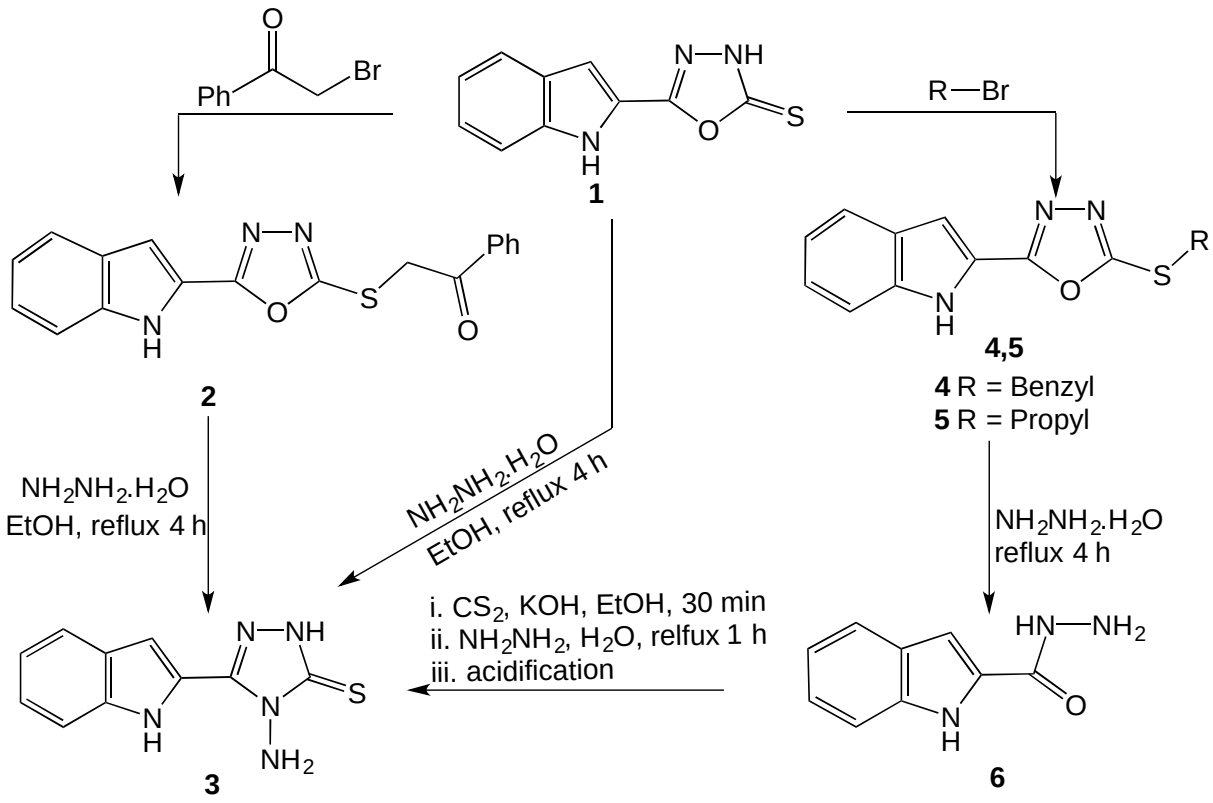
In summary, our present study shows that: (a) hydrazinolysis of *S*-alkylated 1,3,4-oxadiazoles leads to opening of the oxadiazole ring and loss of the alkyl moiety (b) hydrazinolysis of 3-*N*-alkylated 1,3,4-oxadiazolethiones produces 2-*N*-alkyl-4-amino-1,2,-triazolethiones (c) the possibility of allyl migration from sulfur to nitrogen in an aminotriazole without solvent and catalyst at atmospheric pressure.

Results and Discussion

Herein, we intended to study the reactivity of some previously reported *S*-alkylated 1,3,4-oxadiazoles and *N*-alkylated 1,3,4-oxadiazole-thiones[21, 22] with hydrazine giving the possibility of obtainined 4-amino-1,2,4-triazoles from 1,3,4-oxadiazole derivatives.

Hydrazinolysis of oxadiazolethione 1 and some S-alkylated oxadiazoles

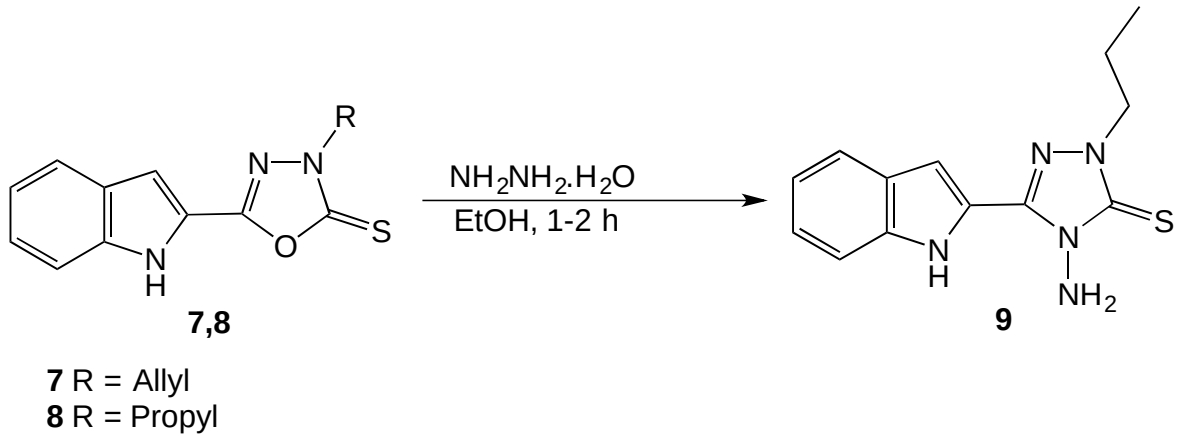
Hydrazinolysis of oxadiazolethione **1** and *S*-phenacylated 1,3,4-oxadiazole **2** in ethanol afforded 4-amino-triazole **3** in a high yield from **1** and low yield from **2**. Whereas, *S*-benzylated/propylated 1,3,4-oxadiazoles **4**, **5** did not react in ethanol solution and in the absence of ethanol, reaction with hydrazine led to the opening of the oxadiazole ring and loss of the alkyl moiety to yield indole-2-carbohydrazide **6**. 4-Amino-triazole **3** was obtained from hydrazide **6** by reflux with CS_2 in ethanol containing aq. KOH followed by addition of $NH_2NH_2.H_2O$ and acidification (Scheme 1).



Scheme 1. Behavior of the parent 1,3,4-oxadiazolethione **1** and some of its S-alkylated derivatives towards hydrazine hydrate

Hydrazinolysis of N-alkylated products

On the other hand, stirring *N*-allylated oxadiazole-thione **7** with hydrazine hydrate in ethanol afforded **9**, in which the oxadiazole-thione had been converted into 4-amino-1,2,4-triazole-3-thione and the allyl side chain had been reduced to propyl. The same product **9** was obtained from hydrazinolysis of *N*-propylated oxadiazolethione **8** (Scheme 2). The literature reports that reduction of olefins by the action of hydrazine needs special conditions such as the presence of Fe_3O_4 nanoparticles as catalyst,[23] so it is significant in the present case that reduction occurred with hydrazine only in the absence of any catalyst.

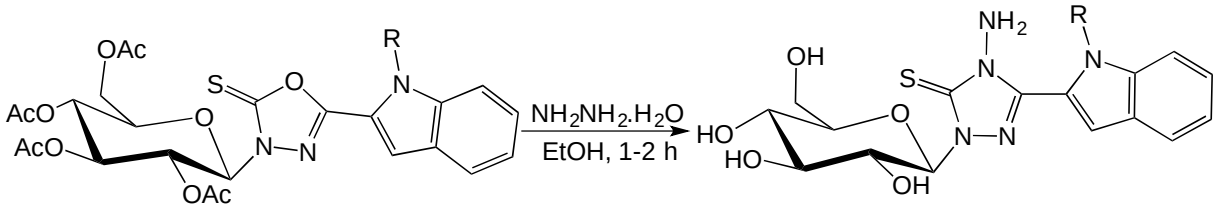


7,8 **9**

7 R = Allyl
8 R = Propyl

Scheme 2. Hydrazinolysis of 3-*N*-allyl/propyl-1,3,4-oxadiazoles.

Reaction of protected glycosyl-1,3,4-oxadiazole-thiones **10**,**11** with hydrazine in ethanol led to the deacetylation of the sugar moiety and conversion of the oxadiazole to triazoles **12**, **13** (Scheme 3).



10,11 **12,13**

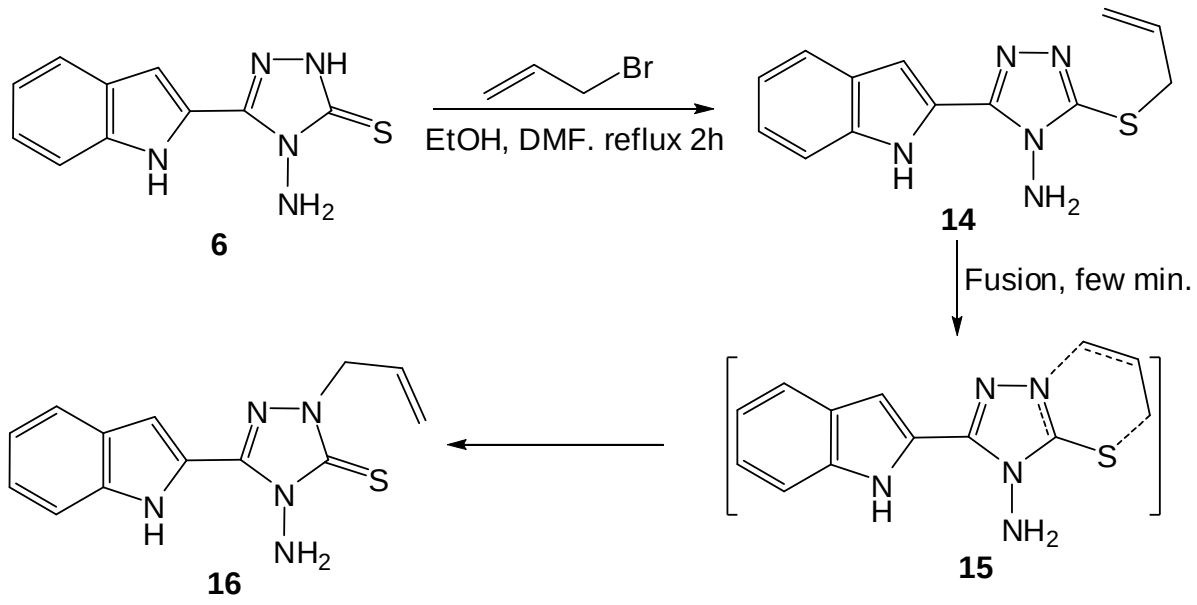
10,12 R = H
11,13 R = -CH_2Ph

Scheme 3. Hydrazinolysis of 3-*N*-acylated glycosyl-1,3,4-oxadiazolethiones.

Allylation of the aminotriazolethione

Reaction of 4-amino-1,2,4-triazolethione **3** with allyl bromide in ethanol containing some DMF and K_2CO_3, afforded regioselectively the S-allylated product **14**.

In a new investigation into thio-aza-Claisen rearrangement with simple procedures, allylsulfanyl-4-amino-1,2,4-triazole **14** was fused for a few minutes in the absence of either solvent or catalyst and afforded the corresponding N-allylated analogue **16**. We assume that the mechanism involves an intramolecular [3,3]-sigmatropic migration of the allyl moiety via a six-membered cyclic transition state **15**, with a concerted six-electron reorganization (Scheme 4). It was previously reported that the migration of the allyl moiety from the exocyclic sulfur to triazole nitrogen needs vacuum pyrolysis at 750-850 ^{o}C (10^{-2}-10^{-3} Torr).[24]



Scheme 4. *S*- and *N*-allylation of 4-amino-1,2,4-triazolethione.

Structure confirmation

^{1}H NMR spectra of all compounds showed signals for the indole CH protons between 7.0-7.70 ppm and the indole NH proton around 11.60 ppm. All indole ^{13}C signals appeared between 101.0-138.0 ppm.

Significant analytical data used for characterization of the individual products in Schemes 1 and 2

The ^{1}H NMR spectra of the aminotriazole **3** showed the protons of the amino group at 5.91 ppm and triazole NH 13.95 ppm. The two triazole carbon signals appeared at 144.3 and 166.5 ppm which strongly suggest the thione form.

The structure of **6** was confirmed from ^{1}H NMR by displaying signals at 4.48 and 9.76 ppm, which are characteristic for -CONHNH$_2$. ^{13}C NMR showed a signal at 161.1 ppm for the carbonyl carbon.

The ^{1}H NMR of the **9** showed three signals as triplet, multiplet and triplet at 0.92, 1.83-1.87 and 4.16 ppm characteristic for the propyl group (CH_3-CH_2-CH_2-$N_{Triazol}$). A signal at 5.99 ppm corresponded to the amino group. The propyl carbon signals appeared at 10.88, 21.12 and 50.48 ppm for (CH_3-CH_2-CH_2-$N_{Triazol}$). The two triazole carbon signals appeared at 143.41 and 165.98 ppm. Electron spray ionization (ESI$^-$) displayed an M-1 peak at *m/z* 292.0970, confirming conversion of the oxadiazole ring into a 4-aminotriazole and the allyl side-chain to propyl.

Significant analytical data used for characterization of the individual products in Scheme 3

The deacetylation of all acetate groups of the acetyl-protected β-glycosides **10**,**11** by the action of hydrazine hydrate was obvious from the absence of acetyl (CH_3C=O) signals in ^{1}H NMR and

^{13}C NMR spectra of **12**,**13**. The spectra in DMSO-d_6 + D_2O showed the anomeric protons at 5.66 and 5.64 ppm with coupling constants ≈ 9.0 Hz. The respective anomeric carbons appeared at 85.4 and 85.24 ppm. The two triazole carbons gave signals at 143.3 and 168.66 ppm indicating conversion of the oxadiazolethione into a 4-aminotriazolethione along with the deprotection of sugar moieties, retaining the β-configuration of the sugar unit.

Significant analytical data used for characterization of the individual products in Scheme 4
The structures of the *S*-allylated triazole **14** and the corresponding *N*-allylated analog **16** were confirmed by the signals arising from the allyl group. The ^{1}H NMR spectrum of **14** showed the SCH_2 as doublet at 3.84 ppm, the olefinic (=CH_2) as two doublets at 5.11 and 5.30 with coupling constants of 10.2 and 16.8 Hz and the olefinic (CH=) as multiplet between 5.95-6.04 ppm. The allyl carbons appeared at 34.04, 118.40 and 133.58 ppm and the two triazole carbon signals at 149.27, 152.49 ppm. Following migration of the ally group to nitrogen, the ^{1}H NMR spectra showed -NCH_2 as doublet at 4.84 and the olefinic (=CH_2) as multiplet between 5.31-5.36 ppm and remaining olefinic (-CH=) as multiplet at 5.95-6.03 ppm. ^{13}C NMR spectrum showed the three allylic carbons at 52.18, 119.65 and 130.45 ppm. The two triazole carbons in **16** appeared at 143.44 and 166.90 ppm. The above data confirms that the allyl group in **14** has been transferred from sulfur to nitrogen in **16**.

Conclusions

In conclusion, reaction of *S*-alkylated-1,3,4-oxadiazole with hydrazine hydrate leads mostly to oxadiazole ring-opening and formation of the hydrazide. On the other hand, reaction of 3-*N*-allyl/protected glycosyl-1,3,4-oxadiazole-thiones with hydrazine hydrate in the presence of ethanol converts the 1,3,4-oxadiazole-thione to 4-amino-1,2,4-triazole-thione and either leads to the reduction of the side-chain as in **9** or induces a deacetylation of an acetyl-protected sugar moiety that hereby maintains its configuration as in **12**,**13**.

Experimental Section

General. Melting points were measured with a Stuart melting-point apparatus (SMP10) in open capillaries and are uncorrected. Flash chromatography was carried out on silica gel 60 (230-400 mesh ASTM). TLC was performed on Merck silica gel 60 F_{254} and spots were detected by absorption of UV light. ^{1}H NMR spectra were done on Bruker Avance NMR spectrometer at 300-600 MHz, whereas ^{13}C NMR spectra were recorded on the same instrument at 75-125 MHz, with TMS as internal standard. Mass spectra were obtained using Finnigan MAT312 and a Jeol JMS.600H for EIMS; HRMS spectra were recorded on a Thermo Finnigan MAT 95XP and Jeol JMS HX110 and ESI mass spectra on a Finnigan ThermoQuest TSQ 7000.

Known compounds 1, **2**, **4**, **5**, **7**, **8**, **10** and **11** used in the study were synthesized following the procedures reported in the literature,[21,22] the melting points and R_f values were compared with references.

4-Amino-5-(1*H*-indol-2-yl)-1,2,4-triazol-3(2*H*)-thione (3)

Method A. A solution of 5-(1*H*-indol-2-yl)-1,3,4-oxadiazole-2(3*H*)-thione **1** or 2-phenacyl-5-(1*H*-indol-2-yl)-1,3,4-oxadiazole **5** (1.0 mmol) and hydrazine hydrate (2 mL) was refluxed in EtOH for 4 h. The unreacted hydrazine was carefully removed using the rotary evaporator, the solution was acidified using dilute HCl and the solid product was crystallized from EtOH.

Method B. 1*H*-Indole-2-carbohydrazide **6** (1.0 mmol) and carbon disulfide (1 mL) were stirred with alcoholic KOH under a gentle reflux for 30 min. Then, hydrazine hydrate (1.0 mL) was added and reflux was continued for 1 hour. After cooling, the solution was acidified with concentrated HCl. The precipitate formed was collected by filtration and crystallized from EtOH. Yield: $75_{\text{from }\mathbf{1}}$, $15_{\text{from }\mathbf{2}}$ %*method A*, 80%*method B* as colorless stick crystals (EtOH). Mp. 293-294 ^{o}C, TLC (EtOAc/*n*-hexane 1:1): R_f 0.59; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 5.91 (s, 2 H, NH_2), 7.05 (dd, 1 H, $J_{4,5}$ 8.0, $J_{5,6}$ 7.2 Hz, H-5_{Indol}), 7.19 (dd, 1H, $J_{5,6}$ 7.2, $J_{6,7}$ 8.3 Hz, H-6_{Indol}), 7.43 (d, 1 H, *J* 1.4 Hz, H-3_{Indol}), 7.45 (d, 1 H, $J_{6,7}$ 8.3 Hz, H-7_{Indol}), 7.64 (d, 1H, $J_{4,5}$ 8.0 Hz, H-4_{Indol}), 11.72 (br. s, 1H, NH_{Indol}), 13.95 (br. s, H, NH_{Triazol}); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 104.64 (C-3_{Indol}), 111.90 (C-7_{Indol}), 119.77 (C-5_{Indol}), 121.06 (C-4_{Indol}), 122.71 (C-2_{Indol}), 123.39 (C-6_{Indol}), 127.17 (C-$3a_{\text{Indol}}$), 136.66 (C-$7a_{\text{Indol}}$), 144.32 (C-5_{Triazol}), 166.50 (C=S); LRMS (EI) *m/z* (Int. %):59.9 (41.8), 63.0 (17.9), 89.1 (44.8), 90.1 (24.2), 114.0 (19.8), 115.0 (35.3), 116.0 (26.8), 131.0 (55.3), 142.1 (83.7), 143.1 (100), 160.0 (16.2), 231.0 (78.48). (HRMS (EI) calcd for $C_{10}H_9N_5S$ [M^+]: 231.0579. Found: 231.0572.

1*H*-Indole-2-carbohydrazide (6). A mixture of 2-(benzyl/propylsulfanyl)-5-(1*H*-indol-2-yl)-1,3,4-oxadiazole **4**, **5** (1.0 mmol) and hydrazine hydrate (2 mL) was heated under reflux for 4 h. The unreacted hydrazine was carefully removed using the rotary evaporator and the solid product was crystallized from EtOH. Yield: $40_{\text{from }\mathbf{4}}$, $45_{\text{from }\mathbf{5}}$ % as colorless crystalline scales (EtOH). mp 247-248 ^{o}C lit.[25] TLC (9:1 CH_2Cl_2/MeOH): R_f 0.43. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 4.48 (d, 2 H, *J* 3.3 Hz, NH_2, D_2O exchangeable), 7.01 (dd, 1 H, $J_{5,6}$ 7.4, $J_{4,5}$ 8.0 Hz, H-5_{Indol}), 7.06 (s, 1 H, H-3_{Indol}), 7.15 (dd, 1 H, $J_{5,6}$ 7.4, $J_{6,7}$ 8.2 Hz, H-6_{Indol}), 7.40 (d, 1 H, $J_{6,7}$ 8.2 Hz, H-7_{Indol}), 7.57 (d, 1 H, $J_{4,5}$ 8.0 Hz, H-4_{Indol}), 9.76 (s, 1 H, NH, D_2O exchangeable), 11.59 (s, 1 H, NH_{Indol}, D_2O exchangeable). ^{13}C NMR (DMSO-d_6, 125 MHz): δ 101.8 (C-3_{Indol}), 112.2 (C-7_{Indol}), 119.6 (C-5_{Indol}), 121.3 (C-4_{Indol}), 123.0 (C-6_{Indol}), 127.0, 130.4, 136.3 (C-2_{Indol}, C-$3a_{\text{Indol}}$, C-$7a_{\text{Indol}}$), 161.1 (C=O). LRMS (EI) *m/z* (Int. %): 63 (33.2), 89.1 (100), 116 (75.4), 144.1 (99.9), 160.1 (17.9), 175.1 (97.8).

Hydrazinolysis of 3-*N*-Alkyl-1,3,4-oxadiazolethiones 7,8 and **10,11.** A solution of 3-*N*-Alkyl-5-(1*H*-indol-2-yl)-1,3,4-oxadiazole-2-thiones **7,8** and **10,11** (1.0 mmol)] and hydrazine hydrate (1 mmol) in EtOH (5 mL) was stirred for 1-2 hours while the reaction progress was monitored by TLC. The solvent and unreacted hydrazine hydrate were carefully removed using the rotary evaporator and the solid product was crystallized from EtOH (**9**,**13**). While, **12** was purified by silica column chromatography using MeOH and CH_2Cl_2 (1:9) as eluent mixture.

4-Amino-5-(1*H*-indol-2-yl)-2-(1-propyl)-1,2,4-triazole-3-thione (9). Yield: 70% as colorless needles (EtOH). mp 147-148 °C, TLC (EtOAc/*n*-hexane 2:8): R_f 0.35,^{1}H NMR (DMSO-d_6, 600 MHz) δ 0.92 (t, 3 H, *J* 7.5 Hz, CH_3), 1.83-1.87 (m, 2 H, CH_2), 4.16 (t, 2 H, *J* 6.9 Hz, NCH_2), 5.99 (s, 2 H, NH_2), 7.05 (dd, 1 H, $J_{4,5}$ 7.8, $J_{5,6}$ 7.2 Hz, H-5_{Indol}), 7.20 (dd, 1 H, $J_{5,6}$ 7.2, $J_{6,7}$ 8.4 Hz, H-6_{Indol}), 7.46 (s, 1 H, H-3_{Indol}), 7.48 (d, 1 H, $J_{6,7}$ 8.4 Hz, H-7_{Indol}), 7.64 (d, 1H, $J_{4,5}$ 7.8 Hz, H-4_{Indol}), 11.74 (s, 1 H, NH_{Indol}); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 10.88 (CH_3), 21.13 (CH_2), 50.48 (NCH_2), 105.24 (C-3_{Indol}), 112.05 (C-7_{Indol}), 119.88 (C-5_{Indol}), 121.15 (C-4_{ndol}), 122.26 (C-2_{Indol}),123.56 (C-6_{Indol}), 127.15 (C-$3a_{Indol}$), 136.79 (C-$7a_{Indol}$), 143.41 (C-$5_{Triazol}$), 165.98 (C=S); HRMS (-ESI): *m/z* calcd for $C_{13}H_{14}N_5S$ [M^-] 272.0970, found 272.0979.

4-Amino-2-β-D-glucopyranosyl-5-(1*H*-indol-2-yl)-1,2,4-1,2,4-triazole-3-thione (12). Yield: 55% as a white solid (MeOH, DCM). mp 268-269 °C, TLC (MeOH/DCM 1:9):R_f 0.13,^{1}H NMR (DMSO-d_6 + D_2O, 600 MHz) δ 3.20 (dd, 1 H, $J_{3,4}$ 9.0, $J_{4,5}$ 9.6 Hz, H-4_{Glc}), 3.33-3.36 (m, 1 H, H-5_{Glc}), 3.39 (dd, 1 H, $J_{2,3} \approx J_{3,4}$ 9.0 Hz, H-3_{Glc}), 3.45 (dd, 1 H, $J_{5,6}$ 6, $J_{6,6'}$ 12 Hz, H-6_{Glc}), 3.68 (dd, 1 H, $J_{5,6'}$ 1.8, $J_{6,6'}$ 12 Hz, H-6′$_{Glc}$), 3.95 (dd, 1 H, $J_{1,2} \approx J_{2,3}$ 9.0 Hz, H-2_{Glc}), 5.66 (d, 1 H, $J_{1,2}$ 9.0 Hz, H-1_{Glc}), 7.06 (dd, 1 H, $J_{4,5}$ 8.4, $J_{5,6}$ 7.2 Hz, H-5_{Indol}), 7.21 (dd, 1 H, $J_{5,6}$ 7.2, $J_{6,7}$ 7.8 Hz, H-6_{Indol}), 7.47-7.49 (m, 2 H, H-3_{Indol}, H-7_{Indol}), 7.65 (d, 1H, $J_{4,5}$ 8.4 Hz, H-4_{Indol}); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 60.75 (C-6_{Glc}), 69.71 (C-4_{Glc}),, 70.63 (C-3_{Glc}), 77.20 (C-2_{Glc}), 79.98 (C-5_{Glc}), 85.4 (C-1_{Glc}), 105.72 (C-3_{Indol}), 112.11 (C-7_{Indol}), 119.89 (C-2_{Indol}), 121.22 (C-4_{ndol}), 122.11 (C-5_{Indol}), 123.65 (C-6_{Indol}), 127.14 (C-$3a_{Indol}$), 136.90 (C-$7a_{Indol}$), 143.70 (C-$5_{Triazol}$), 168.66 (C=S); HRMS (+ESI): *m/z* calcd for $C_{16}H_{20}N_5O_5S$ [M^+] 394.1185, found 394.1181.

4-Amino-2-β-D-glucopyranosyl-5-(1-benzylindol-2-yl)-1,2,4-1,2,4-triazole-3-thione (13). Yield: 80% as colorless needles (MeOH, DCM). mp 225-226 °C, TLC (MeOH/DCM 1.5:8.5):R_f 0.57,^{1}H NMR (DMSO-d_6 + D_2O, 600 MHz) δ 3.12 (dd, 1 H, $J_{3,4}$ 9.0, $J_{4,5}$ 9.6 Hz, H-4_{Glc}), 3.30-3.41 (m, 3 H, H-3_{Glc}, H-5_{Glc}, H-6_{Glc}), 3.68 (dd, 1 H, $J_{5,6'}$ 1.8, $J_{6,6'}$ 12 Hz, H-6′$_{Glc}$), 3.81 (dd, 1 H, $J_{1,2} \approx J_{2,3}$ 9.0 Hz, H-2_{Glc}), 5.64 (d, 1 H, $J_{1,2}$ 9.0 Hz, H-1_{Glc}), 5.70-5.80 (2d, 2 H, *J* 16.2, *J* 16.8 Hz, CH_2Ph), 7.09-7.21 (m, 6 H, H-5_{Indol}, $5H_{Ph}$), 7.26 (dd, 1 H, $J_{5,6}$ 7.2, $J_{6,7}$ 7.8 Hz, H-6_{Indol}), 7.56-7.57 (m, 2 H, H-3_{Indol}, H-7_{Indol}), 7.70 (d, 1H, $J_{4,5}$ 7.8 Hz, H-4_{Indol}); ^{13}C NMR (DMSO-d_6, 150 MHz) δ 47.65 (CH_2Ph), 60.88 (C-6_{Glc}), 69.73, 70.51 (C-3_{Glc}, 70.63 (C-4_{Glc}), 77.05 (C-2_{Glc}), 79.88 (C-5_{Glc}), 85.24 (C-1_{Glc}), 108.30 (C-3_{Indol}), 111.17 (C-7_{Indol}), 120.44 (C-2_{Indol}), 121.56 (C-4_{ndol}), 122.97 (C-5_{Indol}), 124.00 (C-6_{Indol}), 126.53 (C-$3a_{Indol}$), 127.05, 128.33 ($5CH_{Ph}$), 138.01, 138.20 (C-$7a_{Indol}$, C_{Ph}), 143.00 (C-$5_{Triazol}$), 168.32 (C=S); HRMS (+ESI): *m/z* calcd for $C_{23}H_{26}N_5O_5S$ [M^+] 484.1655, found 484.1651.

3-Allylsulfanyl-4-amino-5-(1*H*-indol-2-yl)-1,2,4-triazole (14). A mixture of 4-amino-5-(1*H*-indol-2-yl)-1,2,4-triazol-3(2*H*)-thione **8** (1.0 mmol), allyl bromide (1.1 mmol) and K_2CO_3 (1.1 mmol) in EtOH (10 mL + drops of DMF) was refluxed for 2 h. The solvent was removed using a rotator evaporator; the formed solid was recrystallized from EtOH to give colorless shining crystals. Yield: 65%, mp 234-236 °C, TLC (EtOAc/*n*-hexane 6:4): R_f 0.44, ^{1}H NMR (DMSO-d_6, 300 MHz) δ 3.84 (d, 2 H, *J* 6.9 Hz, SCH_2-CH=CH_2), 5.11 (d, 1 H, J_{cis} 10.2 Hz, SCH_2-CH=C*H*H), 5.30 (d, 1 H, J_{trans} 16.8 Hz, CH=CH*H*), 5.95-6.04 (m, 1 H, SCH_2-C*H*=CH_2), 6.22 (s, 2 H, NH_2), 7.03 (dd, 1H, $J_{4,5}$ 7.8, $J_{5,6}$ 7.2 Hz, H-5_{Indol}), 7.16 (dd, 1H, $J_{5,6}$ 7.2, $J_{6,7}$ 8.1 Hz, H-6_{Indol}),

7.29 (s, 1 H, H-3_{Indol}), 7.45 (d, 1H, $J_{6,7}$ 8.1 Hz, H-7_{Indol}), 7.61 (d, 1H, $J_{4,5}$ 7.8 Hz, H-4_{Indol}), 11.73 (br. s, 1H, NH_{Indol}); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 34.04 (SCH_2), 102.36 (C-3_{Indol}), 111.86 (C-7_{Indol}), 118.40 (CH=*C*H_2), 119.60 (C-5_{Indol}), 120.75 (C-4_{Indol}), 122.81 (C-6_{Indol}), 124.03 (C-2_{Indol}), 127.60 (C-$3a_{Indol}$), 133.58 (*C*H=CH_2), 136.50 (C-$7a_{Indol}$), 149.27 (C-$5_{Triazol}$), 152.49 (C-$3_{Triazol}$); LRMS (EI) *m/z* (Int. %): 89.1 (14.8), 90.1 (10.1), 115.1 (19.5), 116.2), 15.9), 131.2 (10.7), 142.2 (79.0), 143.2 (86.9), 216.2 (100), 217.2 (19.3), 255.3 (21.3), 271.3 (66.8), 272.3 (15.6). HRMS (EI) calcd for $C_{13}H_{13}N_5S$ [M^+]: 271.0892. Found: 271.0894.

2-Allyl-4-Amino-5-(1*H*-indol-2-yl)-1,2,4-triazole-3(2*H*)thione (16). 3-Allylsulfanyl-4-amino-5-(1*H*-indol-2-yl)-1,2,4-triazole **14** was fused for few minutes until all reactants were consumed (TLC). Then, crystallization from EtOH gave colorless sunny crystals. Yield: 30%, mp 142-144 ^{o}C, TLC (EtOAc/*n*-hexane 3:7): R_f 0.61,^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.85 (d, 2 H, *J* 5.6 Hz, NC*H*$_2$-CH=CH_2), 4.95 (s, 2 H, NH_2), 5.31-5.36 (m, 2 H, NCH_2-CH=C*H*$_2$), 5.96-6.03 (m, 1 H, NCH_2-C*H*=CH_2), 7.15 (dd, 1H, $J_{4,5}$ 8.0, $J_{5,6}$ 7.2 Hz, H-5_{Indol}), 7.28 (dd, 1H, $J_{5,6}$ 7.2, $J_{6,7}$ 8.0 Hz, H-6_{Indol}), 7.40 (d, 1H, $J_{6,7}$ 8.0 Hz, H-7_{Indol}), 7.46 (s, 1 H, H-3_{Indol}), 7.67 (d, 1H, $J_{4,5}$ 8.0 Hz, H-4_{Indol}), 9.47 (br. s, 1H, NH_{Indol}); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 52.18 (NCH_2), 105.98 (C-3_{Indol}), 111.42 (C-7_{Indol}), 119.65 (CH=*C*H_2), 120.91 (C-5_{Indol}), 121.83 (C-4_{Indol}), 122.07 (C-2_{Indol}), 124.67 (C-6_{Indol}), 127.66 (C-$3a_{Indol}$), 130.45 (*C*H=CH_2), 136.35 (C-$7a_{Indol}$), 143.44 (C-$5_{Triazol}$), 166.90 (C=S);LRMS (EI) *m/z* (Int. %):56.0 (68.7), 83.0 (49.3), 85.0 (33.2), 90.0 (15.0), 102 (17.6), 114.0 (14.1), 115.0 (26.0), 116 (17.2), 142.0 (90.3), 143.0 (52.1), 216.0 (13.7), 255.0 (24.2), 256.0 (13.2), 271.0 (100), 272.0 (18.8). HRMS (EI) calcd for $C_{13}H_{13}N_5S$ [M^+]: 271.0892. Found: 271.0888

Electronic supplementary material

Compound characterization spectra

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