Unusual reactivity of thiosemicarbazides towards 2,3-diphenylcyclopropenone: synthesis of new pyridazinethiones and 1,2,4-triazolo[4,3-*b*]pyridazinethiones

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Abstract

New pyridazinethiones and 1,2,4-triazolo[4,3-*b*]pyridazinethiones have been obtained during the reaction of thiosemicarbazide and its 1,4-disubstituted derivatives with 2,3-diphenyl-cyclopropenone. The reaction of this cyclopropenone with two equivalents of thiosemicarbazide afforded the corresponding 1,2,4-triazolo[4,3-*b*]pyridazinethiones. However, the reaction of *N*-substituted hydrazino derivatives of thiosemicarbazides with the cyclopropenone occurs with stoichiometric amounts of the starting materials to produce pyridazinethiones. The reaction mechanism, in both cases, was described as a formal [3+3]-cycloaddition.

Keywords: Thiosemicarbazides, 2,3-diphenylcyclopropenone, pyridazinethiones, 1,2,4-triazolo-[4,3-*b*]-pyridazinethiones, [3+3]-cycloaddition

Introduction

Thiosemicarbazides are easily cyclized by the action of acids, bases or oxidants, therefore they are useful versatile building blocks for the preparation of heterocyclic ring systems. Some time ago, we investigated the reactions of thiosemicarbazides with π-deficient compounds. As a result we synthesized many heterocyclic ring systems such as thiazoles, thiazines, thiadiazoles, thiadiazines, pyrazines and indazoles.[1,2]

Cyclopropenones undergo several interesting cycloaddition reactions and they may be useful starting materials for a variety of compounds.[3,4] They are also reactive towards dipolar reagents and compounds having a reactive π-system.[5] The reaction pattern is sometimes complex, but recent extensive investigations have established the utility of these molecules as building blocks for the construction of larger molecules. It is expected that the use of cyclopropenones as C_3 synthetic blocks will find a broader applicability in the field of synthetic chemistry in the future. 2,3-Diphenylcyclopropenone (**1**) can be represented by the resonance structures **1a-c** (equivalent

to **1d**),[5-7] which contain a three-membered ring of sp^2 carbons coupled to the electron-donor substituents on the phenyls seem to stabilize these structures.

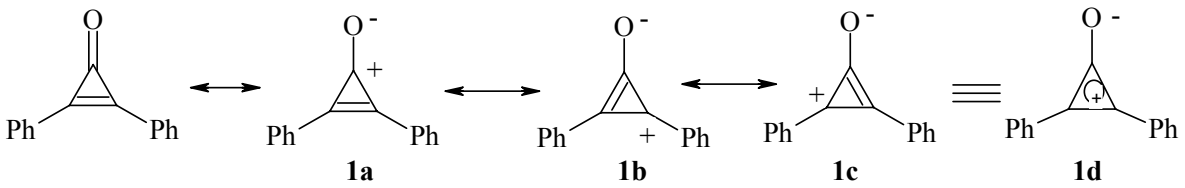


Figure 1. Resonance structures of 2,3-diphenylcyclopropenone

The systematic interest in the use of the cyclopropenone chemistry is to construct a wide variety of heterocycles.[8] Diphenylcyclopropenone (**1**) has been found to react with a wide range of imines and other compounds containing the C=N moiety, usually to form azacyclopentenones (pyrrolinones) *via* formal [2+3] cycloaddition reactions.[9-14] By contrast, the reaction of **1** with guanidine and its alkyl and/or aryl derivatives gave the corresponding 5,6-dihydro-4(1*H*)-pyrimidinone *via* a formal [3+3] cycloaddition reaction.[15] In general, cyclopropenone is amphiphilic, reacting readily with both nucleophilic and electrophilic reagents. Moreover, cyclopropenones are strained ring ambident electrophiles with a tendency to form ring opened products, their reaction with nucleophiles has the possibility of carbonyl or conjugate addition.[9-17] Recently, we have found that the reactions of aroylphenylthioureas with **1** in acetic acid afforded the diasteromers of 3-(3ˈ-aroyl-1-substituted-thioureido)-2,3-diphenylcinnamic acids.[18]

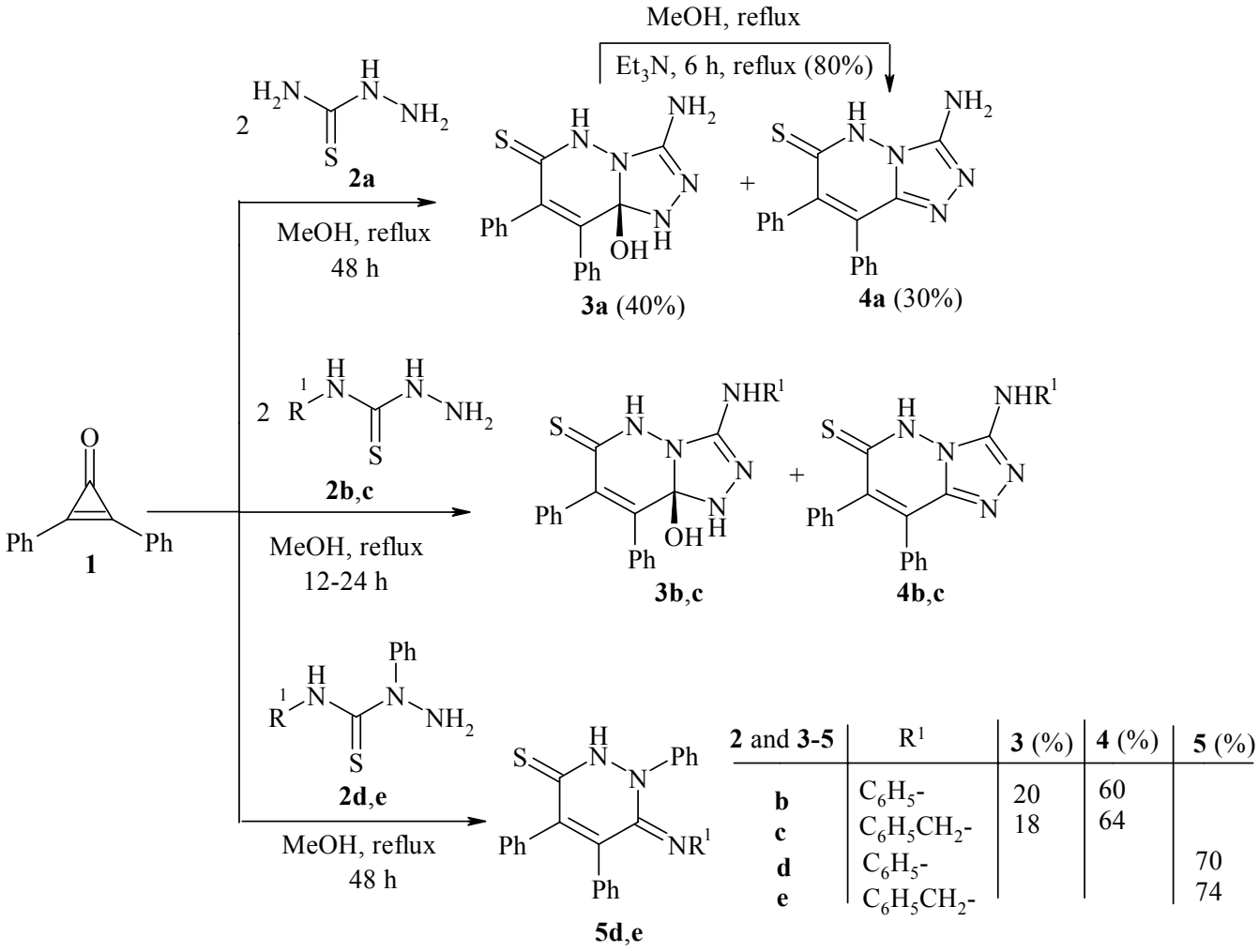
Generally, the N^2 of thiosemicarbazides is described as a softer nucleophilic center than the harder and powerful terminal nitrogen N^1. 2,3-Diphenylcyclopropenone (**1**) is susceptible to nucleophilic attack by N^1 and undergoes cyclization to form six-membered rings; the reaction can be described as a [3+3]-cycloaddition. Therefore, we decided in this publication to study the chemistry of **1**, especially towards bidentate nucleophiles such as thiosemicarbazides.

Results and Discussion

Herein, we report a general overall view of the reaction between thiosemicarbazides **2a-e** and **1** (Scheme 1). In the case of reacting equal equivalents of **2a-c** and **1**, thin layer chromatographic analysis proved that compound **1** was still recovered, whereas **3a-c** and **4a-c** were obtained in low yields. However, the reaction between **1** and two equivalents of **2a-c** proceeded without recovery of **1** and produced compounds **3a-c** and **4a-c**. In different manner, the reaction of **2d**,**e** with **1** was carried out by reacting equal equivalents of the two starting materials to afford compounds **5d**,**e** (Scheme 1). We chose thiosemicarbazides **2a–e** having various different substituents on the NH in the NH-NH_2 group in order to examine their reactivity, which might

affect the course of the reaction (Scheme 1). Elemental analyses and IR, NMR (^{1}H, ^{13}C, COSY C-H and H-H) and mass spectra were in good agreement with the assigned structures of compounds **3a-c** and **4a-c**. For example, the IR spectroscopy of the triazolopyridazines **3a** gave characteristic triazolo-C=N band at ν = 1610, pyridazine C=C at ν = 1560, and NH and NH_2 absorptions at ν = 3300-3180, and a strong OH absorption appeared at ν = 3450 cm^{-1}. The IR spectra of compounds **3b**,**c** showed the presence of pyridazine-NH as a sharp strong band between ν = 3280-3200, whereas the OH absorption was noted between ν = 3480-3450 cm^{-1}. Bands characteristic of vibration coupling of C=S and C-N groups appeared between ν = 1140-1090 cm^{-1}. The ^{1}H NMR spectra of **3b**,**c** revealed two broad singlets at δ = 5.50-5.60 and 9.00-9.10 corresponding to OH and triazole-NH protons, respectively. Additionally, the phenyl- (or benzyl-)NH and pyridazine-NH protons appeared superimposed on the aromatic protons. The elemental analysis and mass spectrum of **3a** proved its molecular formula as $C_{17}H_{15}N_5OS$. The ^{1}H NMR spectra confirmed the structure of compound **3a** by the appearance of four broad singlets at δ = 4.50, 5.40, 7.40 and 9.00 corresponding to NH_2, OH, pyridazine- (along with the aromatic protons) and triazole-NH protons, respectively. The COSY C-H spectra proved the presence of α-quaternary C-OH. The ^{13}C NMR spectra of **3a-c** supported the ^{1}H NMR spectral data by the appearance of the chiral C-OH at δ = 115.0-115.6, whereas the C=S resonated at δ = 180.6-182.4. Direct one-bond attached hydrogen-carbon correlations were established by ^{1}H, ^{13}C- COSY (HETCOR). Accordingly, COSY C-H of compounds **3a** and **4a** indicated the relation between the phenyl carbons and their protons. Besides, a relation was found between the carbon signals of C-7 and C-8 and protons of the phenyl groups attached to these carbon atoms. The NMR spectral data of compounds **4a-c** supported the proposed structures. The mass spectrum and elemental analysis of **4a** established its molecular formula as $C_{17}H_{13}N_5S$. The ^{1}H NMR spectrum of **4a** showed two multiplets for eleven protons. The free NH_2 protons resonated at δ = 5.20, whereas the NH-pyridazine was superimposed on the aromatic protons. The ^{13}C NMR spectrum showed the C-3, -6, -7, -8, -9 at δ = 150.0, 194.0, 122.4, 122.6, 160.4, respectively. The ^{13}C-135/90-DEPT spectra of **4c** supported the presence of the quaternary benzylic-CH_2 at δ = 48.5 (the CH_2 proton appeared in the ^{1}H NMR spectrum as a broad singlet at δ = 4.60). No significant SH resonance appeared in the NMR spectra which suggests that the thione form predominates. The C=S carbon appeared for **4a-c** between δ = 194.0 and 196.0. The formation of **3a-e** and **4a-e** can be rationalized by nucleophilic attack of **2** at its terminal hydrazino nitrogen upon the carbonyl group in **1** to form **6**. The single bond in the strained three-membered ring in **6** is then opened and adds thereafter to the thione group of another molecule of **2** (Figure 2). Then, the nucleophilic NH_2 attacks the activated C=($^+$OH) to form intermediate **7**. A second fused ring is then formed *via* an intramolecular nucleophilic attack of the NH-pyridazine on the thione group. That was accompanied with elimination of one molecule of substituted amine and hydrogen sulfide from **7**, to give the stable fused heterocyclic compound **3** (Figure 2). Dehydration of **3**, under the reaction conditions, occurs to give **4** (Figure 2). Isolation of compounds **3a-c** both confirmed the structure of **4a-c**, and proved elimination of a water molecule to occur as the ultimate step (Figure 2). In our case, the illustrated pathways leading to

3a-c and **4a-c** seem very likely, since compounds having a hydrazino function condensed with **1** to give the corresponding hydrazo derivatives of cyclopropenone (Scheme 1).[19] Moreover, the suggested mechanism was strongly supported by the reported literature[20] especially in the case of the formation of **6** in its tautomer form. Consequently, this tautomer can act as a reactive nucleophile.



2 and 3-5	R^1	3 (%)	4 (%)	5 (%)
b	C_6H_5-	20	60	
c	$C_6H_5CH_2$-	18	64	
d	C_6H_5-			70
e	$C_6H_5CH_2$-			74

Scheme 1. Reactions of thiosemicarbazides **2a-e** with **1.**

The structure of the obtained products (Scheme 1) excluded pathway such as that proposed by Eicher,[9,10] which depends on the nucleophilic attack of the terminal nitrogen of **2** to the olefinic carbon in **1** (pathway **b**). It is also possible that elimination of amine and hydrogen sulfide molecules might occur to give the intermediate **7** and thus produce product **8** (Figure 2). That was also excluded, due to the disappearance of the range of chemical shifts expected for the hydrazino NH-NH protons in the ^{1}H NMR spectra. Previous literature on the chemistry of thiosemicarbazides towards π-acceptors supported the formation of a pyridazino-NH rather than

the formation of the hydrazino NH-NH.[2] The conversion of **3a** into **4a** was carried out experimentally by refluxing compound **3a** in methanol containing a few drops of triethylamine. Product **4a** was then obtained in 80% yield. A long period of refluxing **3a** in the absence of triethylamine gave **4a** in only 30% yield.

Surprisingly, on reacting the substituted hydrazine group **2d**,**e** with **1**, the reaction produced the corresponding pyridazinethiones **5d**,**e** (Scheme 1). The structure of compounds **5d**,**e** is well established using the traditional spectroscopic tools such as IR, NMR (^{1}H, ^{13}C) and mass spectra, in addition to elemental analyses. In NOE experiments of compound **5e,** irradiating the benzylic-CH_2 protons (δ = 5.20) caused a strong positive enhancement to the attached phenyl protons, and also slightly affected the two protons of the other phenyl group.

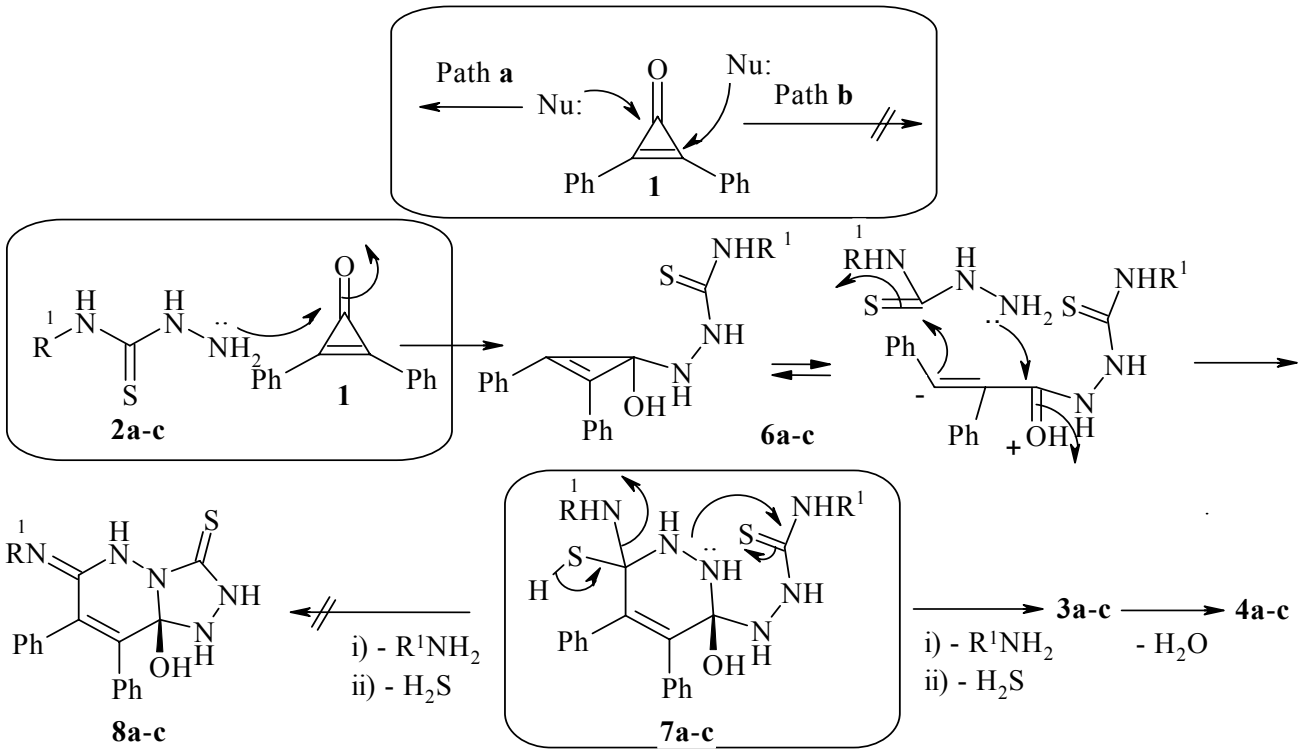


Figure 2. Mechanistic pathway of 1,2,4-triazolo-[4,3-*b*]pyridazine-6-thiones **3a-c** and **4a-c**.

The ^{13}C NMR spectrum of **5e** showed six distinctive carbon signals at δ = 50.4, 122.0, 124.6, 138.9, 150.8 and 190.6 corresponding to benzylic-*C*H_2, *C*-4, -5, Ph-*C*-N, *C*-6 and –3, respectively. ^{1}H, ^{13}C- COSY (HETCOR) of compound **5e** indicated the relations between the phenyl carbons and their protons. Correlation was also found between the carbon signals of C-4 and C-5 and the protons of the phenyl groups connected to these carbon atoms, along with strong correlation between C-6 (δ = 150.8) and the benzyl-CH_2 protons. The proposed mechanism for the formation of **5d**,**e** is based upon normal condensation of the free hydrazine NH_2 with the carbonyl of **1** (Figure 3) to give **9**. Thereafter, we propose that another nucleophilic addition

occurs to the thione group, leaving it as thiolate anion, which spontaneously adds to the azo group in one step to give **10** (Figure 3). Under the reaction conditions, another type of intramolecular rearrangement occurs involving ring opening (to form the stable thione group) accompanied with a proton transfer to give the stable pyridazinethiones **5d**,**e** (Figure 3). The processes showing the formation of intermediates **9** and **10** and including the nucleophilic addition to the thione group from the strained cyclopropenehydrazone followed by bi-cyclic formation, have been shown by other workers during the addition of cyclopropenone to 4-vinyl substituted 1-azetines.[20a]

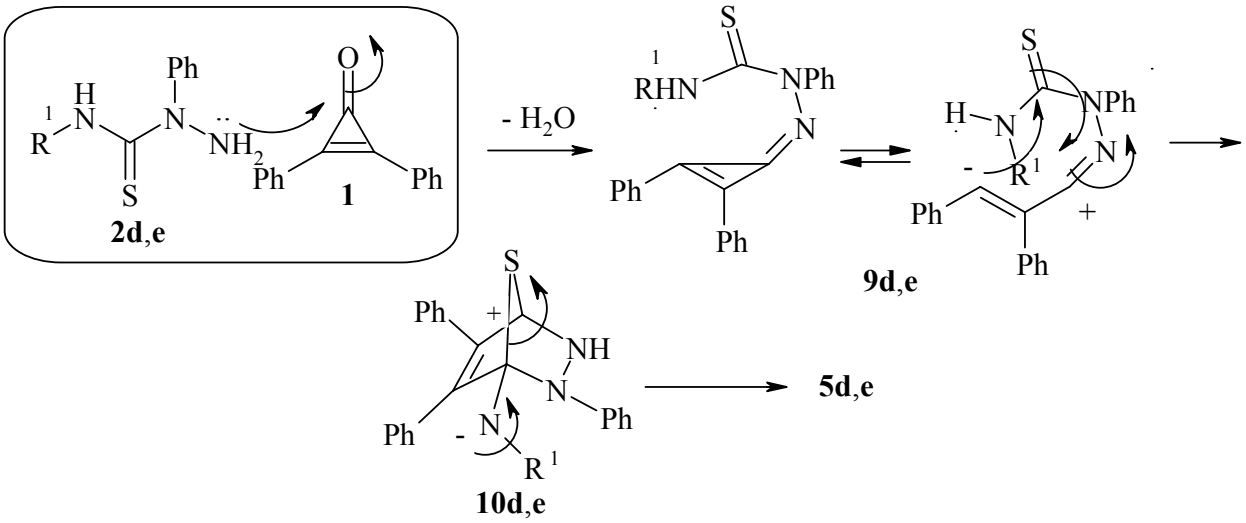


Figure 3. Mechanistic pathway of pyridazinethiones **5d,e**.

The abnormal behavior of **2d**,**e** towards **1** might be attributed to the steric factors arising from the presence of the bulky phenyl group on the nitrogen derived from N^2 of **2d,e**, which prevents further mutual addition between the intermediate **6** (Figure 2) and another molecule of **1**. The comparative higher yield of **5e** related to **5d** can be explained as due to the higher basic character of the benzylic hydrazine **2e** compared with that in **2d** (Scheme 1). Moreover, the stereoview[21] of compounds **5d** and **5e**, as optimized by molecular mechanics, showed that formation **5e** has a lower steric energy value (8.57 Kcal/mol) than **5d** (10.49 Kcal/mol).

In conclusion we have developed a method for the synthesis of pyridazinethione and 1,2,4-triazolopyridazinethione systems. The reaction and products presented here provide insight into spontaneous reactions between thiosemicarbazides **2a-e** and 2,3-diphenylcyclopropenone (**1**). In a fairly complex and multi-step process, triazolopyridazinethiones **3a-c**, **4a-c** and pyridazinethiones **5d**,**e** were formed. The prospective biological and pharmaceutical activities of the obtained products are of great interest.[22-24]

Experimental Section

General Procedures. All mps were recorded on a Gallenkamp apparatus. The IR spectra were obtained on Shimadzu 470 spectrophotometer using potassium bromide pellets. The ^{1}H NMR (400.134 MHz) and ^{13}C NMR (100.6 MHz) spectra were measured in $CDCl_3$ using Bruker a AM 400 with TMS as an internal standard. Coupling constants are expressed in Hz. Mass spectra were recorded on a Finnigan MAT 8430 instrument at 70 eV. Elemental analyses were carried out in the Microanalysis Center of the Institut für Anorganische Chemie, Technische Universität Braunschweig. For preparative thin layer chromatography (PLC), glass plates (20 x 48 cm) were covered with a slurry of silica gel Merck PF_{254} and air-dried using the solvents listed for development. Zones were detected by quenching of indicator fluorescence upon exposure to 254 nm light; elution of the different bands with toluene afforded the pure products. The abbreviations: triaz = triazole and pyrid = pyridazine.

Starting materials

4-Phenylthiosemicarbazide (**2b**),[25,26] 4-benzylthiosemicarbazide (**2c**)[26,27] and 1,4-disubstituted thiosemicarbazides (**2d**,**e**)[28] were prepared according to literature procedures. Thiosemicarbazide (**2a**) and 2,3-diphenylcyclopropenone (**1**) were bought from Fluka.

General experimental procedure

Reactions of 2a-c with 1. A 250 cm^3 two-necked round bottom flask was charged with dry methanol (100 mL) containing 2 mmols of **2a-c** and (0.412 mg, 1 mmol) of **1**. The mixture was gently refluxed under stirring for 12-48 h (the reaction was monitored by TLC). The solvent was evaporated *in vacuo* and the residue was separated by PLC (silica gel) with toluene: ethyl acetate (2:1). Compounds **4a-c** migrated faster than compounds **3a-c**. Products were obtained after recrystallization from the stated solvents.

3-Amino-8α(*S*)-hydroxy-1,8α-dihydro-7,8-diphenyl-1,2,4-triazolo[4,3-*b*]pyridazine-6-thione (3a). Yellow crystals, mp (ethanol) 122 ^{o}C, yield 0.27 g (40%); IR (KBr): ν 3450 (s, OH), 3300–3180 (s, NH and NH_2), 3030-2990 (Ar–CH), 1610 (s, C=N), 1560 (s, C=C), 1115 (m), 998 (s) cm^{-1}; λ_{max} (CH_3CN, lg ε, nm): 398 (3.94); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.50 (2H, br s, NH_2), 5.40 (1H, br s, OH, H-8a), 6.50-6.80 (3H, m, Ph-H), 7.20-7.60 (6H, m, Ph–H and pyrid-NH), 7.86 (2H, dd, *J* = 8.0, 2.0, Ph-H), 9.00 (1H, s, triaz-NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 115.0 (C-8a), 126.0, 126.4 (*para*-Ph-H), 128.2, 129.6, 130.4, 130.6 (Ph–CH), 131.4, 132.8 (C-7 and –8), 133.0, 133.5 (Ph-C), 148.2 (C=N), 180.6 (C-6); EI-MS m/z*:* % 337 [M$^+$] (100), 321 (24), 304 (30), 288 (28), 278 (30), 262 (20), 260 (60), 184 (48), 77 (54), 60 (18). Anal. Calcd. For $C_{17}H_{15}N_5OS$ (337.41): C, 60.52; H, 4.48; N, 20.76; S, 9.50. Found: C, 60.40; H, 4.50; N, 20.80; S, 9.48.

8α(*S*)-Hydroxy-1,8α-dihydro-7,8-diphenyl-3-phenylamino-1,2,4-triazolo[4,3-*b*]pyridazine-6-thione (3b). Yellow crystals, mp (ethanol) 290 ^{o}C, yield 0.17 g (20%); IR (KBr): ν 3460 (m, OH), 3280–3200 (s, NH), 3050-2995 (m, Ar–CH), 1620 (s, C=N), 1585 (s, C=C), 1090 (s), 996

(m) cm^{-1}; λ_{max} (CH_3CN, lg ε, nm): 412 (4.06); ^1H NMR (400 MHz, $CDCl_3$): δ 5.50 (1H, br s, OH, H-8a), 6.56-6.80 (5H, m, Ph-H), 7.60-7.94 (9H, m, Ph–H, pyrid-and Ph-NH), 8.00 (2H, dd, *J* = 8.4, 2.0, Ph-H), 8.10 (1H, dd, *J* = 8.4, 2.0, Ph-H), 9.00 (1H, s, triaz-NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 115.6 (C-8a), 126.0, 126.6, 127.0 (*para*-Ph-H), 128.0, 128.2, 128.4, 129.2, 130.0, 130.4 (Ph–CH), 131.4, 132.0 (C-7 and –8), 132.8, 133.4, 133.8 (Ph-C), 148.8 (C=N), 182.4 (C-6); EI-MS m/z*:* % 413 [M^+] (100), 396 (18), 380 (16), 336 (48), 321 (24), 304 (30), 278 (34), 259 (26), 260 (60), 184 (34), 77 (40), 60 (28). Anal. Calcd. For $C_{23}H_{19}N_5OS$ (413.50): C, 66.81; H, 4.63; N, 16.94; S, 7.75. Found: C, 66.70; H, 4.60; N, 16.90; S, 7.74.

3-Benzylamino-8α(*S*)-hydroxy-1,8α-dihydro-7,8-diphenyl-1,2,4-triazolo[4,3-*b*]pyridazine-6-thione (3c). Pale yellow crystals, mp (ethanol) 240 °C, yield 0.15 g (18%); IR (KBr): ν 3480-3450 (m, OH), 3280–3210 (s, NH), 3080-2980 (w, Ar–CH), 2980-2860 (w, alip-CH), 1630 (s, C=N), 1590 (m, C=C), 1115 (s), 994 (m) cm^{-1}; λ_{max} (CH_3CN, lg ε, nm): 400 (4.08); ^1H NMR (400 MHz, $CDCl_3$): δ 5.60 (1H, s, OH, H-8a), 4.80 (2H, br s, CH_2Ph), 6.60-6.76 (5H, m, Ph-H), 7.40-8.00 (9H, m, Ph–H, pyrid- and benzyl-NH), 8.18 (2H, dd, *J* = 8.2, 2.2, Ph-H), 8.04 (1H, dd, *J* = 8.2, 2.0, Ph-H), 9.10 (1H, s, triaz-H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 54.00 (CH_2-Ph), 115.4 (C-8a), 126.4, 126.8, 127.0 (*para*-Ph-H), 128.0, 128.6, 128.8, 129.6, 130.2, 130.4 (Ph–CH), 132.0, 132.4 (C-7 and –8), 132.6, 133.8, 133.4 (Ph-C), 150.0 (C=N), 181.0 (C-6); EI-MS m/z*:* % 428 [M+1] (30), 427 [M^+] (100), 410 (18), 350 (22), 336 (24), 294 (18), 274 (26), 256 (16), 223 (30), 193 (18), 77 (50), 60 (22). Anal. Calcd. for $C_{24}H_{21}N_5OS$ (427.53): C, 67.43; H, 4.95; N, 16.38; S, 7.50. Found: C, 67.40; H, 4.90; N, 16.30; S, 7.38.

3-Amino-7,8-diphenyl-1,2,4-triazolo[4,3-*b*]pyridazine-6-thione (4a). Orange crystals, mp (methanol) 160 °C, yield 0.19 g (30%); IR (KBr): ν 3290–3250 (s, NH), 3068-2992 (w, Ar–CH), 1610 (s, C=N), 1580 (m, C=C) 1110 (s), 996 (m) cm^{-1}; λ_{max} (CH_3CN, lg ε, nm): 410 (3.98); ^1H NMR (400 MHz, $CDCl_3$): δ 5.20 (2H, br s, NH_2), 6.60-6.70 (2H, m, Ph-H), 7.40-7.68 (9H, m, Ph–H and pyrid-NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 122.4, 122.6 (C-7 and –8), 126.8, 127.2 (*para*-Ph-H), 128.0, 129.2, 130.6, 130.8 (2Ph–CH), 133.4, 133.8 (Ph-C), 150.0 (C-3), 160.4 (C-8a), 194.0 (C-6); EI-MS m/z*:* % 320 [M+1] (20), 319 [M^+] (100), 304 (24), 288 (24), 278 (24), 262 (18), 260 (62), 184 (46), 77 (50), 60 (18). Anal. Calcd. for $C_{17}H_{13}N_5S$ (319.39): C, 63.93; H, 4.10; N, 21.93; S, 10.04. Found: C, 64.00; H, 4.10; N, 21.90; S, 9.98.

7,8-Diphenyl-3-phenylamino-1,2,4-triazolo[4,3-*b*]pyridazine-6-thione (4b). Orange crystals, mp (acetonitrile) 190 °C, yield 0.47 g (60%); IR (KBr): ν 3320–3260 (s, NH), 3060-2985 (w, Ar–CH), 1610 (s, C=N), 1560 (m, C=C), 1112 (s), 998 (s) cm^{-1}; λ_{max} (CH_3CN, lg ε, nm): 430 (4.2); ^1H NMR (400 MHz, $CDCl_3$): δ 6.60-6.80 (5H, m, Ph-H), 7.30-7.82 (10H, m, Ph–H and pyrid-NH), 8.30 (1H, s, Ph-NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 123.0, 123.2 (C-7 and –8), 126.4, 127.6, 128.0 (*para*-Ph-H), 128.4, 128.6, 129.8, 130.2, 130.6, 130.8 (2Ph–CH), 133.6, 134.2 (Ph-C), 138.9 (NH-C-Ph), 152.0 (C-3), 158.9 (C-8a), 194.8 (C-6); EI-MS m/z*:* % 395 [M^+] (100), 362 (18), 318 (42), 302 (38), 288 (28), 278 (30), 262 (30), 226 (24), 184 (18), 77 (34), 60 (22). Anal. Calcd. for $C_{23}H_{17}N_5S$ (395.39): C, 69.85; H, 4.33; N, 17.71; S, 8.11. Found: C, 69.00; H, 4.30; N, 17.66; S, 8.08.

3-Benzylamino-7,8-diphenyl-1,2,4-triazolo[4,3-*b*]pyridazine-6-thione (4c). Orange crystals, mp (acetonitrile) 142 °C, yield 0.52 g (64%); IR (KBr): ν 3240–3220 (s, NH), 3065-2990 (m, Ar–CH), 2980-2960 (m, aliph-CH), 1600 (s, C=N), 1570 (m, C=C), 1110 (m), 996 (m) cm^{-1}; λ_{max} (CH_3CN, lg ε, nm): 412 (4.0); ^1H NMR (400 MHz, $CDCl_3$): δ 4.60 (2H, br, s, CH_2Ph), 6.70-6.90 (5H, m, Ph-H), 7.38-7.90 (11H, m, Ph–H and pyrid-NH), 8.30 (1H, br s, benzyl-NH); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 48.5 (CH_2Ph), 123.2, 123.6 (C-7 and –8), 126.8, 127.4, 128.0 (*para*-Ph-H), 128.6, 128.8, 129.6, 130.0, 130.4 (Ph–CH), 132.4, 134.0 (Ph-C), 152.6 (C-3), 156.8 (C-8a), 196.0 (C-6); EI-MS m/z*:* % 410 [M+1] (22), 409 [M^+] (100), 362 (18), 318 (42), 302 (38), 288 (28), 278 (30), 262 (30), 226 (24), 184 (18), 77 (34), 60 (22). Anal. Calcd. for $C_{24}H_{19}N_5S$ (409.52): C, 70.39; H, 4.68; N, 17.10; S, 7.83. Found: C, 70.20; H, 4.60; N, 17.00; S, 7.78.

Reactions of 2d,e with 1. By the same procedure, dry methanol (50 mL) containing 1 mmol of **2d**,**e** and 1 mmol (0.412 mg) of **1** was gently refluxed under stirring for 48 h (the reaction was monitored by TLC). The solvent was evaporated *in vacuo* and the residue was separated by PLC (silica gel) with toluene: ethyl acetate (3:1). Compounds **5d**,**e** were recrystallized from the stated solvents.

1,4,5-Triphenyl-6[(*Z*)-phenylimino-1,6-dihydro-2*H*-pyridazine-3-thione (5d). Yellow crystals, mp (ethanol) 290 °C, yield 0.30 g (70%); IR (KBr): ν 3280–3220 (s, NH), 3060-2990 (m, Ar–CH), 1580 (s, C=N), 1560 (m, C=C), 1115 (s), 996 (s) cm^{-1}; λ_{max} (CH_3CN, lg ε, nm): 420 (4.0); ^1H NMR (400 MHz, $CDCl_3$): δ 6.62-6.64 (2H, m, *ortho*-Ph-H-C-4), 6.80-7.16 (5H, m, Ph-H), 7.20-7.24 (2H, m, *ortho*-Ph-H- N^1), 7.34-7.48 (5H, m, Ph–H), 7.54-7.56 (2H, m, *ortho*-Ph-H-*N*-C-6), 7.70-7.86 (4H, m, Ph-H), 8.30 (1H, br s, pyrid-H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 124.6, 124.8 (C-4 and –5), 126.0, 126.4, 127.3 (*para*-Ph-H), 128.0, 128.2, 128.4, 128.6, 128.8, 130.0 (2Ph–CH), 131.0, 131.6, 132.6 (Ph-C), 133.0, 133.2 (2Ph-H), 133.6 (*para*-Ph-H), 138.6 (N-C-Ph), 150.6 (C-6), 190.4 (C-3); EI-MS m/z*:* % 431 [M^+] (40), 430 [M-1] (100), 339 (16), 312 (60), 278 (38), 207 (24), 184 (20), 165 (24), 129 (40), 77 (50), 55 (60). Anal. Calcd. $C_{28}H_{21}N_3S$ (431.56): C, 77.93; H, 4.90; N, 9.74; S, 7.43. Found: C, 77.80; H, 4.90; N, 9.70; S, 7.48.

6-[(*E*)-Benzylimino-1,4,5-triphenyl-1,6-dihydro-2*H*-pyridazine-3-thione (5e). Yellow crystals, mp (ethanol) 220 °C, yield 0.33 g (74%); IR (KBr): ν 3200–3180 (m, NH), 3080-2960 (m, Ar–CH), 2960-2850 (w, aliph-CH), 1618 (m, C=N), 1570 (s, C=C), 1112 (s), 996 (m) cm^{-1}; λ_{max} (CH_3CN, lg ε, nm): 418 (3.90); ^1H NMR (400 MHz, $CDCl_3$): δ 5.20 (2H, br, s, CH_2Ph), 6.82-6.84 (2H, m, *ortho*-Ph-H-C-4), 6.90-7.20 (5H, m, Ph-H), 7.30-7.34 (2H, m, *ortho*-Ph-H-N^1), 7.50-7.90 (9H, m, Ph–H), 8.00 (2H, dd, *J* = 8.4, 1.8, Ph-H), 8.34 (1H, s, pyrid-H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 50.4 (CH_2Ph), 122.0, 124.6 (C-4 and –5), 125.6, 126.0, 126.8 (*para*-Ph-H), 127.8, 128.0, 128.2, 128.6, 128.8, 130.4 (2Ph–CH), 131.2, 131.8, 132.4 (Ph-C), 133.2, 133.6 (2Ph-H), 133.8 (*para*-Ph-H), 138.9 (N-C-Ph), 150.8 (C-6), 190.6 (C-3); EI-MS m/z*:* % (EI)] 445 [M^+] (60), 368 (20), 309 (24), 207 (18), 167 (30), 105 (12), 91 (100), 55 (40). Anal. Calcd. for $C_{29}H_{23}N_3S$ (445.59): C, 78.17; H, 5.20; N, 9.43; S, 7.20. Found: C, 78.10; H, 5.22; N, 9.40; S, 7.28.

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