SYNTHESIS OF NEW 1-CHALCOGENAPURINES BY THE REACTION OF 5-AMINOIMIDAZOLE-4-CARBONITRILE WITH ISOCHALCOGENOCYANATES

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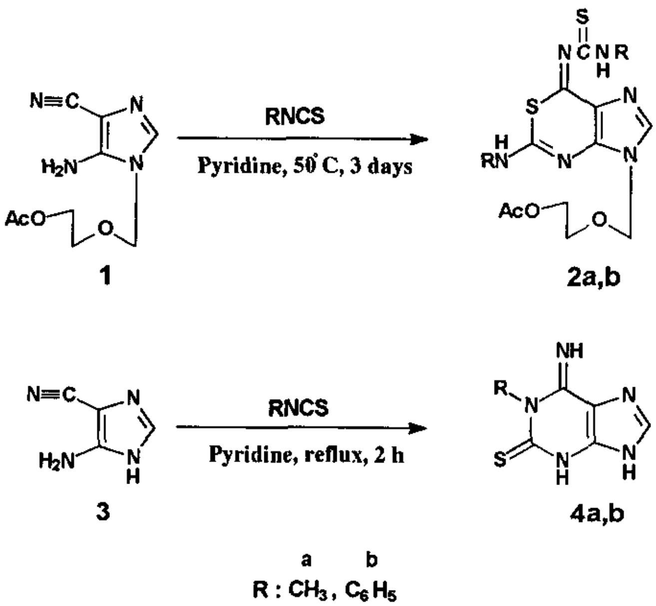
Abstract – 1-Chalcogenapurines[1-thiapurine derivatives (**6,12c,d**) and 1-selenapurine derivative (**15**)] and 1-substituted 1,6-dihydro-6-imino-9*H*-purine-2(3*H*)-chalcogenone (**4a,b, 13**) were synthesized by the reaction of 5(4)-aminoimidazole-4(5)-carbonitrile(**3**)with various isochalcogenocyanates in pyridine. The reaction of **3** with methyl isothiocyanate in pyridine afforded only the 1,6-dihydro-1-methyl-6-imino-9*H*-purine-2(3*H*)-thione (**4a**). On the other hand, the reactions of **3** with ethoxycarbonyl isothiocyanate, benzoyl isothiocyanate or benzhydryl isoselenocyanate preferentially gave the 1-chalcogenapurine derivatives (**12c,d, 15**). In turn, both 1,6-dihydro-1-phenyl-6-imino-9*H*-purine-2(3*H*)-thione (**4b**) and 6,9-dihydro-2-phenylamino-6-(3-phenylthioureido)imino-1-thiapurine (**6**) were produced by the reaction of **3** with phenyl isothiocyanate. Modes of cyclization reactions involving **3** and isochalcogenocyanate (R-N=C=X, X; S,Se) depend in remarkable extent on the chalcogene atom as well as R portion of R-N=C=X.

INTRODUCTION

It is well-known that among purine derivatives including their nucleosides, there are many reagents or drugs[1] of pharmacological, physiological or biological interest. That is, the area of isosteres and analogs of purine (*viz.*, 6-thiopurine,[2,3] acyclovir,[4] arabinosyladenine[5] or oxanosine[6]) is a rich source of "jackpot" for the search of antineoplastic, antiviral agents or immuno-modulators.[7] As far as the synthesis of mimics, with the pyrimidine portion modified, of purines is concerned, 5(4)-aminoimidazole-4(5)-carbonitrile (**3**) is quite versatile starting material. Thus, in our previous paper, we have reported on the reactions of 1-(2- acetoxyethoxy)methyl-5-aminoimidazole-4-carbonitrile (**1**) and a variety of isothiocyanates to give 1–thiapurine derivatives[8]. Independently, Grözinger and Onan[9] have prepared 1–substituted 1,6–dihydro–6–imino–9*H*–purine–2–(3*H*)–thione (**4a,b**) by the reaction of **3** and methyl or phenyl isothiocyanate (Scheme 1). As part of our continuing research program, we prepared additional isosteres and analogs of purine by the reaction of **3** with isothiocyanates.

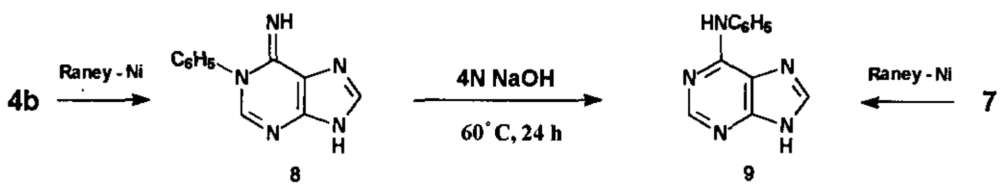
In this paper, we report that the cyclization products of reactions involving **3** and isochalcogenocyanates (R–N=C=X, X; S, Se) depend, in remarkable extent, on the chalcogene atoms, R portion of isochalcogenocyanates, and reaction temperatures.



Scheme 1

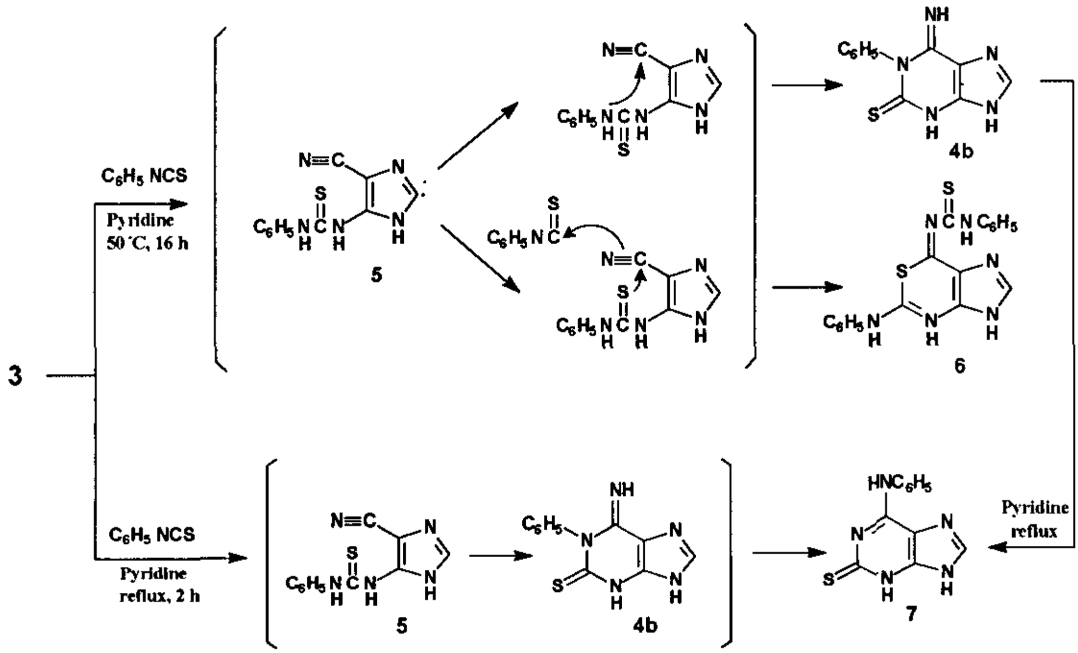
RESULTS AND DISCUSSION

Reaction of **3** with phenyl isothiocyanate in pyridine at 50°C (instead of refluxing temperature ; Scheme 1) for 16h afforded **4b** and **6** in 71% and 23% yields, respectively. Compound (**4b**) was deposited out of the reaction mixture as pale yellow crystals which were collected by filtration and were purified. The residue, obtained from the filtrate, was purified by column chromatography to give **6**. Desulfurization of **4b** with Raney nickel, followed by treatment with 4N NaOH at 60°C for 24h provided **9**, whose uv spectrum was found to be superimposable with that of authentic sample[10]; 6–phenylaminopurine (Scheme 2). Ir spectrum of **4b** showed the presence of the strong absorption at 1676 cm^{-1} probably due to exoC=N stretching vibration.[11] On the basis of these results, the compound (**4b**) was assigned the 1,6–dihydro–1–phenyl–6–imino–9*H*–purine–2(3*H*)–thione structure. Theoretically, a number of tautomers due to the protoropy are possible for the analogs or isosteres of purine. However, the structures in this paper not always correspond to predominant tautomers, but represent one of possible tautomers.



Scheme 2

Then, mass spectral data (including the molecular ion peak) of the compound (6) showed the presence of two sulfur atoms in a shingle molecule, its elemental analysis was also compatible with the chemical formula, $C_{18}H_{14}N_6S_2$. In ir spectrum, the compound (6) had no absorption maximum owing to the cyano group. Its uv spectrum showed the maximum at around 400 nm, which was very similar to that of **2b**.[8] Therefore, the compound (6) was assigned the 6,9–dihydro–2–phenylamino–6–(3–phenyl–thioureido)imino–1–thiapurine structure which was presumably formed by cyclization *via* the sulfur atom rather than the nitrogen atom of the putative 4–cyano–5–(3–phenylthioureido)imidazole intermediate (5) [Scheme 3].



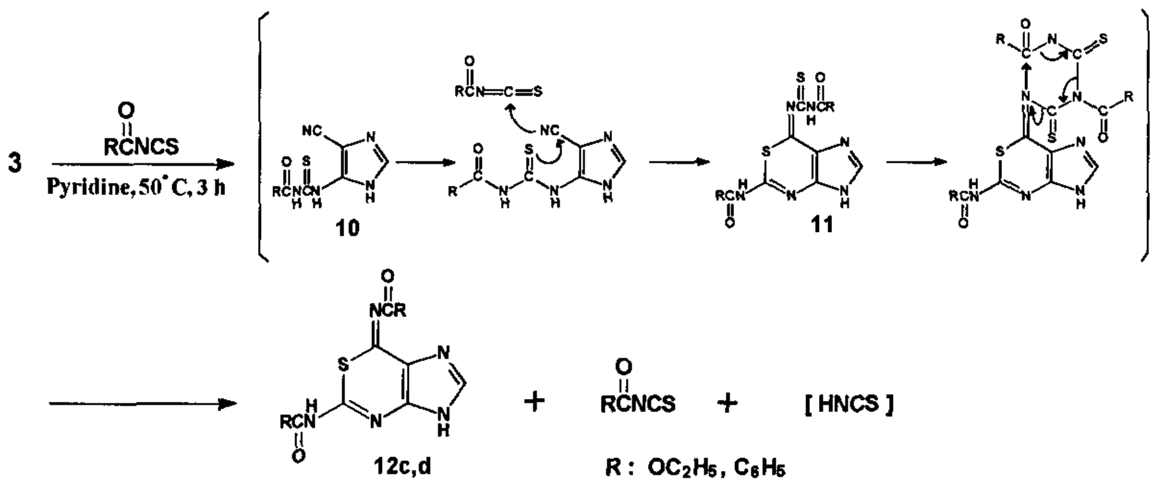
Scheme 3

Surprisingly, a reaction product which was obtained under the reaction conditions employed by Grözinger and Onan[9] (pyridine as solvent and at refluxing temperature, Scheme 1) was not **4b**, but 6–phenylaminopurine–2(3*H*)–thione (7). The structure of 7 was confirmed by spectral (ms, nmr, and ir) data. Above all, ir spectrum was quite helpful for the differentiation between **4b** and 7, because the latter did not show the absorption of the exoC=N stretching vibration (around 1670 cm^{-1}). The compound (7) was also obtained by the Dimroth rearrangement of **4b** at refluxing pyridine. Furthermore, desulfurization of 7 with Raney nickel gave rise to the known compound; 6–phenylaminopurine (9).[10]

On the other hand, the reaction of **3** with methyl isothiocyanate gave rise to 1,6–dihydro–1–methyl–6–imino–9*H*–purine–2(3*H*)–thione (**4a**) alone, irrespective of the reaction temperature ranging from 50°C to refluxing temperature of pyridine. This means that **4a** defied the Dimroth rearrangement at the above–mentioned temperature range.

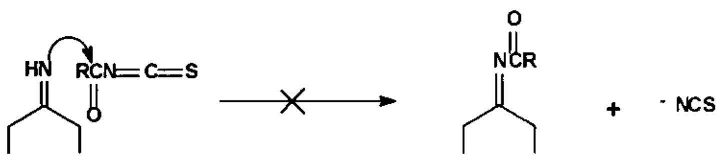
Then, the reaction of **3** with ethoxycarbonyl isothiocyanate was carried out under similar conditions (pyridine/50°C, 3 h). After evaporation of the solvent, addition of ethanol produced yellow precipitates. As this compound showed the absorption maximum at around 350 nm in the uv spectrum, it was initially assumed that 1–thiapurine ring system such as **6** was yielded from one molecule of **3** and two molecules of ethoxycarbonyl isothiocyanate. But, this compound turned out to contain only one sulfur atom on the basis of elemental analysis as well as ms and to show the presence of two carbonyl carbons (^{13}C–nmr; 161.21 and 152.96 ppm) and two N–H protons (^{1}H–nmr; 13.72 and 11.67 ppm) in the nmr spectrum. Based on these spectral data, **12c** was assigned the 6,9–dihydro–2–ethoxycarbonylamino–6–ethoxycarbonylimino–1–thiapurine structure. Yield of **12c** was 60%. Similarly, the reaction of **3** with benzoyl isothiocyanate afforded 6,9–dihydro–2–benzamido–6–benzoylimino–1–thiapurine (**12d**) in 53% yield. Under these reaction conditions, 1–substituted 1,6–dihydro– 6–imino–9*H*–purine–2(3*H*)–thione such as (**4a,b**) was not detectable among the products.

It is worthy to note that even when the reaction was carried out with less than one equivalent of acyl isothiocyanate, **12c,d** were still formed, starting materials being recovered. In addition, in each reaction mixture there was no detectable amount of 2–(substituted amino)–6–imino–1–thiapurine, which would be expected to be formed from **3** by the reaction of one molecule of isothiocyanates. These facts show that in the multi–step synthesis of **12c,d** the first step (the formation of **10** : Scheme 4) must be comparatively very slow and as soon as **10** was formed, it reacts with the second molecule of isothiocyanate to give **11** which in turn reacts with the third molecule of the isothiocyanate to afford the final product (**12c,d**).



Scheme 4

In addition to the above–mentioned facts, by analogy with the proposal by Chern and coworkers[12] and by taking the fact into consideration that there are no precedent that acyl isothiocyanates act as acylating agent (Scheme 5) , we propose the mode of the formation of **12c,d** (Scheme 4) .



Scheme 5

One feature of our proposal consists in the involvement of three molecule of acyl isothiocyanates and eventually one out of the three is recovered.

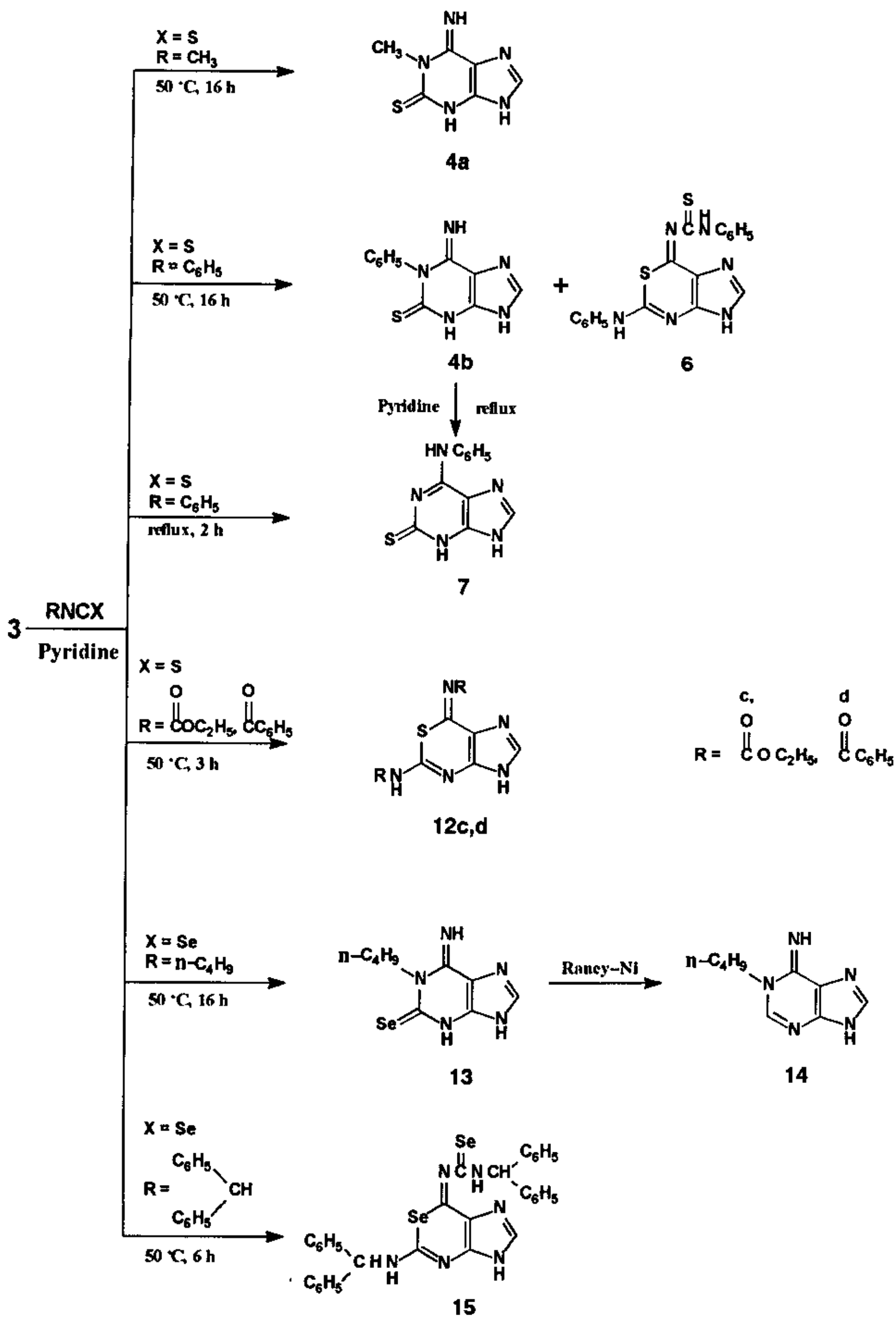
Next, n–butyl isoselenocyanate[13] was allowed to react with **3** in pyridine at 50°C for 16 h. Homogeneous precipitate(s) (**13**) which were deposited during the reaction were collected by filtration. Then, after the mother liquor was evaporated, the residue obtained was purified by column chromatography to have an unknownl compound. Ir spectrum of **13** showed the presence of the strong absorption at 1667 cm^{-1} probably due to exoC=N stretching vibration. Treatment of **13** with Raney nickel gave the 1–n–butyladenine (**14**), whose uv spectrum (λ_{max} 254sh nm, 260 nm, 268 nm in dioxane; λ_{max} 272 nm in methanol) was superimposabl with that of 1–propyladenine.[14] Other spectral (ms and ^{1}H–nmr) data were in keeping with the 1–butyladenine structure. It was demonstrated that 1–methyladenine[15] or 1–methylisoguanine[16] will exist in the imine form. That is, the compound (**13**) was assigned the 1,6–dihydro–1–n–butyl–6–imino–9*H*–purine–2(3*H*)–selenone structure (Scheme 6).

The unknown compound was not different from **13** in terms of chamical composition on the basis of high resolution mass data. Some other spectra of this compound were meansured (see Experimental). This means that **13** and the compound of unknown structure are isomers from each other. However, the structaural assignment is reserved until further infomation is collected.

Predominant formation of purine–type products presumably comes from preferential nucleophilic attack to the imino by the nitrogen atom of the selenoureido intermediate.

On the other hand, the reaction of **3** with benzhydryl isoselenocyanate[17] at 50°C for 16h afforded 1–selenapurine type product; 6,9–dihydro–2–benzhydryl–6–(3–benzhydrylthioureido)imino–1–selenapurine (**15**) in 41% yield. The structure of **15** was confirmed by ms, nmr, and uv spectral data.

These results may be summarized as follows (Scheme 6). In the case where the basicity of N^3–nitrogen atom [$RC(O)N^3HC^2(S)N^1H$–] of the thioureido intermediate (**10**) decreases owing to electron–withdrawing carbonyl group, 1–thiapurine derivatives were preferentially produced. In contrast, the increase in basicity of the N^3–nitrogen atom owing to an electron–donating substituent (alkyl group) of thioureido or selenoureido intermediate preferentially result in the formation of only normal purine ring system. The fact that in the case of phenyl isothiocyanate, the formation of both normal purine ring system and 1–thiapurine ring system may be due to the dual nature (electron–withdrawing and electron–donating) of the phenyl group may substantiate the explanation. It is worthy to note that owing to the high nucleophilicity of selenium atom, as compared with sulfur atom, 1–selenapurine ring system was preferentially formed via 3–benzhydrylselenoureido intermediate.



Scheme 6

EXPERIMENTAL

General. Melting points were determined on a Yanagimoto micro melting point apparatus, and are uncorrected. ^{1}H-Nmr and ^{13}C-nmr spectra were recorded on a JEOL JNM-GX 270 (270 MHz) and JEOL EX 400 (400 MHz) spectrometer with tetramethylsilane as an internal standard, respectively. Chemical shifts are reported in parts per million (δ), and signals are expressed as s (singlet), d (doublet), t (triplet), qui (quintet), sex (sextet), m (multiplet), or br (broad). All exchangeable protons were detected by addition of D_2O. Mass spectra (ms) and high resolution ms were run on a JEOL JMS-DX 303 spectrometer. Infrared (ir) spectra were recorded with a JASCO IRA-1 spectrophotometer in KBr disks. Ultraviolet (uv) spectra were measured on a Shimazu UV-2200 spectrophotometer. Tlc was done on Merck Kieselgel F254 precoated plates. The silica gel used for column chromatography was Merck Kieselgel 60 (70-230 mesh).

1,6-Dihydro-1-methyl-6-imino-9*H*-purine-2 (3*H*)-thione (4a). Methyl isothiocyanate (418 mg, 5.7 mmol) was added to a solution of **3** (400 mg, 3.7 mmol) in dry pyridine (8 ml). The solution was heated at 50°C for 16 h. The precipitated crystals were filtered and washed with ethanol to give **4a** (353 mg, 53% yield), mp : > 300°C ; uv (nm) : λ_{max} ($\varepsilon \times 10^3$) 242 (14.6), 287 (14.7) (0.1 N HCl) ; λ_{max} ($\varepsilon \times 10^3$) 240 (15.8), 290 (13.0) (0.1 N NaOH) ; ir : 1688 cm^{-1} ($\nu_{exoC=N}$) ; ms (EI) : *m/z* 181 (M$^+$) ; ^{1}H-nmr (DMSO-d6) 3.95 (s, 3H, NCH_3), 7.89 (s, 1H, H-8), 8.35 (brs, 1H, NH), 12.50 (brs, 1H, NH). Anal. Calcd for $C_6H_7N_5S$: C, 39.77; H, 3.89; N, 38.65; S, 17.69. Found: C, 39.94; H, 3.91; N, 38.52; S, 17.32.

1,6-Dihydro-1-phenyl-6-imino-9*H*-purine-2(3*H*)-thione (4b) and 6,9-dihydro-2-phenylamino-6-(3-phenylthioureido) imino-1-thiapurine (5). Phenyl isothiocyanate (1.6 ml, 13.7 mmol) was added to a solution of **3** (1.0 g, 9.3 mmol) in dry pyridine (25 ml). The solution was heated at 50°C for 16 h. The yellow crystals, precipitated, were filtered and washed with ethanol to give **4b** (1.6 g, 71% yield), mp: > 300°C; uv (nm) : λ_{max} ($\varepsilon \times 10^3$) 242 (14.6), 291 (14.7), (0.1 N HCl) ; λ_{max} ($\varepsilon \times 10^3$) 240 (15.8), 289 (13.0), (0.1 N NaOH) ; ir : 1676 cm^{-1} ($\nu_{exoC=N}$) ; ms (EI) : *m/z* 243 (M$^+$) ; ^{1}H-nmr (10% CF_3COOD/DMSO-d6) 7.37 ~ 7.92 (m, 5H, Ph-H), 8.19 (s, 1H, H-8), 9.89 (brs, 1H, NH). Anal. Calcd for $C_{11}H_9N_5S \cdot 1/3H_2O$: C, 53.00; H, 3.64; N, 28.22; S, 12.86. Found : C, 53.06; H, 3.55; N, 28.11; S, 12.91.

The filtrate was evaporated to dryness and the residue was purified by column chromatography on silica gel using 2%$CH_3OH/CHCl_3$ as an eluent to give **5** (800 mg, 21% yield), mp : 266~270°C; uv (nm) : λmax ($\varepsilon \times 10^3$) 255 (34.9), 303 (24.4), 419 (20.5), (H_2O) ; λ_{max} ($\varepsilon \times 10^3$) 294 (27.5), 389 (20.2), (0.1 N HCl) ; λ_{max} ($\varepsilon \times 10^3$) 324 (18.3), 354sh (4.3), (0.1 N NaOH) ; ms (FAB) : *m/z* 379 (M + 1) ; ^{1}H-nmr (DMSO-d6) 7.07 ~ 7.63 (m, 10H, Ph-H), 8.00 (s, 1H, H-8), 10.32, 10.40 (brs, 1/2H, NH), 11.09, 11.24 (brs, 1/2H, NH) ; ^{13}C-nmr (DMSO-d6) 120.06, 121.65, 122.73, 123.22, 124.05, 124.98, 128.22, 128.66, 139.52 (Ph-C), 139.54 (C-8), 154.97 (C-4), 156.82 (C-6), 185.00 (C-2), 186.45

(C=S). Anal. Calcd for $C_{18}H_{14}N_6S_2 \cdot 1/3H_2O$: C, 56.23; H, 3.85; N, 21.86; S, 16.68. Found : C, 56.17, H, 3.82; N, 21.58; S, 16.74

6–Phenylamino–9*H*–purine–2(3*H*)–thione (7). The title compound was prepared by reaction of **3** (800 mg, 7.4 mmol) with phenyl isothiocyanate (1.32 ml, 11.1 mmol) according to the procedure of Grözinger and Onan.[9] The yield of **7** was 1.12 g (62%), mp : > 300°C. The data of ^{1}H–nmr, ms and uv agreed with reported values. Anal. Calcd for $C_{11}H_9N_5S$: C, 54.31; H, 3.37; N, 28.91; S, 13.18. Found : C, 53.98; H, 3.58; N, 28.62; S, 12.88.

1,6–Dihydro–1–phenyl–6–imino–9*H*–purine (8). The compound **(4b)** of 200 mg was dissolved in DMF (20 ml) by heating. To the solution was added Raney nickel (1 ml) and the mixture was stirred for 2h at room temperature. The precipitated cystals were sparated from the catalysis by decantation. After evaporation of DMF, methanol (20 ml) was added to the residue. The insoluble crystals were collected by filtration and washed with methanol to give **8** (85 mg), mp : > 290°C; uv (nm) : λ_{max} ($\varepsilon \times 10^3$) 260 (0.92), (H_2O) ; λ_{max} ($\varepsilon \times 10^3$) 259 (10.7), (0.1 N HCl) ; λ_{max} ($\varepsilon \times 10^3$) 274 (11.2), (0.1 N NaOH) ; ms (EI) : *m/z* 211 (M^+) ; ^{1}H–nmr (DMSO–d_6+CF_3COOD) 7.71 (s, 10H, Ph–H), 8.45 (brs, 1H, NH), 8.55 (s, 1H, H–8 or H–2), 8.57 (s, 1H, H–8 or H–2), 9.92 (brs, 1H, NH).

6–Phenylamino–9*H*–purine (9). To a solution of 7 (100 mg) in ethanol (10 ml) and 1N NaOH (1 ml) was added Raney nickel (0.5 ml). The mixture was stirred for 1h at 80°C. The catalysis was filtered off and then the filtrate was neutralized with dilute acetic acid. The precipitated cystals were collected by filtration and washed with water to give **9** (37 mg), mp : 247 ~ 250°C ; uv (nm) : λ_{max} ($\varepsilon \times 10^3$) 290 (20.7), (H_2O) ; λ_{max} ($\varepsilon \times 10^3$) 287 (14.8), (0.1 N HCl) ; 297 (23.7), (0.1 N NaOH) ; ms (EI) : *m/z* 211 (M^+) ; ^{1}H–nmr (DMSO–d_6) 7.03 (t, J=6.84, 1H, p–Ph–H), 7.33 (t, J=7.81, 2H, m–Ph–H), 7.96 (d, 1H, H–8 or H–2), 9.72 (s, 1H, NH), 12.95 (brs, 1H, NH).

6,9–Dihydro–2–ethoxycarbonylamino–6–ethoxycarbonylimino–1–thiapurine (12c). To a stirred solution of **3** (1.2 g, 11 mmol) in dry pyridine (25 ml) was added ethoxycarbonyl isothiocyanate (2.0 ml, 17 mmol), and the mixture was stirred at 50°C for 3 h. After evaporation of the solvent, ethanol (150 ml) was added to the residue. Yellow crystals, precipitated, were collected by filtration and washed with ethanol to give **9c** (840 mg). In addition, The compound **(9c)** of 200 mg was obtained by the concentration of the mother liquor. Total yield was 1.04 g (60%), mp : > 290°C; uv (nm) : λ_{max} ($\varepsilon \times 10^3$) 246 (24.6), 289 (8.3), 298sh (7.5), 352 (14.1), (H_2O) ; uv (nm) : λ_{max} ($\varepsilon \times 10^3$) 248 (39.2), 287 (7.3), 354 (12.7), (0.1 N HCl) ; λ_{max} ($\varepsilon \times 10^3$) 275 (32.2), 378 (14.1), (0.1 N NaOH) ; ms (FAB) : *m/z* 312 (M+1) ; ^{1}H–nmr (DMSO–d_6) 1.25 ~ 1.29 (m, 6H, CH_3), 4.16 ~ 4.23 (m, 4H, CH_2), 8.28 (s, 1H, H–8), 11.67 (s, 1H, NH), 13.72 (br s, 1H, NH) ; ^{13}C–nmr (DMSO–d_6) 14.21 (CH_3), 38.88, 39.10 (CH_2), 112.03 (C–5), 143.52 (C–8), 152.96 (C=O), 156.54 (C–4), 156.95 (C–6), 159.36 (C–2) ,161.21 (C=O). Anal. Calcd for $C_{19}H_{13}N_5O_2S \cdot 3/5H_2O$: C, 59.09; H, 3.55; N, 18.13; S, 8.32. Found : C, 59.36; H, 3.87; N, 17.90; S, 7.98.

6,9-Dihydro-2-n-benzamido-6-benzoylimino-1-thiapurine (12d). The title compound was prepared from **3** and benzoyl isothiocyanate following the procedure described above. The yield was 2.17g (53%), mp : 160 ~ 161°C ; uv (nm) : λ_{max} ($\varepsilon \times 10^3$) 256 (2.6), 313 (8.2), 388 (16.3), (H_2O) ; λ_{max} ($\varepsilon \times 10^3$) 261 (20.7), 367 (15.0), (0.1 N HCl) ; λ_{max} ($\varepsilon \times 10^3$) 256 (22.4), 282 (24.1), 401 (16.0), (0.1 N NaOH) ; ms (EI) : *m/z* 375 (M^+) ; ^{1}H-nmr (DMSO-d6) 7.54 ~ 7.58 (m, 4H, *m*-Ph-H), 7.62 ~ 7.68 (m, 2H, *p*-Ph-H), 8.10 (d, J=7.81, 2H, *o*-Ph-H), 8.43 (d, J=7.32, 2H, *o*-Ph-H), 8.51 (H-8), 12.33 (brs, 1H, NH), 13.81 (brs, 1H, NH) ; ^{13}C-nmr (DMSO-d6) 113.57 (C-5), 128.45 (Ph-C-1), 128.33, 129.84 (Ph-C-2), 132.07 (Ph-C-1), 132.62, 132.81 (Ph-C-4), 135.75 (Ph-C-1), 144.13 (C-8), 156.84 (C-4), 157.88 (C-6), 158.30 (C-2), 166.27, 175.00 (C=0). Anal. Calcd for $C_{19}H_{13}N_5O_2S \cdot 3/5H_2O$: C, 59.09 ; H, 3.55 ; N, 18.13 ; S, 8.33. Found : C, 59.36 ; H, 3.87 ; N, 17.90 ; S, 7.98.

1,6-Dihydro-1-n-butyl-6-imino-9*H*-purine-2(3*H*)-selenone (13). n-Butyl isoselenocyanate[13] (1.3 g, 8 mmol)was added to a solution of **3** (572 mg, 5.3 mmol) in dry pyridine (15 ml), and mixture was heated at 50°C for 16 h. The precipitated crystals were filtered and washed with 50% C_2H_5OH/H_2O to give **13** (563 mg, 39%), mp : > 300°C; uv (nm) : λ_{max} ($\varepsilon \times 10^3$) 249 (19.4) , (0.1 N HCl) ; λ_{max} ($\varepsilon \times 10^3$) 246 (20.10) , 269 (15.9) , (0.1 N NaOH) ; ir : 1667 cm^{-1} ($\nu_{exoC=N}$) ; ms (EI) : *m/z* 271 (M^+) ; high resolution-mass : calcd. for $C_{12}H_{13}N_5Se$, 271.0336; found : 271.0321 ; ^{1}H-nmr (DMSO-d6+CF_3COOD) 0.93 (t, J=7.32, 3H, CH_3), 1.45 (sex, J=7.33, 2H, CH_2), 1.79 (qui, J=7.32, 2H, CH_2), 4.48 (brt, 2H, NCH_2), 8.41 (s, 1H, H-8), 9.65 (brs, 1H, NH) ,9.99 (brs, 1H, NH) ; ^{13}C-nmr (DMSO-d6+CF_3COOD) 13.51 (CH_3), 19.05 (CH_2), 29.11 (CH_2), 51.55 (NCH_2), 143.52 (C-8), 148.02 (C-6), 150.27 (C-2) .

The filtrate was evaporated to dryness and the residue was purified by column chromatography on silica gel using 6% $CH_3OH/CHCl_3$ as an eluent to give an unknown-structural compound (200 mg, 14%) mp : 212~215 °C; uv (nm) : λ_{max} ($\varepsilon \times 10^3$) 276 (10.5), (0.1 N HCl), λ_{max} ($\varepsilon \times 10^3$) 305 (16.2), (0.1 N NaOH) ; ms (EI) : *m/z* 271 (M^+), high resolution-mass : calcd. for $C_{12}H_{13}N_5Se$, 271.0336; found : 271.0307 ; ^{1}H-nmr (DMSO-d₆ + CF_3COOD) 0.67 (t, J=7.32, 3H), 1.09 (sex, J=7.33, 2H), 1.49 (qui, J=7.33, 2H), 3.96 (t, J=6.83, 2H) 7.49 (brs, 2H, N-H), 8.31 (s, 1H) ; ^{13}C-nmr (DMSO-d6 + CF_3COOD) 13.26, 19.92, 31.40, 44.71, 119.35, 142.68, 145.92, 149.578, 150.01.

6,9-Dihydro-2-benzhydrylamino-6-(3-benzhydrylureido)imino-1-selenapurine (15). To a stirred solution of **3** (400 mg, 3.7 mmol) in dry pyridine (30 ml) was added benzhydryl isoselenocyanate[17] (1.5 g, 5.5 mmol), and the mixture was stirred at 50°C for 6 h. After evaporation of the solvent, the residue purified by column chromatography on silica gel using $CHCl_3$ as an eluent to give **15** (1.0 g, 41%), mp : 160 ~ 165 °C; uv (nm) : λ_{max} ($\varepsilon \times 10^3$) 378 (11.3), 437 (9.4), (H_2O) ; λ_{max} ($\varepsilon \times 10^3$) 377 (11.2), 420 (8.1), (0.1 N HCl) ; λ_{max} ($\varepsilon \times 10^3$) 381 (10.5), 428sh (8.1), (0.1 N NaOH) ; high resolution-mass (FAB) : calcd for $C_{32}H_{27}N_6Se_2$ 655.0639, found : 655.0633; ^{1}H-nmr (DMSO-d6) 6.52 (d, J=9.77, 1H, $HCPh_2$), 6.93 (d, J=9.30, 1H, $HCPh_2$), 8.15 (s, 1H, H-8), 9.22 (d, J=7.81, 1H, HN), 10.43 (d, J=8.06, 1H, NH) ; ^{13}C-nmr (DMSO-d_6) 58.94 ($CHPh_2$), 63.55 ($CHPh_2$), 126.15 (C-5), 126.72, 126.95, 127.08, 127.16, 127.36, 127.82, 128.13, 128.33, 128.55, 128.95 (Ph-C), 138.07 (C-8), 140.31, 140.51, 141.29, 141.48 (Ph-C), 142.12 (C-4), 160.70 (C-6), 183.50 (C-2), 188.31 (C=Se).

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