A Series of Novel Acyclic Nucleosides. II. [1]. Synthesis of Acyclic Nucleosides Bearing an Imidazo[4,5-*d*][1,3]oxazine Ring

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Novel acyclic nucleosides **3a,b,c** where N-1 of acyclovir is replaced by oxygen atom were prepared.

Thus, 1-[(2-acetoxyethoxy)methyl]-5-amino-4-ethoxycarbonylimidazole (**9**) was treated with ethoxycarbonyl isothiocyanate or benzoyl isothiocyanate to give **11e,f**. Methylation of the latter with methyl iodide afforded *S*-methylisothiourea derivative **12f** which was treated with alkali and subsequently the mixture was neutralized to give 5-amino-3-[(2-hydroxyethoxy)methyl]-3*H*-imidazo[4,5-*d*][1,3]oxazin-7-one (**3a**). Compounds **3b,c** were obtained by treatment of acetic anhydride or propionic anhydride with sodium 5-amino-1-[(2-hydroxyethoxy)methyl]imidazole-4-carboxylate (**7**) which was prepared *via* 5-amino-[(2-acetoxyethoxy)methyl]-imidazole-4-carboxamide (**5**). Evaluation of acyclic oxanosine analogs for cytotoxicity and activity against herpes simplex virus type 1 (HSV-1) revealed that all the derivatives tested were inactive, but cytotoxicity were similar or less as compared to that of acyclovir.

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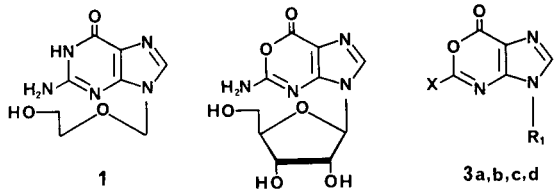
9-[(2-Hydroxyethoxy)methyl]guanine (**1**, acyclovir, Zovirax) may be one of the most efficient and the least cytotoxic drugs in the treatment of viral infection caused by herpes viruses [2]. There are, however, still some problems associated with acyclovir *viz.*, its poor water solubility and rapid development of resistant viruses. In order to search for more effective antiviral agents, chemical synthesis of acyclovir analogs in which the carbohydrate moiety is replaced by an acyclic substituent has been extensively studied [13]. In the course of these studies, several new compounds with significantly improved antiviral activity such as DHPG [4], (S)-HPMPA [5], BRL-39123 [6], and (RS)-2HM-HBG [7] were developed. Modifications of guanine moiety of acyclovir have received relatively minor attention and the studies along this line were limited [8-10]. Only tricyclic derivative which positions 1 and N-2 of acyclovir were linked together by an isopropeno group [9] and 8-substituted acyclovir (8-bromo, 8-iodo, and 8-methyl) [10] have been proven to be active as antiherpetic agents.

Figure 1

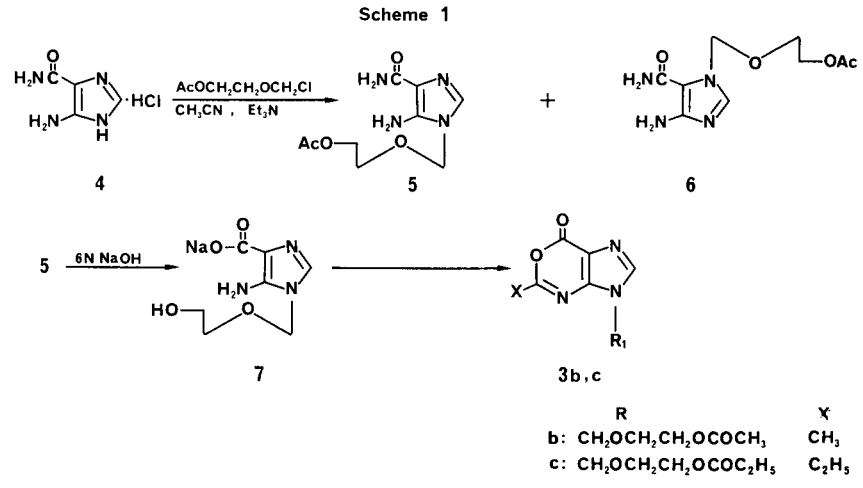


In order to define the function of position 1 in the interaction of drugs with the virus-encoded enzymes to exert antiviral activity, we planned to synthesize analogs in which N-1 is replaced by O, S, Se and sp^2 carbon. The compound that N-1 of acyclovir is substituted by oxygen atom can be also viewed as an analog of antibiotic oxanosine **2**, which was isolated from the Streptomyces by Shimada and coworkers in 1981 [11] and its chemical synthesis was achieved by Yagisawa and colleagues in 1983 [12]. This in a main reason why we initially planned to prepare the analog **3a** in which N-1 is displaced by oxygen atom.

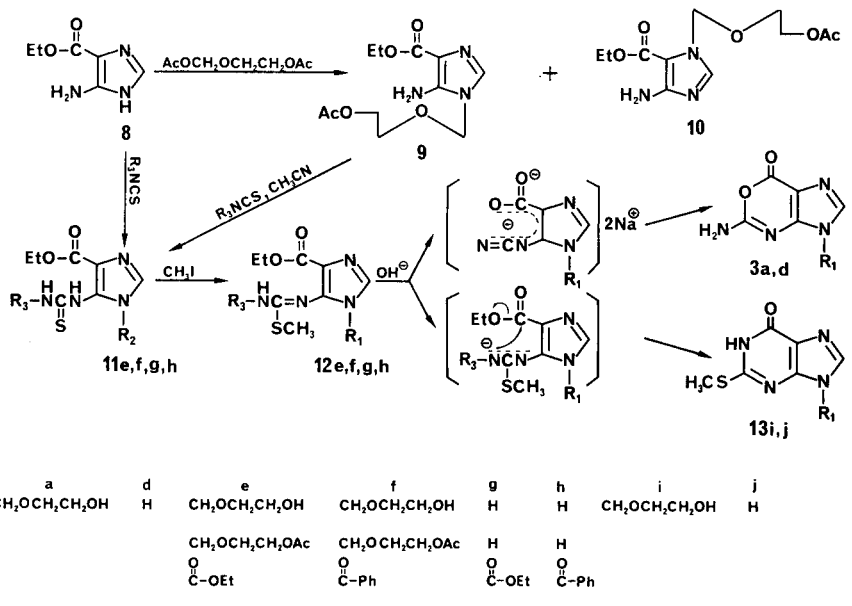
Theoretically the synthesis of the acyclic oxanosine analog, *viz.*, **3a**, would be achieved by several approaches. However, because of comparative stability of the oxanosine ring, we initially attempted to synthesize the acyclic oxanosine analogs by cyclization of the 1-[(2-hydroxyethoxy)methyl]imidazole. To this end, 1-[(2-hydroxyethoxy)methyl]-5-amino-4-carbamoylimidazole (**5**) was prepared in 35% yield according to the method of Beauchamp and coworkers from 4-amino-5-carbamoylimidazole hydrochloride (**4**) [8]. Treatment of **5** with 6*N* sodium hydroxide at reflux temperature for 4 hours provided corresponding sodium carboxylate **7** and it was reacted with acetic or propionic anhydride in refluxing pyridine. The solvent was removed *in vacuo* and then the desired product was isolated by a column chromatography on silica gel. Yield of **3b**, **3c** from **5** was 13%, 38%, respectively. Compound **3b** and **3c** were characterized by ^{1}H-nmr and mass spectrum.

Subsequently, synthesis of the final target where amino group was introduced to position 5 of imidazo[4,5-*d*]

Scheme 1



Scheme 2



[1,3]oxazine ring was accomplished *via* the route as shown in Scheme 2. 2-Acetoxyethoxymethylation of 5(4)-amino-4(5)-ethoxycarbonylimidazole (**8**) was then performed by fusion method (140°, 2 hours), without a catalyst and a pair of isomers **9** and **10** could be obtained in 19% and 32% yield, respectively. Two positional isomers could be easily isolated on column chromatography by using silica gel. In general, fusion method may usually utilize Lewis acid as the catalyst but in the case of alkylation of **8**, it turned out that Lewis acid such as *p*-toluenesulfonic acid or sulfanilic acid was of no use or reduced the yield to a considerable extent. For differentiation of two positional isomers **9** and **10**, ^{1}H-nmr spectra were particularly helpful. Thus, signals due to H-2 of **9** and **10** appeared at δ 7.25 and δ 7.69, respectively. H-2 signal of **9** should be more deshielded because of electron-withdrawing effect of 5-ethoxycarbonyl group. Therefore, the isomer having H-2 at δ 7.25 was assigned the 1-[(2-acetoxyethoxy)methyl]-5-amino-4-ethoxycarbonylimidazole structure and it was found that observed values were consistent with one in other ring system [13].

Compound **9** was then reacted with benzoyl isothiocyanate or ethoxycarbonyl isothiocyanate in acetonitrile (the former at room temperature for 4 hours and the latter at 40-50° for 16 hours). The resulting compounds **11e,f** of the thioureido type were purified by column chromatography on silica gel to give 96%, 88% yield, respectively. Compounds **11g,h** could be prepared in a similar way from **8** by use of benzoyl isothiocyanate or ethoxycarbonyl isothiocyanate in water or *N,N*-dimethylformamide in 80% and 70% yield. Methylation of **11e-h** with methyl iodide under alkaline conditions in an ice-water bath afforded **12e-h** in 82%, 60%, 77% and 66% respectively. When the methylation was carried out at room tempera-

ture, the yield of *S*-methyl derivatives **12e,f** decreased due to the formation of undesirable products **13i**. The structure of these compounds were confirmed by ^{1}H-nmr and mass spectral data.

In particular the use of benzoylthiocarbamoyl derivatives **11f** resulted in reduced yield to a considerable extent. Eventually we were capable of preparing desired acyclic oxanosine **3a** or its aglycon in 18% and 8% yield, respectively by treatment of **12e,g** with 1*N* sodium hydroxide or 6*N* sodium hydroxide at 95-100° followed by neutralization. Compounds **13i,j** were produced in 5% and 3% respective yield under the similar reaction conditions. Low yield of oxanosine aglycon in comparison with the acyclic oxanosine may come from the resistance of 4-ethoxycarbonyl group to hydrolysis due to deprotonation of imidazole moiety under alkaline conditions. Compounds **3a-d** were supported by the data of ^{1}H-nmr and mass spectrum. The uv spectra of **3a** was found to be completely superimposable with reported uv spectrum of oxanosine [11], confirming that the product is indeed 3-[(2-hydroxyethoxy)methyl] derivative.

The stability of **3a** in aqueous solution was examined by determing uv absorbance. It was found that **3a** is quite stable both in acid medium (down to *p*H 2) and alkaline region from *p*H 7 to *p*H 9. At region beyond *p*H 9.8, ring-opening of 1,3-oxazine ring immediately took place.

Results of Antiviral Screening.

New acyclic nucleosides were evaluated in terms of activity against HSV-1 by plaque reduction method. Cytotoxicity of each compound was determined by Vero cells.

The mechanism of action of acyclovir has been well documented. Thus, the drug may be initially phosphorylated by herpes virus-encoded thymidine kinase to the monophosphate [14,15], which may be subsequently phosphorylated to the triphosphate by cellular kinase [16,17]. The latter nucleotide may act as inhibitor against viral DNA polymerase and also acts as a chain terminater [18,19].

Table 1
Antiviral Test of Newly Prepared Oxanosine Analogs

Compound	50% Inhibitory Concentration μM	
	Plaque Reduction Assar HSV-1	Cytotoxicity Vero Calls
3a	100	1000
3b	420	600
3c	400	540
2	0.24	680

These acyclic oxanosine analogs were found to be inactive against HSV-1, but cytotoxicity is similar or less as compared to that of acyclovir (Table I). The lack of antiherpetic activity of **3a** that position 1 of guanine moiety of acyclovir is only displaced by oxygen atom presumably comes from inability to be a substrate for viral thymidine kinase involving the first step of above mentioned mechanism.

Some papers dealing with the substrate specificity of thymidine kinase coded by herpes simplex virus allegedly stated that the specificity is not stringent so far as the base moiety is concerned [14,20]. The present investigation, however, shows that this is not always the case at least with the modification at position 1 in guanine.

EXPERIMENTAL

Melting points were determined on Yanagimoto micro melting point apparatus, and are uncorrected. Nuclear magnetic resonance (nmr) spectra were obtained on JEOL-270 spectrometer using tetramethylsilane as an internal standard. Mass spectral measurements were run on a JEOL D-300 spectrometer. Ultraviolet (uv) spectra were measured on a Hitachi 200-20 spectrophotometer. Column chromatography was performed with Kiesel gel 60 (E. Merck, 70-230 mesh ASTM).

3-[(2-Acetoxyethoxy)methyl]-5-methyl-3*H*-imidazo[4,5-*d*][1,3]-oxazin-7-one (**3b**).

A stirred mixture of 0.5 g (2.1 mmoles) of **5** in 2 ml of 6*N* sodium hydroxide was heated in an oil bath at 100° for 2 hours. After cooling, 5 ml of 2-propanol was added to the reaction mixture and vigorously stirred. A syrup separated from the mixture was dried over phosphorus pentoxide in a vacuum desicator for 24 hours. Resulting powder (0.5 g) of pale brown color was dissolved in a mixture of pyridine (10 ml) and acetic anhydride (5 ml). The mixture was then heated at reflux temperature for 2 hours. After cooling, 5 ml of methanol was added to decompose excess acetic anhydride. The solution was concentrated to dryness *in vacuo*. The residue was chromatographed on a column of silica gel using ethyl acetate as an eluent to yield 72 mg (13%) of solid, mp 64-65°; uv (50% aqueous methanol): λ max 239 (ε 2260), 247 (ε 2330), 268 (ε 1790); (50% methanol-0.1*N* hydrochloric acid): 239 (ε 2510), 247 (ε 2190), 268 (ε 1490); ^{1}H-nmr (DMSO-d_6): δ 1.96 (s, 3H, $COCH_3$), 2.46 (s, 3H, CH_3), 3.68-3.72 (m, 2H, H-3'), 4.06-4.09 (m, 2H, H-4'), 5.52 (s, 2H, H-1'), 8.27 (s, 1H, H-2); ms: m/z 267 (M^+).

Anal. Calcd. for $C_{11}H_{13}N_3O_5$: C, 49.43; H, 4.90; N, 15.73. Found: C, 49.30; H, 4.87; N, 15.47.

5-Ethyl-3-[(2-propanoyl)methyl]-3*H*-imidazo[4,5-*d*][1,3]oxazin-7-one (**3c**).

A pale brown powder (0.35 g) which was obtained from **5** by the use of 6*N* sodium hydroxide as above was dissolved in 5 ml of pyridine and 2.5 ml of propionic anhydride. The mixture was heated at reflux temperature for 2.5 hours. After cooling, a reaction mixture was treated in a similar way as described above to give **3c** as a colorless glass, 190 mg (38%), mp 73-74°; uv (50% methanol-water): λ max 238 (ε 6730), 246 sh (ε 6240), 267 (ε 5220); (50% methanol-0.1*N* hydrochloric acid): 238 (ε 6900), 245 sh (ε 6190), 267 (ε 4030); ^{1}H-nmr (DMSO-d_6): δ 1.13 (t, 3H, CH_2CH_3), 1.35 (t, 3H, $COCH_2CH_3$), 2.31 (q, 2H, CH_2CH_3), 2.78 (q, 2H, $COCH_2CH_3$), 3.75 (t, 2H, H-4'), 4.22 (t, 2H, H-3'), 5.53 (s, 2H, H-1'), 7.84 (s, 1H, H-2); ms: m/z 295 (M^+).

Anal. Calcd. for $C_{13}H_{17}N_3O_5$: C, 52.87; H, 5.80; N, 14.23. Found: C, 52.72; H, 5.84; N, 14.24.

1-[(2-Acetoxyethoxy)methyl]-5-amino-4-ethoxycarbonylimidazole (**9**) and 3-[(2-Acetoxyethoxy)methyl]-5-amino-4-ethoxycarbonylimidazole (**10**).

Compound **6** (500 mg, 3.2 mmoles) and 0.8 ml (5.1 mmoles) of 2-oxa-1,4-butanediol diacetate [21] were placed in 10-ml round bottomed flask. The mixture was fused at 160° (oil bath temperature) and the heating was continued at 140° (oil bath temperature) for 2 hours. The process was repeated eight times. The combined reaction mixture was concentrated to dryness. The residue was chromatographed on a silica gel column, 1% methanol-chloroform being a eluting system. From early fractions, **10** (1.88 g, 27% yield, viscous oil) was obtained. From the latter fractions, **9** (1.33 g, 19% yield) was obtained, mp 86-87°C; uv (water): λ max 238 (ε 4300), 269 (ε 10900); (0.1*N* hydrochloric acid): 247 (ε 7700), 268 (ε 9900); (0.1*N*-sodium hydroxide): 269 (ε 10900); ^{1}H-nmr (DMSO-d_6): δ 1.25 (t, 3H, CH_2CH_3), 1.99 (s, 3H, $COCH_3$), 5.28 (s, 2H, H-1'), 6.12 (s, 2H, NH_2), 7.25 (s, 1H, H-2).

Anal. Calcd. for $C_{11}H_{17}N_3O_5$: C, 48.70; H, 6.32; N, 15.49. Found: C, 48.55; H, 6.45; N, 15.47.

Compound **10** had; uv (water): λ max 233 (ε 5500), 280 (ε 14600); (0.1*N* hydrochloric acid): 239 (ε 8000), 273 (ε 12100); (0.1*N* sodium hydroxide): 281 (ε 13400); ^{1}H-nmr (DMSO-d_6): δ 1.27 (t, 3H, CH_2CH_3), 1.98 (s, 3H, $COCH_3$), 5.47 (s, 2H, H-1'), 5.79 (s, 2H, NH_2), 7.69 (s, 1H, H-2).

Anal. Calcd. for $C_{11}H_{17}N_3O_5$: C, 48.70; H, 6.32; N, 15.49. Found: C, 48.88; H, 6.40; N, 15.52.

1-[(2-Acetoxyethoxy)methyl]-5-(*N*'-ethoxycarbonylthiocarbamoyl)amino-4-ethoxycarbonylimidazole (**11e**).

A mixture of **9**, 1 g (3.7 mmoles) and ethoxycarbonyl isothiocyanate, 0.88 ml (7.4 mmoles) in 15 ml of acetonitrile was heated at 50° for 16 hours. The solvent was removed *in vacuo* and then the residue was chromatographed on a column of silica gel using 0.75% methanol-chloroform as an eluting system to give 1.43 g (96%) of **11e** (viscous oil); uv (water): λ max 218 (ε 13950), 254 (ε 20200), 264 (ε 19920); (0.1*N* hydrochloric acid): 220 (ε 14640), 266 (ε 18830); (0.1*N* sodium hydroxide): 251 (ε 23020); ^{1}H-nmr (DMSO-d_6): δ 1.27 (m, 6H, CH_2CH_3), 3.63 (t, 2H, H-3'), 4.05 (t, 2H, H-4'), 4.21 (m, 4H, CH_2CH_3), 5.31 (s, 2H, H-1'), 7.89 (s, 1H, H-2), 11.13 (s, 1H, S=CNH), 11.69 (s, 1H, O=CNHC=S); ms: m/z 402 (M^+).

Anal. Calcd. for $C_{15}H_{22}N_4O_7S$: C, 44.77; H, 5.51; N, 13.92; S, 7.97. Found: C, 44.57; H, 5.50; N, 13.81; S, 8.02.

1-[(2-Acetoxyethoxy)methyl]-5-(*N*'-benzoylthiocarbamoyl)amino-4-ethoxycarbonylimidazole (**11f**).

A stirred mixture of **9**, 874 mg (3.2 mmoles) and benzoyl isothiocyanate, 0.52 ml (3.8 mmoles) in 8 ml of dry acetonitrile was allowed to stand at room temperature for 4 hours. The reaction mixture was worked up in the manner stated above to afford 1.22 g (88% yield) of **11f** (viscous oil), uv (water): λ max 250 (ε 20500), 285 sh; (0.1*N* hydrochloric acid): 249 (ε 20040), 280 (ε 15890); (0.1*N* sodium hydroxide): 242 (ε 24400); ^{1}H-nmr (DMSO-d_6): δ 1.19 (t, 3H, CH_2CH_3), 2.00 (s, 3H, $COCH_3$), 3.64-3.67 (m, 2H, H-3'), 4.07-4.12 (m, 2H, H-4'), 5.36 (s, 2H, H-1'), 7.53-7.58 (m, 2H, Ar-H, β), 7.65-7.71 (m, 1H, Ar-H, γ), 7.96 (s, 1H, H-2), 7.99-8.30 (m, 2H, Ar-H, α), 12.07 (s, 1H, NH), 12.16 (s, 1H, O=CNHC=S); ms: m/z 434 (M^+).

Anal. Calcd. for $C_{19}H_{22}N_4O_6S$: C, 52.52; H, 5.10; N, 12.90; S, 7.38. Found: C, 52.40; H, 5.11; N, 12.87; S, 7.28.

5-(*N*'-Ethoxycarbonylthiocarbamoyl)amino-4-ethoxycarbonylimidazole (**11g**).

A mixture of **8**, (249 mg, 1.5 mmoles) and 0.2 ml (1.7 mmoles) of ethoxycarbonyl isothiocyanate in 3 ml of dry *N*,*N*-dimethylformamide was stirred for 16 hours at 50°. The solvent was then removed *in vacuo* and the residue was triturated with 3 ml of chloroform. The product was collected by filtration. The yield was 310 mg (70%), mp 176-178°; uv (water): λ max 206 (ε 16730), 253 (ε 13560), 310 (ε 9960); (0.1*N* hydrochloric acid): 252 (ε 14830), 301 (ε 14920); (0.1*N* sodium hydroxide(: 264 (ε 23790), 329 (ε 24240); ^{1}H-nmr (DMSO-d_6): δ 1.25-1.33 (m, 6H, CH_2CH_3), 4.19-4.30 (m, 4H, CH_2CH_3), 7.64 (s, 1H, H-2), 11.53 (s, 1H, NH); ms: m/z 286 (M^+).

Anal. Calcd. for $C_{10}H_{13}N_4O_4S$: C, 41.95; H, 4.93; N, 19.57; S, 11.20. Found: C, 42.15; H, 5.05; N, 19.41; S, 11.35.

5-(*N*'-Benzoylthiocarbamoyl)amino-4-ethoxycarbonylimidazole (**11h**).

A mixture of 500 mg (3.2 mmoles) of **8** and 0.52 ml (3.9 mmoles) of benzoyl isothiocyanate in 20 ml of water was stirred for 2 hours at room temperature. A deposited precipitate was filtered and then washed with water and dried over phosporus pentoxide in a desiccator. The yield of **11h** was 820 mg (80%), mp 189-190°; uv (water): λ max 244 (ε 9540), 276 (ε 10670), 325 (ε 6800); (0.1*N* hydrochloric acid): 250 sh (ε 8150), 278 (ε 12540); 312 (ε 7720); (0.1*N* sodium hydroxide): 240 sh (ε 11790), 292 (ε 8930); ^{1}H-nmr (DMSO-d_6): δ 1.30 (t, 3H, CH_2CH_3), 4.28 (q, 2H, CH_2CH_3), 7.52-7.70 (m, 3H, Ar-H-β,γ), 7.98-8.01 (m, 2H, Ar-H-α), 11.80 (s, 1H, NH); ms: m/z 318 (M^+).

Anal. Calcd. for $C_{14}H_{14}N_4O_3S$: C, 52.82; H, 4.43; N, 17.60; S, 10.07. Found: C, 52.74; H, 4.45; N, 17.55; S, 10.27.

5-(*N*'-Ethoxycarbonyl-*S*-methylisothiocarbamoyl)amino-1-[(2-hydroxyethoxy)methyl]-4-ethoxycarbonylimidazole (**12e**).

Methyl iodide (0.19 ml, 3.13 mmoles) was added to a stirred solution of **11e** (840 mg, 2.09 mmoles) in 5 ml of methanol and 3.5 ml of 1*N* sodium hydroxide in an ice bath. The mixture was allowed to stand at the same temperature for 2.5 hours. The solvent was distilled off and the residue was subjected to a column chromatography on a silica gel using 1.5% methanol-chloroform as a eluting system. Yield of **12c** was 640 mg (82%), mp 100-101°; uv (water): λ max 241 (ε 10520), 288 (ε 4790); (0.1*N* hydrochloric acid): 245 (ε 10790), 285 (ε 6180); (0.1*N* sodium hydroxide): 244 (ε 15690); ^{1}H-nmr (DMSO-d_6): δ 1.18 (m, 6H, CH_2CH_3), 2.36 (s, 3H, SCH_3), 3.24 (m, 4H, CH_2CH_3), 4.01-4.12 (m, 4H, H-3' and H-4'), 5.12 (s, 2H, H-1'), 7.62 (s, 1H, H-2), 10.05 (s, 1H, NH); ms: m/z 374 (M^+).

Anal. Calcd. for $C_{14}H_{22}N_4O_6S$: C, 44.91; H, 5.92; N, 14.96; S, 8.56. Found: C, 45.05; H, 5.94; N, 14.81; S, 8.47.

5-(*N*'-Benzoyl-*S*-methylisothiocarbamoyl)amino-4-ethoxycarbonylimidazole (**12g**).

Methyl iodide (0.2 ml, 3.1 mmoles) was added to a stirred suspension **11h** (820 mg, 2.58 mmoles) in 38 ml of 1*N* sodium hydroxide with ice-water cooling. The mixture was allowed to stand at the same temperature for 1.5 hours. The precipitate was filtered off, washed with water dried. Yield of **12g** was 567 mg (66%), mp 196-200°; uv (water): λ max 252 (ε 25380), 322 (ε 10700); (0.1*N* hydrochloric acid): 246 (ε 32790), 300 sh (ε 10230);

^{1}H-nmr (DMSO-d_6): δ 1.32 (t, 3H, CH_2CH_3) 2.47 (s, 3H, SCH_3), 4.28 (q, 2H, CH_2CH_3), 7.53-8.00 (m, 5H, aromatic protons), 13.23 (s, 1H, NH), 14.06 (s, 1H, H_3SCNH); ms: m/z 332 (M^+).

Anal. Calcd. for $C_{15}H_{16}N_4O_3S$ 1/3H_2O: C, 53.24; H, 4.96; N, 16.55; S, 9.48. Found: C, 53.06; H, 4.76; N, 16.55; S, 9.63.

5-Amino-3-[(2-hydroxyethoxy)methyl]-3*H*-imidazo[4,5-*d*][1,3]-oxazin-7-one (**3a**).

Compound **12e** (100 mg, 0.27 mmole) was dissolved in 2 ml of 1*N* sodium hydroxide. The solution was heated at 95-100° for 30 minutes. After cooling, the reaction mixture was neutralized with dilute acetic acid and then was purified by high performance liquid chromatography (column: Senshu Pack ODS-5201-s, developing solvent: 18% methanol-water). The yield of **3a** was 11.2 mg (18%), mp 190-192°; uv (water): λ max 205 (ε 16700), 246 (ε 9240), 287 (ε 6730); (0.1*N* hydrochloric acid): 248 (ε 8810), 286 (ε 6410); (0.1*N* sodium hydroxide): 273 (ε 7980); ^{1}H-nmr (DMSO-d_6): δ 3.47 (s, 4H, H-3' and H-4'), 5.33 (s, 2H, H-1'), 7.85 (s, 1H, H-2), 7.88 (s, 2H, NH_2); ms: m/z 226 (M^+) high-resolution mass: Calcd. for $C_8H_{10}N_4O_4$: 226.0702. Found: m/z 266.0697.

5-Amino-3*H*-imidazo[4,5-*d*][1,3]oxazin-7-one (**3d**).

Compound **12g** (100 mg, 0.33 mmole) was dissolved in mixture of 1 ml of 6*N* sodium hydroxide and 0.6 ml of water was worked up in the manner stated above. The yield of **3d** was 4 mg (8%), mp 228-230°; uv (water): λ max 208 (ε 6120), 243 (ε 7440), 287 (ε 6420); (0.1*N* hydrochloric acid): 206 (ε 3300), 246 (ε 8270), 288 (ε 5780); (0.1*N* sodium hydroxide): 250 sh, 282 (ε 10950); ^{1}H-nmr (DMSO-d_6): δ 763 (s, 2H, NH_2), 7.73 (s, 1H, H-2), 12.71 (s, 1H, NH); ms: m/z 152 (M^+), high-resolution mass: Calcd. for $C_5H_4O_2N_4$: 152.0334. Found: m/z 152.0352.

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