The synthesis of potential DNA intercalators.
Part 3. Triazanaphthalenes, tetraaza-anthracenes and -phenanthrenes from isoxazolones

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Abstract
The reaction of bis-isoxazolinyl pyrimidines and pyrazines with bases leads to a novel synthesis of tri- and tetra azaheterocycles, capable of intercalation with DNA.

Keywords: 2,4-Dichloropyrimidine, 3,6-dichloropyridazine, 4-ethoxycarbonyl isoxazolone, bis-isoxazolinylpyrimidines, bis-isoxazolinylpyridazine

Introduction
We have previously shown\textsuperscript{1,2} that 2-isoxazolinyl azaheterocycles undergo rearrangement in the presence of bases, resulting in the annulation of a pyrimidine ring onto the azaheterocycle (Scheme 1). By contrast, the use of triethylamine,\textsuperscript{3} photolysis\textsuperscript{4} or pyrolysis\textsuperscript{5} led to annelation of an imidazole ring onto the azaheterocycle (Scheme 1).

\begin{center}
\textbf{Scheme 1}
\end{center}
This work was extended to the reaction of bis-isoxazolinyldiazaheterocyclic systems, in which the rearrangements underwent more complex, but mechanistically consistent, pathways (Scheme 2).

Scheme 2

When the isoxazoline moiety contained an arylamino group at C-3, base induced rearrangements led to competitive cyclisation through the arylamino group or the azaheterocycle, depending on the nucleophilicity of the latter (Scheme 3).

Scheme 3

Since imidazo[1,2-α]azaheterocycles such as those in Scheme 3 above may be converted to larger heterocycles that can be expected to intercalate with DNA because of their H-bonding donor and acceptor groups, this work was extended to bis-isoxazolinyldiazaheterocycles.

Structures 1, 2, and 4 are clearly well set up as precursors for polycyclic structures which are of considerable interest as pharmacophores for therapeutic drugs. Such compounds have been used to reduce neurotoxin injury associated with anoxia or ischemia, or as antiviral agents. Tricyclic aza-heterocycles also display platelet-derived growth factor inhibitory activity.
Unfortunately, no definitive pattern emerged, that would allow prediction of the structure of the products from their reaction with bases. Thus, while the quinoxaline 3 gave the bis-imidazoquinoxaline 4, the corresponding phthalazine 5 underwent partial annelation through the benzene ring to give 6 (Scheme 4).

Scheme 4

In this paper we intended to extend the range of bis-isoxazolones investigated, in the hope of more clearly defining the synthetic utility of this mode of heterocyclic synthesis. Herein we report the synthesis of the bis-isoxazolinylypyrimidines (7-14) and pyridazines (15-17), and the base catalysed reactions of 7-10, 13 and 15.
Results and Discussion

2,4-Dichloro-6-methylpyrimidine reacted with the 4-ethoxycarbonylisoxazolone 18 when heated briefly to 130 °C to give the bis substituted pyrimidine 7. Similarly, heating the pyrimidine with the 3-phenylamino- 19 or 3-(3-bromophenyl)aminoisoxazolone 20 gave the bis substituted pyrimidines 8 and 9 respectively (Scheme 5).

Scheme 5

Reaction of pyrimidine 7 with potassium carbonate in THF gave the bis-annelated tetraazaphenanthrene 21, rather than the anticipated 22: a suggested pathway for such a product is shown in Scheme 6. Some support for this pathway was found in the observation that reaction of 7 with potassium carbonate in ethanol gave the product 23 (Scheme 7).
The reaction of the aminoaryl derivatives 8 and 9 with potassium carbonate in THF followed the hoped pathway, with the annelation of two imidazole rings onto the pyrimidine to give 24 and 25 (Scheme 8).
Scheme 8

Reaction of 4,6-dichloro-5-nitropyrimidine with the isoxazolones 18 by heating neat under nitrogen at 130 °C gave bis substituted pyrimidine 10, but only mono substituted pyrimidines 11 and 12 were formed by heating the isoxazolones 19 and 20 with 4,6-dichloro-5-nitropyrimidine (Scheme 9).
Scheme 9

The reaction of 10 with sodium hydroxide at room temperature gave 26 while under reflux conditions afforded 27 (Scheme 10). A number of alternative tautomeric structures for 26 and 27 can be written.

Scheme 10
Similarly, 13 and 14 were obtained from the isoxazolones 18 and 19 with 4,6-dichloropyrimidine. The 4,6-bisisoxazolinylpyrimidines 13 reacted with sodium hydroxide at 40 °C to give the tetraazaanthracene 28 (Scheme 11).

![Scheme 11](image)

Similarly, the bis-isoxazolinyl derivative 15 reacted with sodium hydroxide to afford the tetraazaanthracene 29 (Scheme 12).

![Scheme 12](image)

**Conclusions**

The above base-catalyzed rearrangements again illustrate that the synthesis of several new tri- and tetra heterocycles appears possible, and because of their multiple H-bonding and H-acceptor sites, these compounds could be expected to intercalate with DNA.\(^8\)\(^{-10}\) They could also serve as intermediates for new planar polycyclic heterocycles.
Experimental Section

General. Freshly distilled solvents were used throughout, and anhydrous solvents were dried according to Perrin and Armarego. Melting points were determined on a Philip Harris C4954718 apparatus and are uncorrected. Infrared spectra were recorded on a Thermonicolet (Nexus 670) FT-infrared spectrometer, using sodium chloride cells and measured as film or KBr disks. 1H (300 MHz) and 13C (75.5 MHz) NMR measurements were recorded on a Bruker 300 spectrometer in DMSO-d6, CD2Cl2 or CDCl3 using TMS as the internal reference. Mass spectra were recorded on a Varian Matt 311 spectrometer and relative abundances of fragments are quoted in parentheses after the m/z values.

General Procedure. 6-Methyl-2,4-bis(4-ethoxycarbonyl-5-oxo-2,5-dihydroisoxazolin-2-yl)pyrimidine (7)
Ethyl 5-oxo-2,5-dihydroisoxazole-4-carboxylate (18) (100 mg, 0.637 mmol) and 2,4-dichloro-6-methylpyrimidine (52 mg, 0.318 mmol) were heated neat under nitrogen at 130 °C for 15 min. The resulting product was recrystallised from ethanol to give the bis-isoxazolinyl derivative 7 (103 mg, 80%) as a white solid, mp 201-204 °C (lit16, 202-204 °C).

1H NMR (DMSO-d6) δ 1.29 (t, J=7.2 Hz, 6H), 2.49 (s, 3H), 4.27 (q, J=7.2 Hz, 2H), 4.28 (q, J=7.2 Hz, 2H), 7.35 (s, 1H), 10.25 (s, 1H), 10.33 (s, 1H); 13C NMR (DMSO-d6) δ 14.68, 24.47, 60.89, 61.05, 96.33, 97.01, 103.34, 148.68, 149.38, 151.03, 153.38, 160.69, 160.9, 163.1, 163.66, 173.78; FT-IR (KBr) νmax / cm⁻¹: 1805, 1783, 1708, 1556, 1440, 1240, 1213, 1023, 765.

6-Methyl-2,4-bis(4-ethoxycarbonyl-3-phenylamino-5-oxo-2,5-dihydroisoxazolin-2-yl)pyrimidine (8).
The same procedure as above with ethyl 5-oxo-3-phenylamino-2,5-dihydroisoxazole-4-carboxylate (19) (100 mg, 0.4 mmol) gave 8 (82 mg, 70%) as a cream solid, mp 174-175 °C.

1H NMR (CDCl3) δ 1.28 (t, J=7.2 Hz, 3H), 1.39 (t, J=7.2 Hz, 3H), 2.25 (s, 3H), 4.27 (q, J=7.2 Hz, 2H), 4.37 (q, J=7.2 Hz, 2H), 6.86 (s, 1H), 6.95 (d, J=7.8 Hz, 2H), 7.04-7.32 (m, 8H), 10.13 (s, 1H), 10.4 (s, 1H); 13C NMR (CDCl3) δ 14.21, 14.38, 23.98, 60.98, 61.09, 78.73, 79.03, 106.36, 121.19, 121.39, 125.97, 126.27, 129.23, 129.4, 137.53, 137.64, 152.96, 157.16, 159.54, 160.32, 162.66, 162.92, 163.63, 164.9, 171.15; FT-IR (KBr) νmax / cm⁻¹: 3423, 1786, 1617, 1585, 1371, 1350, 1013, 764; MS m/z (%) 586(M⁺, 4), 538(22), 497(12), 404(24), 216(54), 214(28), 178(27), 144(76), 76(100).

6-Methyl-2,4-bis(4-ethoxycarbonyl-3-(3-bromophenylamino)-5-oxo-2,5-dihydroisoxazolin-2-yl)pyrimidine (9).
The same procedure as above with ethyl 3-(3-bromophenyl)amino-5-oxo-2,5-dihydroisoxazole-4-carboxylate (20) (100 mg, 0.3 mmol) gave 9 (85 mg, 75%) as a cream solid, mp 185-187 °C. 1H NMR (CDCl3) δ 1.27 (t, J=7.2 Hz, 3H), 1.36 (t, J=7.2 Hz, 3H), 2.18 (s, 3H), 4.26 (q, J=7.2 Hz, 2H), 4.35 (q, J=7.2 Hz, 2H), 6.92 (s, 2H), 7.06 (t, J=7.2 Hz, 1H), 7.16-7.35 (m, 6H), 10.21 (s, 1H), 10.5 (s, 1H); 13C NMR (CDCl3) δ 14.21, 14.34, 24.11, 61.19, 61.29, 79.29, 79.74, 105.56, 119.88, 120.54, 122.71, 122.83, 124.51, 124.95, 129.06, 129.28, 130.48, 130.84, 138.93, 139.01, 152.77, 157.19, 158.97, 159.95, 162.34, 162.52, 163.04, 164.47, 171.23;
FT-IR (KBr) ν<sub>max</sub> / cm<sup>-1</sup>: 3432, 1789, 1612, 1586, 1370, 1348, 1202, 1030; MS m/z (%) 744(M<sup>+</sup>) 4, 700(10), 656(21), 652(29), 563(12), 292(66), 180(100), 153(69), 88(92), 45(100).

4,6-Bis(4-ethoxycarbonyl-5-oxo-2,5-dihydroisoxazolin-2-yl)-5-nitropyrimidine (10). Ethyl 5-oxo-2, 5-dihydroisoxazole-4-carboxylate (18) (100 mg, 0.637 mmol) and 2,4-dichloro-5-nitropyrimidine (61.7 mg, 0.318 mmol) were heated neat under nitrogen at 130 °C for 15 min. The resulting product was recrystallised from ethanol to give the isoxazolone (10) (111 mg, 80%) as white solid, mp 206-208 °C. ¹H NMR (DMSO-d<sub>6</sub>) δ 1.27 (t, J=7.2 Hz, 6H), 4.25 (q, J=7.2 Hz, 4H), 9.04 (s, 1H), 9.77 (s, 2H); ¹³C NMR (DMSO-d<sub>6</sub>) δ 14.45, 61.48, 98.44, 145.04, 149.62, 157.77, 159.86, 162.35; FT-IR (KBr) ν<sub>max</sub> / cm<sup>-1</sup>: 1816, 1708, 1538, 1447, 1373, 1196, 1021, 980, 770; MS m/z (%) 435(M<sup>+</sup>), 26, 389(5), 314(3), 268(3), 117(10), 68(39), 52(100).

4-Chloro-6-(4-ethoxycarbonyl-3-phenylamino-5-oxo-2,5-dihydroisoxazolin-2-yl)-5-nitropyrimidine (11). Using the same procedure as above with 5-oxo-3-phenylamino-2,5-dihydroisoxazole-4-carboxylate (19) (6) (100 mg, 0.4 mmol) gave 11 (119 mg, 73%) as white crystals, mp 192-194 °C.

General procedure. 4,6-Bis-(4-ethoxycarbonyl-5-oxo-2,5-dihydroisoxazolin-2-yl)pyrimidine (13) Ethyl 5-oxo-2,5-dihydroisoxazole-4-carboxylate (18) (100 mg, 0.637 mmol) and 2,4-dichloropyrimidine (47.4 mg, 0.318 mmol) were heated neat under nitrogen at 130 °C for 15 min. The resulting product was recrystallised from ethanol to give the isoxazolone 13 (111 mg, 80%) as a white solid, mp 206-208 °C. ¹H NMR (CDCl<sub>3</sub>) δ 1.39 (t, J=7.2 Hz, 6H), 4.38 (q, J=7.2 Hz, 4H), 7.24 (s, 1H), 8.73 (s, 1H), 9.37 (s, 2H); ¹³C NMR (CDCl<sub>3</sub>) δ 14.24, 61.58, 90.91, 98.54, 145.36, 145.05, 158.26, 160.05, 162.08; FT-IR (KBr) ν<sub>max</sub> / cm<sup>-1</sup>: 1808, 1716, 1599, 1518, 1473, 1192, 1023, 78; MS m/z (%) 390(M<sup>+</sup>), 345(6), 301(23), 211(12), 118(12), 68(13).

4,6-Bis(4-ethoxycarbonyl-3-phenylamino-5-oxo-2,5-dihydroisoxazolin-2-yl)pyrimidine (14). Using the same procedure as above with isoxazolone (19) (100 mg, 0.4 mmol) gave 14 (86.5 mg, 75%) as white crystals, mp 178 °C dec. ¹H NMR (CDCl<sub>3</sub>) δ 1.2 (t, J=7.2 Hz, 6H), 4.15 (q, J=7.2 Hz,
4H), 7.12-7.34 (m, 11H), 8.16 (s, 1H), 10.41 (s, 2H); $^{13}$C NMR (CDCl$_3$) δ 14.13, 60.95, 79.11, 97.17, 122.03, 126.43, 129.37, 137.75, 155.37, 157.56, 159.1, 162.47, 162.98; FT-IR (KBr) $\nu_{\text{max}}$ / cm$^{-1}$: 3434, 1795, 1701, 1588, 1520, 1454, 1348, 1198, 1025, 777; MS m/z (%) 528[(M$^+$-CO$_2$), 8], 485(18), 439(10), 393(15), 252(22), 216(73), 145(53), 105(100).

3,6-Bis(4-ethoxycarbonyl-5-oxo-2,5-dihydroisoxazolin-2-yl)pyridazine (15). The isoxazolone 18 (100 mg, 0.637 mmol) and 3,6-dichloropyridazine (47.4 mg, 0.318 mmol) were heated neat under nitrogen at 130 °C for 15 min. The resulting product was recrystallised from ethanol to give the isoxazolone 15 (105 mg, 85%) as pale yellow crystals, mp 209-211 °C dec (lit$^{17}$, 210 °C dec).

3,6-Bis(4-ethoxycarbonyl-3-phenylamino-5-oxo-2,5-dihydroisoxazolin-2-yl)pyridazine (16). The isoxazolone 19 (100 mg, 0.4 mmol) and 3,6-dichloropyridazine (30 mg, 0.2 mmol) were refluxed in ethanol for 48h. The solvent was removed under reduced pressure to give a yellow semi solid which was recrystallised from aqueous ethanol (30%) to afford 16 (59 mg, 51%) as pale yellow crystals, mp 143-145 °C.

3,6-Bis(3-(3-bromophenylamino)-4-ethoxycarbonyl-5-oxo-2,5-dihydroisoxazolin-2-yl)pyridazine (17). Using the same procedure as above with the isoxazolone 20 (100 mg, 0.3 mmol) gave 17 (67 mg, 60%) as white crystals, mp 143-145 °C. $^1$H NMR (CDCl$_3$) δ 1.31 (t, $J$=7.1 Hz, 6H), 4.28 (q, $J$=7.1 Hz, 4H), 7.03 (d, $J$=7.4 Hz, 4H), 7.06 (t, $J$=7.4 Hz, 2H), 7.17 (t, $J$=7.4 Hz, 4H), 7.5 (s, 2H), 7.68 (s, 2H), 9.99 (s, 2H); $^{13}$C NMR (CDCl$_3$) δ 13.28, 60.01, 78.05, 121.69, 123.85, 125.93, 128.41, 135.08, 152.9, 162.09, 162.65, 163.11; FT-IR (KBr) $\nu_{\text{max}}$ / cm$^{-1}$: 3430, 1801, 1710, 1685, 1632, 1587, 1040; MS m/z (%) 590[(M$^+$+H)$_2$, 13], 586(20), 546(5), 501(7), 324(23), 322(38), 217(48), 248(51), 202(100), 103(64), 44(63).

Ethyl 2,8-dihydroxy-5-methyl-4,10-dioxo-1,6,7,11-tetraaza-1,4,10,11-tetrahydrophenanthrene-9-carboxylate (21). The bis-isoxazolinyl derivative 7 (100 mg, 0.25 mmol) was refluxed in THF (8 mL) with potassium carbonate (34.5 mg, 0.25 mmol) for 24h. The solvent was removed under reduced pressure, water was added to the residue and the solution acidified to pH 2 with concentrated HCl. The pale yellow solid was filtered to give 21 (25 mg, 29%), mp 153-156 °C. $^1$H NMR (DMSO-d$_6$) δ 1.2 (bs, 1H); FT-IR (KBr) $\nu_{\text{max}}$ / cm$^{-1}$: 3421, 3255, 2918, 1736, 1703, 1618, 1438, 1318, 1283, 1181, 1078; MS m/z (%) 686[(M$^+$-CO$_2$), 7], 642(6), 596(3), 497(3), 368(6), 276(12), 218(18), 197(23), 196(30), 90(30), 69(51), 46(100).

Ethyl 6-[2,2-bis-(ethoxycarbonyl)-acetamido]-2-hydroxy-8-methyl-4-oxo-4H-pyrimido[1,2-a]pyrimidine-3-carboxylate (23). The bis-isoxazolinyl derivative 7 (100 mg, 0.25 mmol) was refluxed in ethanol (8 mL) with potassium carbonate (34.5 mg, 0.25 mmol) for 24h. The solution was cooled, quenched with HCl (5 mL) and the resulting products filtered to afford compound
26 (62 mg, 56%), mp 175 °C dec. \(^1\)H NMR (DMSO-\(d_6\)) \(\delta\) 1.19 (t, \(J=7.2\) Hz, 9H), 2.89 (s, 3H), 4.08 (q, \(J=7.2\) Hz, 2H), 4.19 (q, \(J=7.2\) Hz, 4H), 5.03 (s,1H), 7.63 (s, 1H), 11.89 (s, 1H), 12.22 (bs, 1H); \(^{13}\)C NMR (DMSO-\(d_6\)) \(\delta\) 14.42, 14.78, 24.19, 44.65, 60.98, 62.24, 104.22, 106.83, 157.05, 158.35, 159.51, 164.48, 164.91, 165, 168.03, 170.23; FT-IR (KBr) \(\nu_{\text{max}} / \text{cm}^{-1}\): 3423, 3299, 1761, 1715, 1655, 1202, 1083; MS m/z (%) 450(M\(^+\), 4), 404(5), 345(20), 264(10), 205(21), 187(50), 177(80), 160(100), 114(44), 87(68).

**Diethyl 5-methyl-2,8-bis(phenylamino)diimidazo[1,2-a:1',2'-c]pyrimidine-3,9-dicarboxylate (24).** The bis-isoxazolinyl derivative 8 (100 mg, 0.171 mmol) was refluxed in THF (8 mL) with potassium carbonate (23.5 mg, 0.171 mmol) for 24h. The solvent was removed under reduced pressure and the residue was recrystallized from ethanol to give 24 (59.5 mg, 70%), mp 182 °C dec. \(^1\)H NMR (DMSO-\(d_6\)) \(\delta\) 0.69 (t, \(J=7.2\) Hz, 3H), 0.98 (t, \(J=7.2\) Hz, 3H), 2.27(s, 3H), 3.45 (q, \(J=7.2\) Hz, 2H), 3.89 (q, \(J=7.2\) Hz, 2H), 6.66 (d, \(J=7.5\)Hz, 2H), 6.74(t, \(J=7.2\)Hz, 1H), 7.04-7.22 (m, 7H), 7.78 (s, 1H); \(^{13}\)C NMR (DMSO-\(d_6\)) \(\delta\) 14.32, 14.34, 24.32, 58.16, 59.96, 77.82, 103.54, 120.35, 120.88, 122.87, 125.65, 128.43, 129.08, 138.76, 154.66, 155.71, 155.85, 159.42, 162.38, 163.32, 164.11, 166.3, 168.53; FT-IR (KBr) \(\nu_{\text{max}} / \text{cm}^{-1}\): 3448, 1725, 1618, 1585, 1351, 1048, 695; MS m/z (%) 498(M\(^+\), 4), 339(6), 316(8), 213(24), 196(33), 169(24), 128(61), 93(100), 66(34).

**Diethyl 2,8-bis(3-bromophenylamino)-5-methylimidazo[1,2-a:1',2'-c]pyrimidine-3,9-dicarboxylate (25).** Using the same procedure as above with the bis-isoxazolone 9 (100 mg, 0.134 mmol) gave 25 (60 mg, 68%) as white crystals, mp 190 °C dec. \(^1\)H NMR (DMSO-\(d_6\)) \(\delta\) 0.78 (t, \(J=7.2\) Hz, 3H), 1.01 (t, \(J=7.2\) Hz, 3H), 2.32 (s, 3H), 3.5 (q, \(J=7.2\) Hz, 2H), 3.89 (q, \(J=7.2\) Hz, 2H), 6.63 (d, \(J=7.8\) Hz, 1H), 6.77 (s, 1H), 6.87 (d, \(J=7.8\)Hz, 1H), 6.99 (t, \(J=7.8\)Hz, 1H), 7.1-7.19 (m, 3H), 7.28 (s, 1H) 7.71 (s, 1H); \(^{13}\)C NMR (DMSO-\(d_6\)) \(\delta\) 14.38, 14.45, 24.39, 58.27, 59.78, 72.25, 103.33, 120.04, 121.62, 121.99, 122.57, 123.5, 125.81, 130.11, 130.68, 153.39, 155.82, 156.64, 158.95, 162.18, 162.99, 165.96, 168.77; FT-IR (KBr) \(\nu_{\text{max}} / \text{cm}^{-1}\): 3443, 1725, 1611, 1580, 1378, 1040, 684.

**Diethyl 2,5,8-trihydroxy-10-nitro-4,6-dioxo-1,4a,5a,9-tetraaza-1,4,5,5a,6,9-hexahydroanthracene-3,7-dicarboxylate (26).** To bis-isoxazolinyl derivative 10 (100 mg, 0.23 mmol) was added 2.5M sodium hydroxide solution (10 mL) and the mixture was stirred at 40 °C for 10 min, after which time a homogenous solution formed. This solution was acidified to pH 2 with 2M HCl and the resulting precipitate was filtered to give 26 (60 mg, 68%) as a brown solid, mp> 300 °C. \(^1\)H NMR (DMSO-\(d_6\)) \(\delta\) 1.24 (t, \(J=7.2\) Hz, 3H), 1.27 (t, \(J=7.2\) Hz, 3H), 4.21 (q, \(J=7.2\) Hz, 2H), 4.3 (q, \(J=7.2\) Hz, 2H), 12.76 (bs,1H), 13.62 (s, 1H); \(^{13}\)C NMR (DMSO-\(d_6\)) \(\delta\) 14.32, 14.6, 31.14, 60.97, 62.24; FT-IR (KBr) \(\nu_{\text{max}} / \text{cm}^{-1}\): 3413, 1697, 1637, 1569, 1473, 1375, 1233, 1127, 1081; MS m/z (%) 435[M\(^+\)-H\(_2\)O, 4], 407(20), 354(9), 310(19), 250(8), 205(26), 137(24), 105(40), 91(100), 90(90).

**Diethyl 2,5,8-trihydroxy-10-nitro-4,6-dioxo-1,4a,5a,9-tetraaza-1,4,5,5a,6,9-hexahydroanthracene-3,7-dicarboxylic acid (27).** The bis-isoxazolinyl derivative 10 (100 mg, 0.23 mmol) was refluxed in 2.5M sodium hydroxide solution (10 mL) for 15 min. The cooled solution was acidified to pH 2 and the resulting precipitate was filtered to give 27 (55.5 mg, 61%) as a black solid, mp> 300
Diethyl 2,5,8-trihydroxy-4,6-dioxo-1,4,5,5a,6,9-hexahydroanthracene-3,7-dicarboxylate (28). This compound was prepared as described for 22 using bis-isoxazolinyl derivative 13 (100 mg, 0.256 mmol) to afford the compound 28 (73 mg, 70%) as a black solid, mp > 300 °C. 1H NMR (DMSO-d6) δ 5.05 (bs, 2H), 5.14 (s, 1H), 7.21 (s, 1H), 13.6 (bs, 1H) ; 613C NMR (DMSO-d6) δ 31.13, 34.75, 117.13, 120.74, 122.31, 124.92, 131.46, 141.4, 159.63, 174.84; FT-IR (KBr) ν max / cm⁻¹: 3413, 1630, 1508, 1430, 1092, 812; MS m/z (%) 396 [(M⁺-1), 4], 319(4), 304(5), 255(10), 236(13), 110(23), 96(49), 82(68), 68(81), 54(100).

Ethyl 10-ethoxycarbonyl-3,6,11-trihydroxy-8,9-dioxo-1,5,8a-tetraaza-3,4,8a-tetrahydropyrimido[1,2-a]naphthalene-7-carboxylate (29). The same procedure as above with the bis-isoxazolinyl derivative 15 (100 mg, 0.256 mmol) gave 29 (73 mg, 70%) as a brown solid, mp 257 °C dec. 1H NMR (DMSO-d6) δ 1.22 (t, J=7.2 Hz, 6H), 3.03 (d, J=6.6 Hz, 1H), 3.66 (d, J=6.6 Hz, 1H), 3.71 (s, 2H), 4.17 (q, J=7.2 Hz, 4H), 11.91 (s, 2H); 13C NMR (DMSO-d6) δ 14.59, 32.36, 53.01, 60.83, 155.33, 156.17, 162.36, 163.18, 166.4, 168.39, 172.63, 173.33; FT-IR (KBr) ν max / cm⁻¹: 3492, 1763, 1675, 1581, 1556, 1425, 1264, 1192, 682; MS m/z (%) 408(M⁺, 6), 407(8), 367(8), 303(4), 235(12), 110(13), 96(27), 82(33), 68(40), 54(100).

References