Synthesis of N-(2-Phenyl-cyclopropyl)-Substituted Nucleoside Analogues

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A novel class of nucleoside analogues containing adenine, hypoxanthine, thymine, uracil, thioracil and cytosine as the heterocyclic moieties have been prepared starting from 2-phenylcyclopropylamine. These compounds showed weak antitumor activity. The resolution of the racemates on an analytical scale was performed by HPLC using chiral phases.

Introduction

An attractive strategy in the development of new inhibitors of enzymes consists in the introduction of cyclopropane units into analogues of the enzymes’ substrate [1]. This concept has been used for the synthesis of excellent inhibitors of the enzymes lactate-dehydrogenase [2], alcohol-dehydrogenase [3], myocardial c-AMP-phosphodiesterase [4], mitochondrial mono-aminooxidase A [5, 6] and bacterial gyrase [7]. Furthermore, a series of bifunctionalized cyclopropanes that were derived from 2-amino-1-aryl-cyclopropane carboxylic acid has to be regarded as structural prototypes of antidepressive agents, the therapeutic action of which is strongly associated with the presence of the cyclopropane moiety [8]. During ongoing QSAR studies of antitumor active cyclopropanoid nucleoside analogues we became interested in the synthesis and biological evaluation of N-(2-phenylcyclopropyl)-substituted nucleoside analogues [9–11].

Results and Discussion

The synthesis of the adenine analogue (±)-1 started from easily available (±)-(RS,SR)-trans-2-phenylcyclopropylamine [(±)-2]. Thus reaction of (±)-2 with 5-amino-4,6-dichloro-pyrimidine in n-butanol/triethylamine for 20 h gave 62% of (±)-3 whose reaction with triethylorthoformate in the presence of hydrochloric acid furnished the 6-chloro-purine derivative (±)-4 [12]. Treatment of (±)-4 with ammonia in an autoclave for 22 h finally afforded the adenine derivative (±)-1. (±)-4 served as a starting material for the hypoxanthine derivative (±)-5 by treatment of 4 with sodium hydroxide for 4 h at 100 °C.

The pyrimidine derivative (±)-6 was obtained starting from (±)-2 that was allowed to react with in situ prepared 3-ethoxy-acryloylisocyanate (7) [13–15] to afford (±)-8 followed by a ring closure reaction mediated by 2 N sulfuric acid to result in a 78% yield of the uracil derivative (±)-6. In a similar way the thymine derivative (±)-9 became available from the cyclization of (±)-10; 10 was obtained from the reaction of (±)-2 with in situ prepared 2-methyl-acryloylisocyanate (11) [13–15].

The uracil derivative 6 served as a valuable starting material [16] for the synthesis of the cytosine derivative (±)-12. Thus, reaction of 6 with phosphorpentasulfide in pyridine for 6 h at 110 °C gave the thioracil derivative (±)-13. Reaction of 13 with methylidioide/sodium hydroxide followed by an ammonolysis afforded the cytosin derivative (±)-12 in 86% yield.

Preliminary screening of racemic 1, 5, 9, 6, 12 and 13 revealed weak antitumor activity for several of these compounds. It is well established that the biological activity of many nucleoside analogues resides only in one of the enantiomers [17]. To access the pure enantiomers of the analogues two prerequisites have to be fulfilled. First, the starting material 2 must be at one’s disposal in...
form of its pure enantiomers; this task has been accomplished recently in our laboratories [18]. On the other hand analytical methods have to be elaborated to check the enantiomeric purity of the final compounds. According to our preceding experiences in this field HPLC seemed to be the method of choice.

The chromatographic resolution of the enantiomers of (±)-1, (±)-9 and (±)-12 was performed by HPLC on a Daicel Chiralcel OD column using 2-propanol/hexane mixtures + 0.1% diethylamine as the solvent; although a clean baseline separation was also obtained without the presence of diethylamine the addition of this additive is of great advantage for the shortening of the retention times. No separation could be achieved, however, under a variety of conditions for the uracil and thiouracil derivatives (±)-6 and (±)-13 with the OD-column but switching to reversed-phase conditions on a Daicel Chiralcel OD-R column with methanol as the eluent brought about a nice separation of the respective enantiomers. Two typical chromatograms are depicted in Fig. 1; the conditions for a separation of the enantiomers are enlisted in Tab. I. Presently a chemoenzymatic approach for the synthesis of the pure enantiomers is under investigation in our labs.

Experimental

General – Melting points are uncorrected (Reichert hot stage microscope); NMR spectra were recorded using either a Bruker AM250 or a Varian XL300 instrument (δ given in ppm, J in Hz, internal Me4Si, C' and H' correspond to the atoms of the heterocycle or its synthetic precursor), IR spectra (film or KBr pellet) on a Perkin-Elmer 1605 FT-IR, UV spectra on a Perkin-Elmer Lambda 14, MS spectra were taken either on a MAT311A or a Varian-112S instrument; for elemental analysis a Foss-Heraeus Vario EL instrument was used. TLC was performed on silica gel (Merck 5554, detection by dipping in an ethanolic ninhydrine (1%) solution followed by gentle heating, or by UV detection at 254 nm). HPLC was performed on a Merck-Hitachi L6200A/L4000/D2500 instrument (UV detection at 260 nm) using either a Chiralcel OD (4.6x250 mm, 10 μm, Daicel Chemical Industries) or a Chiralcel OD-R (4.6x250 mm, 10 μm, Daicel Chemical Industries) column.

9-[(1 RS,2 SR)-2-Phenylcyclopropyl]-9 H-6-purin-amine [(±)-1]

Ammonolysis of (±)-4 (0.22 g, 0.82 mmol) in dry liquid ammonia (15 ml) in an autoclave for 22 h at 63 °C and 12 bar pressure gave an oil that was purified by chromatography (ethyl acetate/hexane 1:1 → ethyl acetate → ethyl acetate/methanol 10:1) to afford (±)-1 (0.18 g, 87%); m.p. 202–204 °C, Rf (ethyl acetate/methanol 15:1)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Column</th>
<th>Eluent</th>
<th>Flow [ml/min]; pressure [kg/cm²]</th>
<th>tR [min]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OD</td>
<td>Hexane/2-propanol (80/20) + 0.1% DEA</td>
<td>0.8; 21</td>
<td>(+): 16.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hexane/2-propanol (90/10)</td>
<td>0.8; 18</td>
<td>(-): 18.06</td>
</tr>
<tr>
<td>9</td>
<td>OD</td>
<td>Hexane/2-propanol (80/20) + 0.1% DEA</td>
<td>0.8; 21</td>
<td>(+): 27.98</td>
</tr>
<tr>
<td>6</td>
<td>OD-R</td>
<td>MeOH</td>
<td>0.4; 14</td>
<td>(+): 30.32</td>
</tr>
<tr>
<td>13</td>
<td>OD-R</td>
<td>MeOH</td>
<td>0.4; 14</td>
<td>(+): 34.59</td>
</tr>
<tr>
<td>12</td>
<td>OD</td>
<td>Hexane/2-propanol (80/20) + 0.1% DEA</td>
<td>0.8; 21</td>
<td>(+): 31.84</td>
</tr>
</tbody>
</table>

Table I. HPLC conditions for the separation of the enantiomers (25 °C, UV detection at λ = 260 nm)
N4-[(1RS,2SR)-2-Phenylcyclopropyl]-6-chloropyrimidine-4,5-diamine ([±]-3)

(1RS,2SR)-2-Phenylcyclopropylamine sulfate (tranylcypromine-sulfate, 3.0 g, 8.24 mmol) was dissolved in aqueous sodium hydroxide (20%, 30 ml) and extracted with diethylether (4×30 ml). The combined organic phases were evaporated and the remaining oil of ([±]-2 (2.06 g, 94%) was used without further purification. To a solution of ([±]-2 (1.47 g, 11.07 mmol) in dry triethylamine (30 ml) a suspension of 5-amino-4,6-dichloropyrimidine (2.18 g, 13.28 mmol) in n-butanol (80 ml) was added and the mixture was heated under reflux for 20 h under argon. After cooling to 25 °C the solvents were removed and the residue subjected to column chromatography (ethyl acetate/hexane 1:5 → 1:3 → 1:1) to afford ([±]-3 (1.78 g, 0.21; UV (methanol): λ_max = 258 nm, log ε = 4.165; IR (KBr): 3298m, 3145s, 1793w, 1734w, 1718w, 1700m, 1696m, 1669s, 1604s, 1570s, 1560m, 1534w, 1522w, 1507m, 1500m, 1473m, 1437m, 1417m, 1396m, 1371m, 1330m, 1302s, 1258m, 1214m, 1192m, 1123m, 1061m, 1023m, 986w; 1H NMR (300 MHz, d_6-DMSO): 8.22 (s, 1H, H−C(2′)), 8.16 (s, 1H, H−C(8′)), 7.41−7.28 (m, 5H, H−C(phenyl)), 7.25 (s, 2H, NH₂, exchangeable with D₂O), 3.70 (ddd, J = 7.4, 4.1, 3.7, 1H, H−C(1)), 2.61 (ddd, J = 10.0, 6.8, 3.7, 1H, H−C(2)), 1.92 (ddd, J = 10.0, 6.3, 4.1, 1H, H_A−C(3)), 1.58 (ddd, J = 7.4, 6.8, 6.3, 1H, H_B−C(3)); 13C NMR (75 MHz, d_6-DMSO): 155.77 (s, C(6′)), 152.39 (d, C(2′)), 140.24 (d, C(4′)), 139.72 (s, C_q(phenyl)), 128.17, 126.36, 126.05 (d, C(phenyl)), 118.85 (s, C(5′)), 34.14 (d, C(1)), 23.59 (d, C(2)), 14.35 (t, C(3)); MS (EI, 80 eV, 151 °C): 252 (19.9%), 251 (95.9%), 250 (100.0%), 223 (6.4%), 174 (8.6%), 148 (21.2%), 136 (81.4%), 135 (10.9%), 117 (64.8%), 116 (61.2%), 115 (81.7%), 91 (26.1%).

Analysis for C_{14}H_{13}N_{5} (251.29)  
Calcd. C 66.92 H 5.21%  
Found C 67.00 H 5.16%  

Fig. 2. Synthesis of the analogues.
62%); m.p. 63–65 °C, \( R_F \) (ethyl acetate/hexane 1:2) 0.24; IR (KBr): 3484, 3242, 3025, 1734, 1718, 1700, 1696, 1684, 1635, 1636, 1576, 1496, 1457, 1437, 1419, 1387, 1336, 1253, 1199m, 1110m, 979w; \( ^1 \)H NMR (300 MHz, \( d_2 \)-DMSO): 7.75 (s, 1H, \( H-C(2') \)), 7.30–7.14 (m, 5H, H–C(phenyl) and 1H, NH, exchangeable with \( D_2 \)O), 5.04 (s, 2H, NH), exchangeable with \( D_2 \)O, 3.07–3.03 (m, 1H, H–C(1)), 2.00 (ddd, \( J = 7.5, 7.5, 3.0 \) 1H, H–C(2)), 1.28 (ddd, \( J = 7.5, 6.5, 2.0 \) 2H, \( H_{A-B}-C(3) \)); ^13C NMR (75 MHz, \( d_2 \)-DMSO): 152.42 (s, C(6')), 145.67 (d, C(2')), 141.43 (s, C(phenyl)), 136.86 (s, C(4')), 128.17, 125.93, 125.53 (d, C(phenyl)), 123.59 (s, C(5')), 34.51 (d, C(1)), 24.61 (d, C(2)), 15.74 (t, C(3)); MS (EI, 80 eV, 137 °C): 262 (26.0%), 261 (22.9%), 260 (77.8%), 259 (28.4%), 246 (3.4%), 244 (9.5%), 234 (2.1%), 171 (48.9%), 169 (100.0%), 157 (23.9%), 155 (64.6%), 144 (27.0%), 132 (20.6%), 128 (20.0%), 117 (100.0%), 115 (99.2%), 91 (66.1%).

Analysis for \( C_{13}H_{12}ClN_4 \) (260.73)
Calcd. C 59.89 H 5.03%
Found C 59.91 H 5.21%

6-Chloro-9-[(I RS,2 SR)-2-phenylcyclopropyl]-9H-purine \((\pm)-4\)

To a suspension of \((\pm)-3\) (0.40 g, 1.54 mmol) in triethyl orthoformate (3.7 g, 24.7 mmol) hydrochloric acid (36%, 0.18 g, 1.86 mmol) was added and the mixture was stirred for 2 h. After addition of water (6 ml) and ethyl acetate (10 ml) the pH was adjusted to 8–9 by the careful addition of solid sodium hydrogen carbonate. The aqueous phase was extracted with ethyl acetate (3×10 ml) and the combined organic phases were dried (MgSO₄), the solvent was removed under reduced pressure and the residue subjected to column chromatography (ethyl acetate/methanol 10:1) to afford \((\pm)-5\) (0.08 g, 34%); m.p. 227–230 °C, \( R_F \) (ethyl acetate/methanol 8:1) 0.36; UV (methanol): \( \lambda_{max} = 244 \) nm, \( \log \epsilon = 4.038, \lambda_{max} = 250 \) nm, \( \log \epsilon = 4.024 \); IR (KBr): 3406w, 3074w, 3007m, 2971w, 2905m, 2867m, 2802m, 2635m, 1970w, 1710s, 1590s, 1550m, 1517m, 1499m, 1461m, 1419m, 1337m, 1229m, 1180m, 1165m, 1132m, 1078w, 1042w; \( ^1 \)H NMR (300 MHz, \( d_6 \)-DMSO): 12.33 (br s, 1H, NH), 8.18 (s, 1H, H–C(8')), 7.36–7.22 (m, 5H, H–C(phenyl)), 3.73 (ddd, \( J = 7.2, 4.7, 3.7 \) 1H, H–C(1)), 2.60 (ddd, \( J = 10.1, 6.6, 3.7 \) 1H, H–C(2)), 1.90 (ddd, \( J = 10.1, 5.8, 4.7 \) 1H, H–C(3)), 1.59 (ddd, \( J = 7.2, 6.6, 5.8 \) 1H, H–C(3)); ^13C NMR (75 MHz, \( d_6 \)-DMSO): 156.27 (s, C(6')), 149.19 (s, C(4')), 145.28 (s, C(2')); 149.37 (d, C(8')), 149.19 (s, C(4')), 145.28 (s, C(2')); 139.53 (d, C(8')), 139.36 (s, C(phenyl)), 128.04, 126.23, 125.99 (each d, C(phenyl)), 124.02 (s, C(5')), 34.16 (d, C(1)), 23.62 (d, C(2')); 14.25 (t, C(3)); MS (EI, 80 eV, 193 °C): 254 (0.8%), 253 (5.6%), 252 (45.9%), 251 (16.2%), 137 (43.3%), 117 (100.0%), 116 (50.6%), 115 (83.2%), 91 (34.5%), 77 (14.0%), 67 (16.2%); HRMS calcd. for \( C_{13}H_{12}N_4O \): 252.1001; found: 252.1009.

1-[(I RS,2 SR)-2-Phenylcyclopropyl]-1,2,3,4-tetrahydro-2,4-pyrimidine-dione \((\pm)-6\)

A solution of \((\pm)-8\) (0.3 g, 1.1 mmol) in sulfuric acid (2 N, 2 ml) was boiled under reflux for 4 h. After cooling to 25 °C and neutralization with so-

Analysis for \( C_{14}H_{11}ClN_{4} \) (270.72)
Calcd. C 62.11 H 4.09%
Found C 62.42 H 4.16%

9-[(I RS,2 SR)-2-Phenylcyclopropyl]-1,9-dihydro-6-purinone \((\pm)-5\)
mium hydroxide (2 N) the reaction mixture was extracted with ethyl acetate (3 × 30 ml). The combined organic phases were dried (MgSO₄), the solvent was removed in vacuo and the residue subjected to chromatography (ethyl acetate/hexane 1:1 → 3:1) to afford (±)-6 (0.19 g, 78%); m.p. 181–183 °C, R₂ (ethyl acetate/hexane 1:1) 0.16; UV (methanol): λ_max = 265 nm, log ε = 4.049; IR (KBr): 3129, 3027, 2862, 2814, 2345, 1844, 1772, 1695, 1670, 1617, 1604, 1570, 1559, 1540, 1534, 1521, 1517, 1442, 117, 116, 91 (12.2%).

- The reagent 3-ethoxyacryloyl-isocyanate (7) [prepared from 3-ethoxy-acryloylchloride (0.45 g, 3.37 mmol) in dry benzene (1.5 ml) and silver cyanate (1.0 g, 6.78 mmol) in dry benzene (7 ml)] was added at −15 °C to a solution of (±)-2 (0.3 g, 2.25 mmol) in dry dimethylformamide (10 ml) under argon over a period of 30 min. Stirring at that temperature was continued for another 30 min and then for 1 h at 25 °C. After addition of an ice cold saturated solution of sodium hydrogencarbonate (20 ml) the reaction mixture was extracted with ethyl acetate (40 × 30 ml); the combined organic phases were dried (MgSO₄) and the solvents removed under reduced pressure. The residue was subjected to column chromatography (ethyl acetate/hexane 1:3 → 1:1) to afford (±)-8 (0.55 g, 88%); m.p. 164–167 °C, R₂ (ethyl acetate/hexane 1:1) 0.55; IR (KBr): 3253, 3086, 3062, 3029, 2982, 2935, 2886, 2842, 1704, 1674, 1609, 1544, 1496, 1475, 1464, 1395, 1345, 1335, 1243, 1214, 1176, 1161, 1108, 1095, 1067, 1031, 1013, 1000; ¹H NMR (300 MHz, d₆-DMSO): 10.13 (s, 1 H, OC(O)CH₃), 7.69 (d, J = 7.2, 1 H, H₆), 7.68 (d, J = 7.2, 1 H, H₅), 7.62 (s, 1 H, H₄), 7.43 (d, J = 7.2, 1 H, H₃), 7.34 (d, J = 7.2, 1 H, H₂), 7.27 (t, J = 7.2, 1 H, CH₂), 4.30 (q, J = 7.2, 2 H, CH₂-O), 3.75 (t, J = 7.2, 1 H, OCH₂), 3.56 (t, J = 7.2, 1 H, OCH₂), 3.07 (s, 3 H, OCH₃), 2.27 (s, 3 H, CH₃), 1.40 (s, 3 H, CH₃), 1.28 (s, 3 H, CH₃), 1.15 (s, 3 H, CH₃), 1.10 (s, 3 H, CH₃). Analysis for C₁₄H₉N₂O₃ (274.32)

Calcd. C 65.68 H 6.61 N 10.21%
Found C 65.86 H 6.47 N 9.95%

N-(3-Ethoxycarbonyl-3-isocyano-propyl)-N'-[(1RS,2SR)-2-phenyl-cyclopropyl]-urea [(±)-9]

According to the preparation of (±)-6 from the reaction of (±)-10 (0.34 g, 1.22 mmol) with sulfuric acid (2 N, 3 ml) for 4 h (reflux) (±)-9 (0.2 g, 66%) was obtained; m.p. 206–208 °C, R₂ (ethyl acetate/hexane 1:1) 0.31; UV (methanol): λ_max = 270 nm, log ε = 4.363; IR (KBr): 3253, 3086, 3062, 3029, 2982, 2935, 2886, 2842, 1704, 1674, 1609, 1544, 1496, 1475, 1464, 1395, 1345, 1335, 1243, 1214, 1176, 1161, 1108, 1095, 1067, 1031, 1013, 1000; ¹H NMR (300 MHz, d₆-DMSO): 10.13 (s, 1 H, OC(O)CH₃), 7.69 (d, J = 7.2, 1 H, H₆), 7.68 (d, J = 7.2, 1 H, H₅), 7.62 (s, 1 H, H₄), 7.43 (d, J = 7.2, 1 H, H₃), 7.34 (d, J = 7.2, 1 H, H₂), 7.27 (t, J = 7.2, 1 H, CH₂), 4.30 (q, J = 7.2, 2 H, CH₂-O), 3.75 (t, J = 7.2, 1 H, OCH₂), 3.56 (t, J = 7.2, 1 H, OCH₂), 3.07 (s, 3 H, OCH₃), 2.27 (s, 3 H, CH₃), 1.40 (s, 3 H, CH₃), 1.28 (s, 3 H, CH₃), 1.15 (s, 3 H, CH₃), 1.10 (s, 3 H, CH₃). Analysis for C₁₄H₉N₂O₃ (274.32)

Calcd. C 65.68 H 6.61 N 10.21%
Found C 65.86 H 6.47 N 9.95%
Analysis for C_{14}H_{14}N_{2}O_2 (242.28)
Calcd. C 69.41  H 5.82  N 11.56%.
Found C 69.22  H 5.65  N 11.38%.

N-[(E)-3-Methoxy-2-methyl-2-propenoyl]-N'-[(1RS,2SR)-2-phenyl-cyclopropyl]-urea [(±)-10]

According to the preparation of (±)-8 from the reaction of (±)-2 (0.3 g, 2.23 mmol) in dry dimethylformamide (10 ml) with 3-methoxy-2-methylacryloylisocyanate [prepared from 3-methoxy-2-methylacryloylchloride (0.46 g, 3.38 mmol) in dry benzene (1.5 ml) and silver cyanate (1.1 g, 6.77 mmol) in dry benzene (7 ml)] at -15 °C for 1 h and at 25 °C for 2 h (±)-10 was obtained after column chromatography (ethyl acetate/hexane 1:7 → 1:3) as a white solid (0.4 g, 65%), m.p. 119-127 °C; 'H NMR (300 MHz, d_6-DMSO): 9.79 (1 H, C (5')), 7.37-7.17 (m, 5 H, H-C(phenyl)), 3.80 (s, 3 H, CH_3), 2.84 (dddd, J = 3.9, 3.7, 3.4, 1 H, H-C(1)), 2.04 (dddd, J = 9.4, 6.3, 3.4, 1 H, H-C(2)), 1.62 (d, J = 1.1, 3 H, CH_3), 1.24-1.17 (m, 2 H, H_{A,B}-(C-3)); 13C NMR (75 MHz, d_6-DMSO): 169.32 (s, C (2)), 157.97 (d, C(6')), 154.23 (s, C(2')), 141.03 (s, C_4 (phenyl)), 128.01, 125.68, 125.46 (each d, C(phenyl)), 106.72 (s, C(5')), 61.02 (q, OCH_3), 32.33 (d, C(1)), 24.28 (d, C(2)), 15.78 (t, C(3)), 8.86 (q, CH_3); MS (EI, 80 eV, 173 °C): 228 (5.4%), 227 (37.4%), 226 (5.1%), 199 (2.9%), 198 (3.2%), 156 (4.9%), 136 (20.3%), 123 (69.9%), 122 (13.8%), 117 (47.4%), 116 (39.8%), 115 (5.4%), 104 (13.6%), 97 (5.9%), 96 (55.1%), 95 (100.0%), 91 (22.8%), 79 (15.0%), 77 (15.7%), 70 (30.0%), 68 (77.0%); HRMS calcd. for C_{13}H_{13}N_3O_2: 227.1058; found: 227.1058.

I-[(1RS,2SR)-2-Phenyl-cyclopropyl]-4-thioxo-1,2,3,4-tetrahydro-2-pyrimidinone [(±)-13]

To a solution of (±)-6 (0.092 g, 0.44 mmol) in dry pyridine (5 ml) phosphorus pentasulfide (0.31 g, 1.41 mmol) was added and stirred at 100-110 °C for 6 h. After cooling to 25 °C ice water (10 ml) was added and the mixture extracted with ethyl acetate (3×30 ml). The combined organic layers were dried (MgSO_4), the solvents removed under reduced pressure and the residue was subjected to chromatography (ethyl acetate/hexane 1:10 → 1:5); m.p. 188-190 °C, R_F (ethyl acetate/hexane 1:3) 0.31; UV (methanol): λ_max = 335 nm, log ε = 4.261, λ_max2 = 245 nm, ε_2 = 3.426; IR (KBr): 3425 cm\(^{-1}\), 3200 m, 3089 m, 1844 w, 1830 w, 1793 m, 1772 w, 1762 w, 1751 w, 1734 m, 1700 s, 1684 s, 1653 m, 1647 m, 1635 m, 1612 s, 1570 m, 1560 m, 1554 m, 1534 m, 1521 m, 1517 m, 1507 m, 1499 m, 1477 m, 1457 s, 1441 s, 1395 m, 1355 m, 1315 m, 1293 s, 1217 m, 1156 m, 1149 s, 1110 m, 1092 m, 1069 m, 1056 m, 1004 m; 1^H NMR (250 MHz, d_6-DMSO): 12.65 (s, 1 H, NH), 7.54 (d, J = 7.4, 1 H, H-C(6')), 7.33-7.21 (m, 5 H, H-C(phenyl)), 6.22 (d, J = 7.4, 1 H, H-C(5')), 1.44 (dddd, J = 7.4, 6.8, 6.8, 1 H, H_{A,B}-(C-3)).
C(6'), 139.50 (s, Cₛ(phenyl)), 128.04, 126.43,
126.03 (each d, C(phenyl)), 111.68 (d, C(5'));
MS (EI, 80 eV, 115 °C): 246 (1.0%), 245 (2.4%), 244
(15.1%), 130 (2.0%), 129 (12.9%), 118 (8.9%), 117
(100.0%), 116 (29.3%), 115 (34.2%), 103 (4.3%),
97 (3.4%), 91 (18.3%), 70 (15.7%).

Analysis for C₁₃H₁₂N₂O₅S (244.31)
   Calcd. C 64.41 H 4.95 N 11.47 S 13.12%,
   Found C 63.63 H 4.92 N 11.45 S 13.30%.

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