Efficient and Convenient Polyethylene Glycol (PEG)-Mediated Synthesis of Spiro-oxindoles

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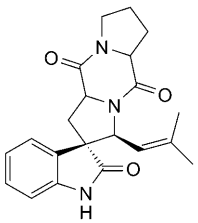
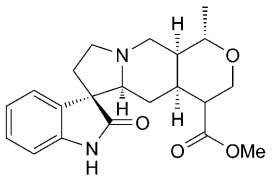
Polyethylene glycol (PEG) has been reported as an efficient and convenient medium for the three-component synthesis for spiro-oxindole.

Introduction. – The indole moiety constitutes a core structure of many therapeutically active compounds [1]. It is also found in many biologically active natural products [2]. For example, spirotryprostatin-A has been found as a novel inhibitor of microtubili assembly [3], and pteropodine and isopterodine have been shown to modulate the function of muscarinic serotonin receptors [4]. Because of their conformational rigidity, they confer favorable physiological properties for bioavailability. Hence, they have found application as pharmaceuticals.



Spirotryprostatin A

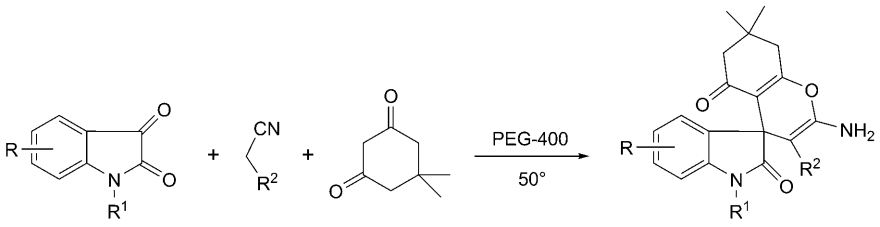


Pteropodine

Synthesis of spiro-oxindoles has been reported by three-component reaction of isatin, malononitrile, and naphthol in the presence of $InCl_3$ [5]. A synthesis of spiro-oxindoles is also accomplished using microwave [6]. Recently, tetrabutylammonium fluoride (Bu_4NF) has been described as a catalyst for a three-component reaction [7].

Results and Discussion. – Recently, polyethylene glycol (PEG) has attracted interest as solvent [8] because of its unique properties like low cost, reduced toxicity, recyclability, reduced inflammability, easy degradability, and miscibility with a wide variety of organic solvents. Encouraged by this advantage of PEG, we planned to synthesize spiro-oxindoles using PEG as a medium. Here, we report the results of PEG-mediated synthesis of spiro-oxindoles (*Scheme 1*).

Scheme 1



R = H, 7-Cl, 4-Br, 6-Br, 5-Me, 5-NO_2
R^1 = H, Me, Ac, $PhCH_2$, Ph
R^2 = CN, COOMe

1 – 13

To optimize the reaction conditions, a mixture of isatin, malononitrile, and dimedone was stirred with 0.3 ml of PEG at room temperature. TLC showed formation of a product in low yield (10%). Therefore, the same mixture was heated at 50° for 60 min to accomplish the reaction. After workup, spiro-oxindole was the only product isolated in high yield. We noticed also that reducing in the quantity of PEG (0.1 ml) decreased the efficiency of the reaction. To study the electronic effect of substituents on the reaction, we have examined a variety of substrates. It was observed that electron-withdrawing substituents reduce efficiency of the reaction, whereas electron-donating substituents facilitate the reaction. For example, the reaction of 5-nitroisatin (*Table 1*, *Entry 9*) under optimized conditions resulted in 86% yield of the spiro-oxindole **9**, whereas 5-methylisatin (*Entry 5*) gave 90% yield of expected product **5** in short time (60 min).

It was also noticed that substituents on the N-atom increase the efficiency of the reaction. For example, *N*-substituted isatins (*Entries 10–13*) reacted with malononitrile and dimedone in presence of PEG to afford the corresponding products **10**–**13** in high yield in short time (45 min).

Table 1. *PEG-400-Catalyzed Three-Component Synthesis of Spiro-oxindoles* **1**–**13**

Entry	Compound	R	R^1	R^2	Time [min]	Yield [%]
1	**1**	H	H	COOMe	80	87
2	**2**	6-Br	H	COOMe	70	89
3	**3**	7-Cl	H	COOMe	80	82
4	**4**	H	H	CN	60	92
5	**5**	5-Me	H	CN	60	90
6	**6**	4-Br	H	CN	60	91
7	**7**	6-Br	H	CN	60	87
8	**8**	7-Cl	H	CN	65	89
9	**9**	5-NO_2	H	CN	80	86
10	**10**	H	$PhCH_2$	CN	45	92
11	**11**	H	Me	CN	45	93
12	**12**	H	Ph	CN	45	91
13	**13**	H	Ac	CN	50	88

After these encouraging results, we further tested this protocol for barbituric acid and 4-hydroxycoumarin. The reaction of isatin (*Table 2*, *Entries 1–3*), malononitrile, and barbituric acid proceeded smoothly leading to the corresponding products **14**–**16** in good yield. Analogously, 4-hydroxycoumarin reacted with isatins (*Entries 4–6*) under optimized conditions and gave the expected products **17**–**19** again in high yields.

Scheme 2

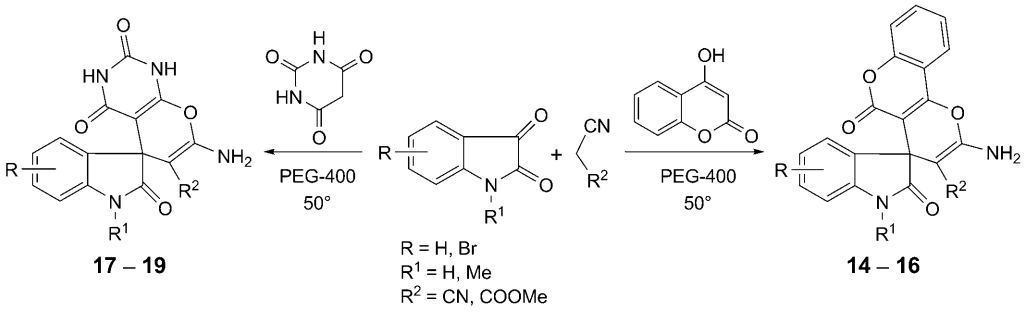


Table 2. *PEG-400-Catalyzed Three-Component Synthesis of Spiro-oxindoles* **14**–**19**

Entry	Compound	R	R^1	R^2	Time [min]	Yield [%]
1	**14**	H	Me	COOMe	85	88
2	**15**	H	H	CN	90	91
3	**16**	4-Br	H	CN	80	90
4	**17**	H	H	COOMe	85	85
5	**18**	H	H	CN	80	87
6	**19**	H	Me	CN	85	87

Conclusions. – We have developed a general and efficient method using PEG as an efficient and convenient medium for the three-components synthesis of spiro-oxindoles. The products are isolated in high yield. Easy workup, high yield, and inexpensive catalyst are the advantages of the present procedure.

The authors *D. A. K.*, *B. R. V. P.*, and *P. R. G.* thank *CSIR* and *UGC New Delhi* for fellowships.

Experimental Part

General. All reactions were carried out without any special precautions in an atmosphere of air. Chemicals were purchased from *Fluka* and *S. D. Fine Chemicals.* TLC: Precoated silica-gel plates (*60* F_{254}, 0.2-mm layer; *E. Merck*). ^{1}H-NMR Spectra: *Varian 200* or *Bruker 300* spectrometer; in (D_6)DMSO; δ in ppm, *J* in Hz. MS: *VG Autospec*; in *m*/*z*.

General Procedure. To a suspension of isatin (1 mmol) in PEG (0.3 ml), malononitrile (1 mmol) and dimedone (1 mmol) were added. This mixture was stirred at 50° until completion of the reaction (monitored by TLC). The mixture was diluted with H_2O, and the solid was filtered off and again washed with H_2O to obtain the purified product. The compounds were recrystallized from appropriate solvents. The products thus obtained were characterized by means of IR, NMR, and MS.

*Methyl 2-Amino-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]indole]-3-carboxylate* (**1**). White solid. M.p. 255–256°. IR: 3366, 3241, 3187, 2955, 1690, 1614,

1520, 1471, 1304, 1225, 1167, 1054, 928, 746. ^{1}H-NMR: 10.22 (*s*, NH); 7.88 (br. *s*, NH_2); 7.05–7.11 (*m*, 1 arom. H); 6.90 (*d*, *J* = 6.0, 1 arom. H); 6.82 (*t*, *J* = 7.8, 1 arom. H); 6.76 (*d*, *J* = 6.9, 1 arom. H); 3.32 (*s*, Me); 2.66 (*d*, *J* = 17.4, CH); 2.55 (*d*, *J* = 17.4, CH); 2.23 (*d*, *J* = 15.66, CH); 2.07 (*d*, *J* = 15.66, CH); 1.10 (*s*, Me); 1.01 (*s*, Me). EI-MS: 368 (M^+). Anal. calc. for $C_{20}H_{20}N_2O_5$: C 65.21, H 5.47, N 7.60; found: C 65.47, H 5.35, N 7.68.

*Methyl 2-Amino-6′-bromo-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]indole]-3-carboxylate* (**2**). White solid. M.p. 270–272°. IR: 3356, 3280, 3124, 2943, 1721, 1686, 1617, 1538, 1411, 1303, 1217, 1142, 1058, 917. ^{1}H-NMR: 10.30 (*s*, NH); 7.82 (br. *s*, NH_2); 6.94 (*d*, *J* = 10.4, 1 arom. H); 6.70–6.82 (*m*, 2 arom. H); 3.30 (*s*, Me); 2.59 (*d*, *J* = 20.0, 1 H, CH_2); 2.48 (*d*, *J* = 20.0, 1 H, CH_2); 2.16 (*d*, *J* = 21.2, CH); 2.02 (*d*, *J* = 21.6, CH); 1.02 (*s*, Me); 0.95 (*s*, Me). EI-MS: 446 (M^+), 448 ($[M+2]^+$). Anal. calc. for $C_{20}H_{19}BrN_2O_5$: C 53.71, H 4.28, N 6.26; found: C 53.96, H 4.31, N 6.19.

*Methyl 2-Amino-7′-chloro-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]indole]-3-carboxylate* (**3**). White solid. M.p. 279–280°. IR: 3365, 3280, 3119, 2990, 1717, 1679, 1616, 1520, 1416, 1315, 1214, 1130, 1042, 898, 730, 642, 555. ^{1}H-NMR: 10.50 (*s*, NH); 7.84 (br. *s*, NH_2); 7.10–7.14 (*m*, 1 arom. H); 6.73–6.79 (*m*, 2 arom. H); 3.25 (*s*, Me); 2.42–2.6 (*m*, CH_2); 2.13 (*d*, *J* = 21.2, CH); 2.05 (*d*, *J* = 21.2, CH); 1.04 (*s*, Me); 0.95 (*s*, Me). EI-MS: 402 (M^+). Anal. calc. for $C_{20}H_{19}ClN_2O_5$: C 59.63, H 4.97, N 6.95; found: C 56.70, H 4.64, N 6.83.

*2-Amino-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]indole]-3-carbonitrile* (**4**). White solid. M.p. 287–289°. IR: 3380, 3308, 3142, 2195, 1723, 1659, 1608, 1466, 1350, 1219, 1059, 908, 748. ^{1}H-NMR: 10.41 (*s*, NH); 7.22 (br. *s*, NH_2); 7.11 (*t*, *J* = 10.0, 1 arom. H); 7.01–6.73 (*m*, 3 arom. H); 2.56 (*s*, CH_2); 2.23–2.03 (*m*, CH_2); 1.03 (*s*, Me); 1.00 (*s*, Me). EI-MS: 335 (M^+). Anal. calc. for $C_{19}H_{17}N_3O_3$: C 68.05, H 5.11, N 12.53; found: C 68.24, H 5.22, N 12.61.

*2-Amino-1′,2′,5,6,7,8-hexahydro-5′,7,7-trimethyl-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]indole]-3-carbonitrile* (**5**). White solid. M.p. 277–279°. IR: 3364, 3310, 3143, 2967, 2192, 1721, 1659, 1607, 1497, 1350, 1221, 1165, 1049, 914. ^{1}H-NMR: 10.24 (*s*, NH); 7.16 (br. *s*, NH_2); 6.92 (*d*, *J* = 10.4, 1 arom. H); 6.76 (*s*, 1 arom. H); 6.67 (*d*, *J* = 7.6, 1 arom. H); 2.51–2.55 (*m*, CH_2); 2.18 (*s*, Me); 2.10–2.15 (*m*, CH_2); 1.02 (*s*, Me); 0.99 (*s*, Me). EI-MS: 349 (M^+). Anal. calc. for $C_{20}H_{19}N_3O_3$: C 68.75, H 5.48, N 12.03; found: C 68.56, H 5.57, N 12.11.

*2-Amino-4′-bromo-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]-indole]-3-carbonitrile* (**6**). White solid. M.p. 312–315°. IR: 3363, 3310, 3152, 2962, 2199, 1724, 1659, 1605, 1497, 1350, 1219, 1048, 928. ^{1}H-NMR: 10.41 (*s*, NH); 7.28 (br. *s*, NH_2); 7.14 (*t*, *J* = 7.6, 1 arom. H); 6.98 (*d*, *J* = 7.2, 1 arom. H); 6.78 (*d*, *J* = 7.6, 1 arom. H); 2.56 (*d*, *J* = 7.6, CH_2); 2.17 (*d*, *J* = 15.6, CH); 2.08 (*d*, *J* = 16.0, CH); 1.03 (*s*, Me); 1.00 (*s*, Me). EI-MS: 413 (M^+), 415 ($[M+2]^+$). Anal. calc. for $C_{19}H_{16}BrN_3O_3$: C 55.09, H 3.89, N 10.14; found: C 55.19, H 3.97, N 10.19.

*2-Amino-6′-bromo-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]-indole]-3-carbonitrile* (**7**). White solid. M.p. 318–320°. IR: 3357, 3312, 3170, 1721, 1667, 1605, 1486, 1358, 1219, 1049, 918, 802. ^{1}H-NMR: 10.59 (*s*, NH); 7.35 (br. *s*, NH_2); 7.09 (*d*, *J* = 7.6, 1 arom. H); 6.93 (*s*, 1 arom. H); 6.78 (*d*, *J* = 7.6, 1 arom. H); 2.53 (*d*, *J* = 7.6, CH_2); 2.17 (*d*, *J* = 16.0, CH); 2.10 (*d*, *J* = 16.0, CH); 1.02 (*s*, Me); 1.00 (*s*, Me). EI-MS: 413 (M^+), 415 ($[M+2]^+$). Anal. calc. for $C_{19}H_{16}BrN_3O_3$: C 55.09, H 3.89, N 10.14; found: C 55.34, H 3.26, N 10.22.

*2-Amino-7′-chloro-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]-indole]-3-carbonitrile* (**8**). White solid. M.p. 278–280°. IR: 3352, 3315, 3152, 2960, 2189, 1729, 1675, 1605, 1490, 1352, 1225, 1042, 910, 807, 744, 665, 572. ^{1}H-NMR: 10.45 (*s*, NH); 7.42 (br. *s*, NH_2); 7.13–7.23 (*m*, 1 arom. H); 6.79–6.87 (*m*, 2 arom. H); 2.49–2.54 (*m*, CH_2); 2.02–2.13 (*m*, CH_2); 1.04 (*s*, Me); 0.95 (*s*, Me). EI-MS: 369.5 (M^+). Anal. calc. for $C_{19}H_{16}ClN_3O_3$: C 61.71, H 4.36, N 11.36; found: C 61.80, H 4.56, N 11.63.

*2-Amino-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-5′-nitro-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]-indole]-3-carbonitrile* (**9**). White solid. M.p. 302–304°. IR: 3390, 3252, 3197, 2959, 2876, 2190, 1741, 1681, 1645, 1473, 1343, 1289, 1224, 1168, 1061, 913. ^{1}H-NMR: 11.44 (*s*, NH); 8.39–8.46 (*m*, 1 arom. H); 8.21–8.27 (*m*, 1 arom. H); 7.79 (br. *s*, NH_2); 7.31 (*d*, *J* = 8.6, 1 arom. H); 2.81–2.94 (*m*, CH_2); 2.35–2.51 (*m*, CH_2); 1.29 (*s*, 2 Me). EI-MS: 380 (M^+). Anal. calc. for $C_{19}H_{16}N_4O_5$: C 60.0, H 4.24, N 14.73; found: C 60.28, H 4.35, N 14.64.

*2-Amino-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-2′,5-dioxo-1′-(phenylmethyl)spiro[4*H*-1-benzopyran-4,3′-[3*H*]indole]-3-carbonitrile* (**10**). White solid. M.p. 267–269°. IR: 3384, 3320, 3204, 2962, 2198, 1713, 1668, 1612, 1487, 1352, 1229, 1168, 1052, 894, 744. ^{1}H-NMR: 7.47 (*d*, *J* = 9.6, 2 arom. H); 7.21–7.35 (*m*, 3 arom. H, NH_2); 7.05–7.14 (*m*, 2 arom. H); 6.94 (*t*, *J* = 10.0, 1 arom. H); 6.67 (*d*, *J* = 10.0, 1 arom. H); 4.88 (*d*, *J* = 7.6, CH_2); 2.53–2.59 (*m*, CH_2); 2.22 (*d*, *J* = 21.2, CH); 2.10 (*d*, *J* = 21.2, CH); 1.03 (*s*, Me); 1.00 (*s*, Me). EI-MS: 425 (M^+). Anal. calc. for $C_{26}H_{23}N_3O_3$: C 73.39, H 5.45, N 9.88; found: C 73.66, H 5.34, N 9.97.

*2-Amino-1′,2′,5,6,7,8-hexahydro-1′,7,7-trimethyl-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]indole]-3-carbonitrile* (**11**). White solid. M.p. 253–255°. IR: 3377, 3318, 3172, 2959, 2194, 1705, 1678, 1608, 1493, 1355, 1227, 1165, 1052, 903. ^{1}H-NMR: 7.24 (br. *s*, NH_2); 7.19–7.22 (*m*, 1 arom. H); 6.93–7.04 (*m*, 3 arom. H); 3.12 (*s*, Me); 2.50–2.55 (*m*, CH_2); 2.04–2.16 (*m*, CH_2); 1.02 (*s*, Me); 0.98 (*s*, Me). EI-MS: 349 (M^+). Anal. calc. for $C_{20}H_{19}N_3O_3$: C 68.75, H 5.48, N 12.03; found: C 69.01, H 5.39, N 12.12.

*2-Amino-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-2′,5-dioxo-1′-phenylspiro[4*H*-1-benzopyran-4,3′-[3*H*]-indole]-3-carbonitrile* (**12**). White solid. M.p. 304–306°. IR: 3430, 3310, 2955, 2192, 1713, 1655, 1500, 1465, 1350, 1319, 1218, 1052. ^{1}H-NMR: 7.84 (*t*, *J* = 7.7, 2 arom. H); 7.71 (*t*, *J* = 7.36, 1 arom. H); 7.59–7.63 (*m*, 2 arom. H, NH_2); 7.37–7.46 (*m*, 2 arom. H); 7.28 (*t*, *J* = 7.36, 1 arom. H); 6.89 (*d*, *J* = 7.74, 1 arom. H); 2.71–2.76 (*m*, CH_2); 2.34–2.51 (*m*, CH_2); 1.29 (*s*, Me); 1.26 (*s*, Me). EI-MS: 411 (M^+). Anal. calc. for $C_{25}H_{21}N_3O_3$: C 72.98, H 5.14, N 10.21; found: C 72.74, H 5.25, N 10.29.

*1′-Acetyl-2-amino-1′,2′,5,6,7,8-hexahydro-7,7-dimethyl-2′,5-dioxospiro[4*H*-1-benzopyran-4,3′-[3*H*]-indole]-3-carbonitrile* (**13**). Yellow solid. M.p. 248–251°. IR: 3409, 3325, 3245, 3195, 2966, 2905, 2193, 1717, 1685, 1658, 1597, 1462, 1353, 1264, 1165, 1043, 967, 912, 793, 770, 592, 516, 515. ^{1}H-NMR: 8.04 (*d*, *J* = 8.48, 1 H); 7.49 (*s*, NH_2); 7.33–7.28 (*m*, 1 arom. H); 7.19 (*d*, *J* = 3.7, 2 arom. H); 2.64 (*d*, *J* = 1.5, CH_2); 2.55 (*s*, Me); 2.15–2.18 (*m*, CH_2); 1.02 (*s*, Me); 1.00 (*s*, Me); 1.02 (*s*, Me); 0.95 (*s*, Me). EI-MS: 377.13 (M^+). Anal. calc. for $C_{21}H_{19}N_3O_4$: C 66.8, H 5.07, N 11.13; found: C 66.83, H 5.05, N 11.15.

*Methyl 2′-Amino-1,2-dihydro-1-methyl-2,5′-dioxospiro[3*H*-indole-3,4′-[4*H*,5*H*]pyrano[3,2-*c*][1]benzopyran]-3′-carboxylate* (**14**). White solid. M.p. 244–246°. IR: 3503, 3426, 3318, 3160, 2202, 1692, 1654, 1578, 1468, 1390, 1188, 1134, 826, 771. ^{1}H-NMR: 12.53 (br. *s*, NH); 12.04 (br. *s*, NH); 10.92 (br. *s*, NH); 7.88 (br. *s*, NH_2); 7.14 (*t*, *J* = 10.0, 1 arom. H); 6.98 (*d*, *J* = 10.4, 1 arom. H); 6.81–6.86 (*m*, 2 arom. H); 3.21 (*s*, Me); 3.08 (*s*, Me). EI-MS: 370 (M^+). Anal. calc. for $C_{17}H_{14}N_4O_6$: C 55.14, H 3.81, N 15.13; found: C 55.27, H 3.74, N 15.27.

*2′-Amino-1,2-dihydro-2,5′-dioxospiro[3*H*-indole-3,4′-[4*H*,5*H*]pyrano[3,2-*c*][1]benzopyran]-3′-carbonitrile* (**15**). White solid. M.p. 273–274°. IR: 3448, 3280, 3142, 3033, 2204, 1697, 1643, 1511, 1443, 1396, 1242, 1114, 1003, 846, 663. ^{1}H-NMR: 12.40 (br. *s*, NH); 12.02 (br. *s*, NH); 10.52 (br. *s*, NH); 7.41 (br. *s*, NH_2); 7.17 (*t*, *J* = 8.0, 2 arom. H); 6.91 (*t*, *J* = 7.6, 1 arom. H); 6.79 (*d*, *J* = 7.6, 1 arom. H). EI-MS: 323 (M^+). Anal. calc. for $C_{15}H_9N_5O_4$: C 55.73, H 2.81, N 21.66; found: C 55.40, H 2.89, N 21.68.

*2′-Amino-4-bromo-1,2-dihydro-2,5′-dioxospiro[3*H*-indole-3,4′-[4*H*,5*H*]pyrano[3,2-*c*][1]benzopyran]-3′-carbonitrile* (**16**). White solid. M.p. 253–255°. IR: 3502, 3420, 3325, 2198, 1690, 1657, 1580, 1472, 1385, 1340, 1250, 1185, 1065, 776. ^{1}H-NMR: 12.62 (br. *s*, NH); 12.22 (br. *s*, NH); 10.30 (br. *s*, NH); 7.02 (*t*, *J* = 8.0, 1 arom. H); 6.95 (*d*, *J* = 8.0, 1 arom. H); 6.89 (br. *s*, NH_2); 6.71 (*d*, *J* = 7.6, 1 arom. H). EI-MS: 401 (M^+), 403 ($[M+2]^+$). Anal. calc. for $C_{15}H_8BrN_5O_4$: C 44.80, H 2.01, N 17.41; found: C 44.66, H 2.09, N 17.49.

*Methyl 7′-Amino-1,1′,2,2′,3′,4′-hexahydro-2,2′,4′-trioxospiro[3*H*-indole-3,5′-[5*H*]pyrano[2,3-*d*]pyrimidine]-6′-carboxylate* (**17**). White solid. M.p. 273–275°. IR: 3380, 3312, 3094, 1712, 1668, 1613, 1530, 1443, 1288, 964, 910, 760, 665. ^{1}H-NMR: 10.42 (*s*, NH); 8.02 (br. *s*, NH_2); 8.04 (*d*, *J* = 8.0, 1 arom. H); 7.74 (*t*, *J* = 8.0, 1 arom. H); 7.53 (*t*, *J* = 7.6, 1 arom. H); 7.45 (*d*, *J* = 8.4, 1 arom. H); 7.11 (*t*, *J* = 7.6, 1 arom. H); 7.01 (*d*, *J* = 7.2, 1 arom. H); 6.79 (*t*, *J* = 7.6, 1 arom. H); 6.75 (*d*, *J* = 7.6, 1 arom. H); 3.22 (*s*, Me). EI-MS: 390 (M^+). Anal. calc. for $C_{21}H_{14}N_2O_6$: C 64.62, H 3.62, N 7.18; found: C 64.84, H 3.55, N 7.11.

*7′-Amino-1,1′,2,2′,3′,4′-hexahydro-2,2′,4′-trioxospiro[3*H*-indole-3,5′-[5*H*]pyrano[2,3-*d*]pyrimidine]-6′-carbonitrile* (**18**). White solid. M.p. 290–292°. IR: 3350, 3300, 3195, 2954, 2199, 1720, 1667, 1613, 1522, 1474, 1364, 1224, 1132, 1072, 972, 748. ^{1}H-NMR: 10.64 (*s*, NH); 7.95 (*d*, *J* = 8.0, 1 arom. H); 7.77 (*t*, *J* = 7.6, 1 arom. H); 7.67 (br. *s*, NH_2); 7.57 (*t*, *J* = 7.6, 1 arom. H); 7.50 (*d*, *J* = 8.4, 1 arom. H); 7.22 (*t*, *J* = 7.6, 2 arom. H); 6.93 (*t*, *J* = 7.6, 1 arom. H); 6.85 (*d*, *J* = 8.0, 1 arom. H). EI-MS: 357 (M^+). Anal. calc. for $C_{20}H_{11}N_3O_4$: C 67.23, H 3.10, N 11.76; found: C 67.49, H 3.02, N 11.86.

*7′-Amino-1,1′,2,2′,3′,4′-hexahydro-1-methyl-2,2′,4′-trioxospiro[3*H*-indole-3,5′-[5*H*]pyrano[2,3-*d*]pyrimidine]-6′-carbonitrile* (**19**). White solid. M.p. 285–286°. IR: 3408, 3300, 3192, 2195, 1716, 1670, 1612, 1468, 1237, 1116, 1059, 968, 754. ^{1}H-NMR: 7.93 (*d*, *J* = 10.8, 1 arom. H); 7.76 (*t*, *J* = 10.8, 1 arom. H); 7.71 (br. *s*, NH_2); 7.55 (*t*, *J* = 10.8, 1 arom. H); 7.49 (*d*, *J* = 10.8, 1 arom. H); 7.26–7.34 (*m*, 2 arom. H); 6.98–7.08 (*m*, 2 arom. H); 3.19 (*s*, Me). EI-MS: 371 (M^+). Anal. calc. for $C_{21}H_{13}N_3O_4$: C 67.92, H 3.53, N 11.32; found: C 67.65, H 3.65, N 11.23.

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