The synthesis of some polycyclic N-H acids with quinoxaline and [1,2,4]triazines[1]

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Abstract
3-(4-Aminophenyl)-1,2-dihydro-quinoxaline-2-one (**2b**), 3-(2-aminophenyl)-6,7-dimethyl-1,2-dihydro-quinoxaline-2-one (**1b**), its 3-(4-aminophenyl)-isomer (**3b**), 3-(2-aminobenzyl)-1,2-dihydro-quinoxaline-2-one (**4b**), its 3-(4-aminobenzyl)-isomer (**6b**), 3-(2-aminobenzyl)-6,7-dimethyl-1,2-dihydro-quinoxaline-2-one (**5b**) and its 3-(4-aminobenzyl)-isomer (**7b**) were diazotised and the resulting diazonium salts were coupled with ethyl cyanoacetylcarbamate, 3-methyl-1,2-dihydro-quinoxaline-2-one, 3,6,7-trimethyl-1,2-dihydro-quinoxaline-2-one and 3-methyl-6,7-dichloro-1,2-dihydro-quinoxaline-2-one. In this manner the corresponding hydrazones with one 1,2-dihydro-quinoxaline-2-one ring (**1d, 3d, 5d, 7d**) and hydrazones with two 1,2-dihydro-quinoxaline-2-one rings (**3e-3g, 4e-4g, 5e-5g, 6e-6g, 7e-7g**) were obtained. Cyclization of hydrazones (**1d, 3d, 5d, 7d**) afforded compounds (**1h, 3h, 5h, 7h**) containing 6-azauracil and also 1,2-dihydroquinoxaline-2-one rings. The starting amino derivative (**1b**) was prepared by the reaction of N-acetylisatine with 4,5-dimethyl-o-phenylenediamine followed by hydrolysis of the N-acetyl derivative. The amino derivative (**5b**) was prepared by the condensation of 2-nitrophenylpyruvic acid with 4,5-dimethyl-o-phenylenediamine and by reduction of the formed nitro derivative (**5a**). The amino derivative (**3b**) was prepared by the condensation of 4-acetylaminophenylglyoxylic acid with 4,5-dimethyl-o-phenylenediamine and hydrolysis of the N-acetyl derivative. The amino derivative (**7b**) resulted from the condensation of 4,5-dimethyl-o-phenylenediamine with 4-aminophenylpyruvic acid.

Keywords: Anti-prion compounds, 1-aryl-6-azauracils, 1,2-dihydroquinoxaline-2-ones

Introduction

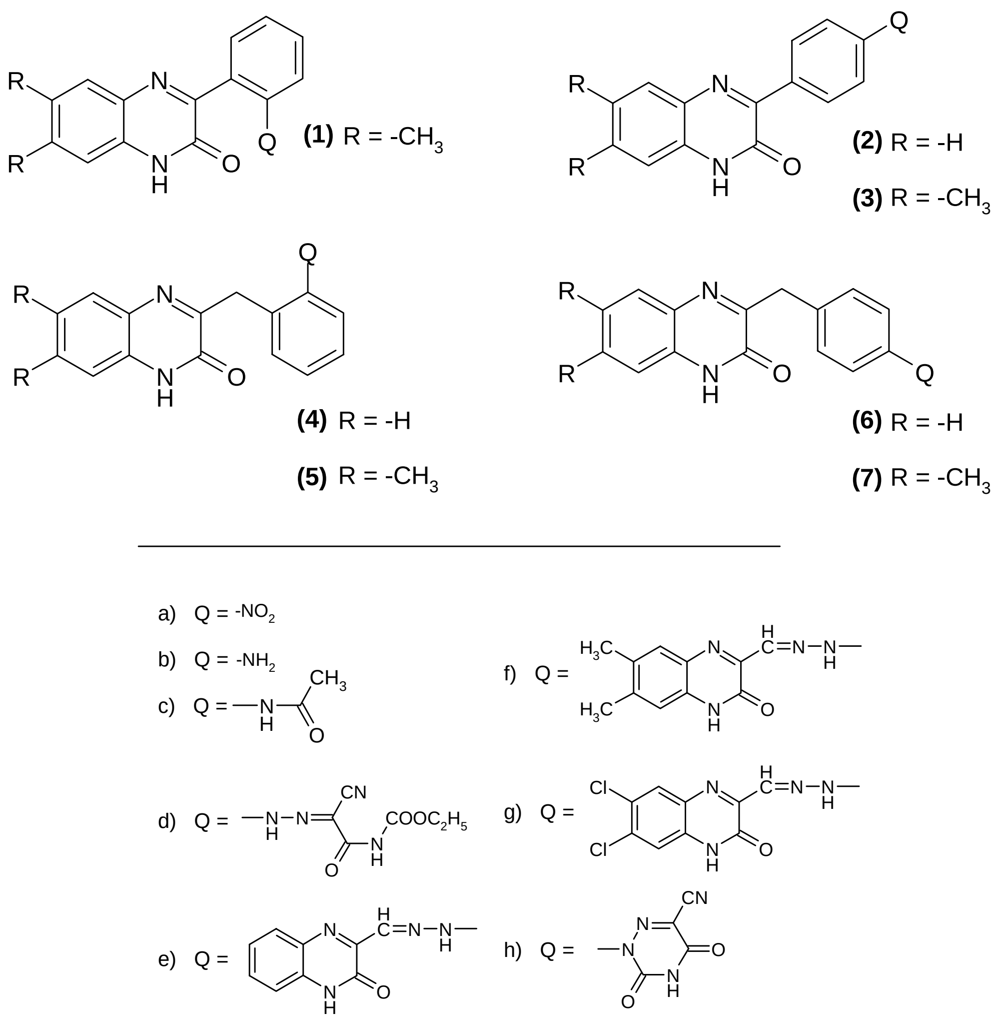
Neurological diseases such as Creutsfeldt-Jacob disease, bovine spongiform encephalopathy and scrapie are caused by induced conformational changes of a normal host protein designated as PrP^c to an abnormally folded protein designated as PrP^{Sc}. Compounds which can affect the conformation of the protein chain could be helpful in treatment of such diseases. The newly discovered anti-prion compounds can be grouped into branched polyamines or rigid condensed heterocycles with tetrapyrrole or acridine skeletons[2].

Also, some non-condensed polyatomic heterocyclic compounds in which free rotation of individual cycles can offer several conformations could be suitable in controlling conformations of the protein chain. Such molecules can adapt themselves to the spatial arrangement of a certain part of the protein chain but, at the same time, due to bonding and non-bonding interactions they can change the conformation of this chain.

Following some previous communications,[3-5] we have focused on the synthesis of compounds containing 6-azauracil and quinoxaline cycles.

Results and Discussion

6,7-Dimethyl-1,2-dihydro-quinoxaline-2-ones substituted with 2-aminophenyl-, 4-aminophenyl-, 2-aminobenzyl-, and 4-aminobenzyl- groups in the 3-position were key intermediates in the synthesis of the aforementioned compounds**.**



Scheme 1

The amino derivatives (**1b**), (**2b**), (**3b**), (**4b**), (**5b**), (**6b**) and (**7b**) were diazotised and the resulting diazonium salts coupled with ethyl cyanoacetylcarbamate, 3-methyl-1,2-dihydro-quinoxaline-2-one, 3,6,7-trimethyl-1,2-dihydro-quinoxaline-2-one and 3-methyl-6,7-dichloro-1,2-dihydro-quinoxaline-2-one in an aqueous solution of sodium acetate to provide hydrazones (**1d-1g, 2e-2g, 3d-3g, 4e-4g, 5d-5g, 6e-6g, 7d-7g**) in good yields. Cyclization of hydrazones (**1d, 3d, 5d, 7d**) in alkaline solution led to compounds (**1h, 3h, 5h, 7h**) with 6-azauracil and 1,2-dihydro-quinoxaline-2-one rings. Hydrazones (**1e-1g, 2e-2g, 3e-3g, 4e-4g, 5e-5g, 6e-6g, 7e-7g**) provided compounds with two 1,2-dihydro-quinoxaline-2-one moieties.

Starting amino derivatives were prepared in good yields from simple and easily accessible compounds. Compound (**1b**) was prepared from N-acetylisatine and 4,5-dimethyl-o-phenylenediamine according to a modified[6] procedure of Schunck and Marchlewski[7]. Compound (**5b**) was prepared by the condensation of 4,5-dimethyl-o-phenylenediamine with 2-nitrophenylpyruvic acid followed by reduction of o-nitrobenzyl derivative (**5a**). The amino derivative (**3b**) was prepared by the condensation of 4-acetylaminophenylglyoxylic acid with 4,5-dimethyl-o-phenylenediamine followed by hydrolysis of the N-acetyl derivative (**3c**). The amino derivative (**7b**) was obtained by the condensation of 4,5-dimethyl-o-phenylenediamine with 4-aminophenylpyruvic acid.

In the IR spectra of compounds (**1d-1h, 3d-3h, 5d-5h, 7d-7h**) the N-H valence vibrations were observed between 3440-3325 cm^{-1}, resp. 3260-3240 cm^{-1}. The nitrile group in compounds (**1d-1h, 3d-3h, 5d-5h, 7d-7h**) vibrated near 2200 cm^{-1}. In the ^{1}H NMR spectra of compounds (**1d-1h, 3d-3h, 5d-5h, 7d-7h**) the chemical shifts of the methyl groups were between 2.30-2.34 ppm, the aromatic hydrogen atoms between 7.31-8.23 ppm and NH at 10.63-13.26 ppm.

Experimental Section

3-(4-Aminophenyl)-6,7-dimethyl-1,2-dihydroquinoxaline-2-one (3b). A mixture of acetyl derivative (**3c**) (3.89 g; 12.66 mmole) and a solution of KOH (6.5 g) in a mixture of ethanol (30 ml) and water (25 ml) was heated until a solution formed. The solution was then refluxed for 5 hours. The ethanol was evaporated from the reaction mixture by heating on a water bath and the solution was acidified with acetic acid to pH 5. The next day, a yellow crystalline compound was collected with suction, washed with water and dried in air. For further details see tables 1-3 in the supplementary material section.

3-(4-Acetylaminophenyl)-6,7-dimethyl-1,2-dihydroquinoxaline-2-one (3c). To a solution of 4,5-dimethyl-o-phenylenediamine (272,4 mg; 2,0 mmole) in hot ethanol (5 ml), was added a solution of p-acetylaminophenylglyoxylic acid[8] (414,38 mg; 2,0 mmole) in hot ethanol (8 ml). The reaction mixture was refluxed for 5 minutes. The next day upon cooling, a crystalline compound was collected with suction, washed with water and dried in air. For further details see tables 1-3 in the supplementary material section.

3-(2-Nitrobenzyl)-6,7-dimethyl-1,2-dihydroquinoxaline-2-one (5a). To the solution of o-nitrophenylpyruvic acid[9] (417.6 mg; 1.99 mmole) in ethanol (10 ml) was added a solution of 4,5-dimethyl-o-phenylenediamine (305.09 mg; 2.24 mmole) in hot ethanol (4 ml). The reaction mixture was refluxed for 5 minutes. The ethanol was evaporated and water (20 ml) was added to the reaction mixture. The next day, a crystalline compound was collected with suction, washed with water and dried in air. For further details see tables 1-3 in the supplementary material section.

3-(2-Aminobenzyl)-6,7-dimethyl-1,2-dihydroquinoxaline-2-one (5b). To solution of $FeSO_4 \cdot 7H_2O$ (1.39 g; 5.0 mmole) in water (7 ml) was added to a solution of $Ba(OH)_2.8H_2O$ in hot water (15 ml). The mixture of $Fe(OH)_2$ and $BaSO_4$ was quickly collected with suction and washed with hot ethanol. The mixture was added to a solution of 3-(2-nitrobenzyl)-6,7-dimethyl-1,2-dihydroquinoxaline-2-one (**5a**) (154,66 mg; 5,0 mmol) in hot ethanol (60 ml). The reaction mixture was refluxed for 90 minutes on a water bath and then filtered with suction and washed with hot ethanol. The filtrate was evaporated and the solution was mixed with a little water. The product was collected with suction, washed with water and dried in air. For further details see tables 1-3 in the supplementary material section.

3-(4-Aminobenzyl)-6,7-dimethyl-1,2-dihydroquinoxaline-2-one (7b). A solution of p-aminophenylpyruvic acid hydrochloride[10] (413.36 mg; 2.0 mmol) in ethanol (40 ml) was added to a solution of 4,5-dimethyl-o-phenylenediamine (272.4 mg; 2.0 mmol) in hot ethanol (8 ml). The reaction mixture was refluxed for 5 minutes and then evaporated to dryness. The resultant solid was dissolved in water (60 ml), and the pH was adjusted to 7 using ammonia solution. The next day, a crystalline compound was collected with suction, washed with water and dried. For further details see tables 1-3 in the supplementary material section.

General procedure of the synthesis of 1,2-dihydro-quinoxaline-2-ones substituted in position 3 (1d-7d, 1e-7e, 1f-7f, 1g-7g)

A solution of $NaNO_2$ (140.0; 2.0 mmole) in ice-cold water (4 ml) was added portionwise under stirring to a solution (2.02 mmole) of the corresponding aromatic amine **2b-8b** in a mixture of hydrochloric acid (37 %, 3.0 ml) and water (10-30 ml), which was cooled in an ice-bath. The solution was left to stand for 30-60 min and then was added portionwise during 10 min to a stirred mixture obtained by dissolving the following compounds as stated below.

For preparation of compounds (**1d-7d**): ethyl cyanoacetylcarbamate (0.42 g; 2.691 mmole) in warm water (110 ml), cooling on an ice bath, adding CH_3COONa (5 g) and crushed ice.

For preparation of compounds (**1e-7e**): 3-methyl-1,2-dihydro-quinoxaline-2-one (324mg; 2.02 mmole) in water (2 ml) and acetic acid (15 ml), adding CH_3COONa (1.0 g) and crushed ice.

For preparation of compounds (**1f-7f**): 3,6,7-trimethyl-1,2-dihydro-quinoxaline-2-one (380.2mg; 2.02 mmole) in water (2 ml) and acetic acid (30 ml), adding CH_3COONa (2.0 g) and crushed ice.

In each case, the next day, a crystalline compound was collected with suction, washed with water and dried in air.

For compounds (**1g-7g**): 3-methyl-6,7-dichloro-1,2-dihydro-quinoxaline-2-one (462.0 mg; 2.02 mmole) in pyridine (30 ml) was used.

The next day, the reaction mixture was diluted with water and the next day, crystalline compound was collected with suction, washed with water and dried in air.

The data for these compounds are outlined in tables 1-3 in the supplementary material section.

2-[2-(2-Oxo-1,2-dihydro-6,7-dimethyl-quinoxalin-3-yl)-phenyl]-3,5-dioxo-2,3,4,5-tetra-hydro-1,2,4-triazin-6-carbonitrile (1h). A mixture of hydrazone (**1d**) (0.432 g; 1.0 mmole), Na_2CO_3 (120.0 mg) and water (10 ml) was heated on a boiling water bath until a solution was formed and then for an additional 15 minutes. The solution was then allowed to cool and acidified with hydrochloric acid (37 %) to pH 1. After several hours, the crystalline solid was collected by suction, washed with a little water and dried in air.

Compounds (**3h**), (**5h**) and (**7h**) were prepared by analogy to (**1h**) from hydrazones (**3d**), (**5d**) and (**7d**).

For further details see tables 1-3 in the supplementary material section.

Melting points (Boetius) were not corrected. Infrared spectra were measured as potassium bromide disks and scanned on an ATI Unicam Genesis FTIR instrument. The NMR spectra were measured in DMSO-d_6 solutions on a Bruker AMX-360 spectrometer (360 MHz) with TMS as an internal standard. Elemental analyses were performed using an EA 1108 Elemental Analyzer (Fison Instrument).

Supplementary Information

See Table 1 on page 70. Characteristic data of compounds **1-7.**
See Table 2 on page 72. ^{1}H-NMR spectra of compounds **1-7.**
See Table 3 on page 74. IR spectra of compounds **1-7.**

Acknowledgments

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Table 1. Characteristic data of compounds **1-7**

Compound	M.p. (°C) Yield (%)	Formula M.w.	Elemental Analysis (Calcd./Found) %C	%H	%N
1d	219-220 70.1	$C_{22}H_{20}N_6O_4$ 432.44	61.11 61.00	4.66 4.59	19.43 19.30
1h	184-185 69.3	$C_{20}H_{14}N_6O_3$ 386.37	62.17 62.00	3.65 3.70	21.75 21.67
2e	265-267 80.0	$C_{23}H_{16}N_6O_2$ 408.42	67.64 67.50	3.95 3.77	20.58 20.69
2f	249-250 78.9	$C_{25}H_{20}N_6O_2$ 436.47	68.80 68.61	4.62 4.55	19.25 19.34
2g	290-291 70.4	$C_{23}H_{14}N_6O_2Cl_2$ 477.4	57.87 57.66	2.96 3.12	17.60 17.79
3b	239-240 89.0	$C_{16}H_{15}N_3O$ 265.31	72.43 72.22	5.70 5.89	15.84 15.91
3c	254-255 89.9	$C_{18}H_{17}N_3O_2$ 307,.5	70.34 70.20	5.57 5.58	13.67 13.52
3d	239-241 87.2	$C_{22}H_{20}N_6O_4$ 432.44	61.11 61.23	4.66 4.78	19.43 19.50
3e	239-240 89.0	$C_{25}H_{20}N_6O_2$ 436.47	68.80 68.91	4.62 4.73	19.25 19.00
3f	278-280 70.9	$C_{27}H_{24}N_6O_2$ 464.53	69.81 69.67	5.21 5.33	18.09 18.00
3g	240-241 88.8	$C_{25}H_{18}N_6O_2Cl_2$ 505.46	59.41 59.48	3.59 3.47	16.63 16.73
3h	244-245 97.9	$C_{20}H_{14}N_6O_3$ 386.37	62.17 62.32	3.65 3.71	21.75 21.81
4e	330-331 88.7	$C_{24}H_{18}N_6O_2$ 422.45	68.24 68.10	4.29 4.41	19.89 19.99
4f	255-256 87.8	$C_{26}H_{22}N_6O_2$ 450.50	69.32 69.09	4.92 5.03	18.65 18.64
4g	277-278 75.4	$C_{24}H_{16}N_6O_2Cl_2$ 491.43	58.66 58.79	3.28 3.44	17.10 16.99
5a	215-217 59.8	$C_{17}H_{15}N_3O_3$ 309.32	66.01 66.00	4.89 4.76	13.58 13.64
5b	171-172 65.9	$C_{17}H_{17}N_3O$ 279.34	73.10 73.02	6.13 6.04	15.04 14.92
5d	225-226 68.9	$C_{23}H_{22}N_6O_4$ 446.46	61.88 61.86	4.97 4.55	18.82 18.70
5e	240-242 87.1	$C_{26}H_{22}N_6O_2$ 450.5	69.32 69.48	4.92 5.05	18.65 18.79

Table 1. Continued

Compound	M.p. (°C) Yield (%)	Formula M.w.	Elemental Analysis (Calcd./Found) %C	%H	%N
5f	245-247 86.6	$C_{28}H_{26}N_6O_2$ 478.55	70.28 70.09	5.48 5.55	17.56 17.57
5g	269-272 83.0	$C_{26}H_{20}N_6O_2Cl_2$ 519.48	60.11 60.00	3.88 3.64	16.18 16.09
5h	169-171 61.0	$C_{21}H_{16}N_6O_3$ 400.4	63.00 62.90	4.03 4.12	20.99 20.89
6e	239-240 89.0	$C_{24}H_{18}N_6O_2$ 422.45	68.24 68.44	4.29 4.10	19.89 19.85
6f	290-291 70.4	$C_{26}H_{22}N_6O_2$ 450.50	69.32 69.13	4.92 5.00	18.65 18.69
6g	239-240 89.0	$C_{24}H_{16}N_6O_2Cl_2$ 491.43	58.66 58.82	3.28 3.40	17.10 16.99
7b	250-251 89.9	$C_{17}H_{17}N_3O$ 279.34	73.10 73.19	6.13 6.21	15.04 14.99
7d	264-265 86.2	$C_{23}H_{22}N_6O_4$ 446.46	61.88 61.76	4.97 4.64	18.82 18.79
7e	242-244 93.0	$C_{26}H_{22}N_6O_2$ 450.5	69.32 69.47	4.92 5.11	18.65 18.66
7f	250-251 79.3	$C_{28}H_{26}N_6O_2$ 478.55	70.28 70.33	5.48 5.61	17.56 17.65
7g	250-251 89.9	$C_{26}H_{20}N_6O_2Cl_2$ 519.48	60.11 59.98	3.88 3.94	16.34 16.31
7h	233-234 78.9	$C_{21}H_{16}N_6O_3$ 400.4	63.00 62.93	4.03 4.05	20.99 20.91

Table 2. ^{1}H NMR spectra of compounds **1-7**

Compound	^{1}H NMR spectrum, δ [ppm]
1d	1.28 (t, 3H, J=7.0, CH_3); 2.29 (s, 3H, CH_3); 2.32 (s, 3H, CH_3); 4.16 (q, 2H, J=7.0, CH_2); 7.31 (m, 2H, ArH); 7.57 (m, 1H, ArH); 7.81 (s, 1H, ArH); 8.23 (m, 2H, ArH); 10.63 (s, 1H, NH); 12.77 (s, 1H, NH); 13.26 (s, 1H, NH).
1h	2.30 (s, 3H, CH_3); 2.34 (s, 3H, CH_3); 7.13 (s, 1H, ArH); 7.54 (s, 1H, ArH); 7.66 (m, 3H, ArH); 8.01 (d, 1H, J=8.03, ArH); 12.72 (s, 1H, NH); 13.20 (s, 1H, NH).
2e	7.,19 (t, 1H, J = 7.39, ArH); 7.36 (m, 4H, ArH); 7.50 (d, 1H, J=7.94, ArH); 7.60 (m, 4H, ArH); 8.01 (d, 1H, J=7.89, ArH); 8.04 (d, 1H, J=7.92, ArH); 8.25 (s, 1H, CH); 10.79 (s, 1H, NH;, 12.60 (s, 1H, NH).
2f	2.,27 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 7.22 (t, 1H, J = 7.42, ArH); 7.26 (m, 4H, ArH); 7.57 (m, 1H, ArH); 7.62 (m, 3H, ArH); 8.03 (d, 1H, J=7.90, ArH); 8.27 (s, 1H, CH); 10.80 (s, 1H, NH), 12.61 (s, 1H, NH).
2g	7.08 (t, 1H, J = 7.39, ArH); 7.30 (m, 2H, ArH); 7.44 (m, 1H, ArH); 7.60 (m, 4H, ArH); 8.10(m, 1H, ArH); 8.14 (m, 1H, ArH); 8.32 (s, 1H, CH); 10.90 (s, 1H, NH); 12.69 (s, 1H, NH).
3b	2.31 (s, 3H, CH_3); 2.35 (s, 3H, CH_3); 5.70 (s, 2H, NH_2); 6.60 (d, 2H, J = 5.14, ArH); 7.06(d, 1H, J = 7.68, ArH); 7.65 (s, 1H, ArH); 8.24 (d, 2H, J = 7.70, ArH); 12.23 (s, 1H, NH).
3c	2.11 (s, 3H, CH_3); 2.33 (s, 3H, CH_3); 2.35 (s, 3H, CH_3); 7.11 (s, 1H, ArH); 7.68 (m, 3H, ArH); 8.34 (m, 2H, ArH); 10.19 (s, 1H, NH); 12.25 (s, 1H, NH).
3d	1.35 (t, 3H, J=7.00, CH_3); 2.31 (s, 3H, CH_3); 2.35 (s, 3H, CH_3); 4.39 (d, 2H, J=7.00, CH_2); 6.60 (m, 2H, ArH); 7.06 (s, 1H, ArH); 7.65 (s, 1H, ArH); 8.24(d, 2H, J= 8.85, ArH); 10.75 (s, 1H, NH); 12.24 (s, 1H, NH); 12.23(s, 1H, NH).
3e	2.31 (s, 3H, CH_3); 2.33 (s, 3H, CH_3); 7.19 (t, 1H, J = 7.39, ArH); 7.36 (m, 3H, ArH); 7.50 (d, 1H, J=7.94, ArH); 7.60 (m, 3H, ArH); 8.01 (d, 1H, J=7.89, ArH); 8.04 (m, 1H, ArH); 8.06 (s, 1H, CH); 10.79 (s, 1H, NH); 12.60 (s, 1H, NH).
3f	2.27 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 2.33 (s, 6H, CH_3); 7.19 (t, 1H, J = 7.39, ArH); 7.36 (m, 3H, ArH), 7.50 (d, 1H, J=7.94, ArH); 7.60 (m, 2H, ArH); 8.01(d, 1H, J=7.89, ArH); 8.06 (s, 1H, CH); 10.79 (s, 1H, NH); 12.60 (s, 1H, NH).
3g	2.28 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 7.19 (m, 1H, ArH); 7.40 (m, 3H, ArH); 7.55 (d, 1H, J=7.88, ArH); 7.63 (m, 2H, ArH); 8.10 (m, 1H, ArH); 8.12 (s, 1H, CH); 10.88 (s, 1H, NH),; 12.33 (s, 1H, NH).
3h	2.31 (s, 3H, CH_3); 2.35 (s, 3H, CH_3); 6.60 (d, 2H, J = 7.80, ArH); 7.06 (s, 1H, ArH); 7.65 (s, 1H, ArH); 8.24 (m, 2H, ArH); 12.28 (s, 1H, NH); 12.31 (s, 1H, NH).
4e	4.25 (s, 2H, CH_2); 7.10 (t, 1H, J = 7.40, ArH); 7.29 (m, 5H, ArH), 7.52 (d, 1H, J=7.90, ArH); 7.59 (m, 3H, ArH); 8.00 (d, 1H, J=7.91, ArH); 8.02 (d, 1H, J=7.88, ArH); 8.17 (s, 1H, CH); 10.76 (s, 1H, NH), 12.44 (s, 1H, NH).
4f	2.25 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 4.20 (s, 2H, CH_2); 7.20 (m, 1H, ArH); 7,23 (m, 3H, ArH); 7.60 (m, 1H, ArH); 7.62 (m, 3H, ArH); 8.03 (m, 1H, ArH); 8.10 (m, 1H, ArH); 8.12 (s, 1H, CH); 11.00 (s, 1H, NH); 12.71 (s, 1H, NH).
4g	4.33 (s, 2H, CH_2); 7.26 (t, 1H, J = 7.22, ArH); 7.40 (m, 4H, ArH); 7.51 (d, 1H, J=7.96, ArH); 7.59 (m, 2H, ArH); 7.88 (d, 1H, J=7.91, ArH); 8.04 (d, 1H, J=7.93, ArH); 8.19 (s, 1H, CH); 10.99 (s, 1H, NH); 12.55 (s, 1H, NH).
5a	2.27 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 4.56 (s, 2H, CH_2); 7.00 (m, 1H, ArH); 7.24 (t, 1H, J = 7.41, ArH); 7.44 (m, 2H, ArH); 7.60 (m, 2H, ArH); 12.30 (s, 1H, NH).

Table 2. Continued

Compound	^{1}H NMR spectrum, δ [ppm]
5b	2.28 (s, 3H, CH_3); 2.32 (s, 3H, CH_3); 4.06 (s, 2H, CH_2); 5.18 (s, 2H, NH_2); 6.89 (m, 3H, ArH); 7.51 (m, 3H, ArH); 12.26 (s, 1H, NH).
5d	1.25 (t, 3H, J =7.1, CH_3); 2.30 (s, 3H, CH_3); 2.32 (s, 3H, CH_3); 4.16 (q, 2H, J =7.3, CH_2); 4.50 (s, 2H, CH_2); 7.28 (m, 2H, ArH); 7.30 (m, 1H, ArH); 7.81 (s, 1H, ArH); 8.22 (m, 2H, ArH); 10.78 (s, 1H, NH); 12.00 (s, 1H, NH); 13.11(s, 1H, NH).
5e	2.28 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 4.21 (s, 2H, CH_2); 7.08 (m, 3H, ArH); 7.33 (m, 3H, ArH); 7.56 (m, 1H, ArH); 7.59 (m, 2H, ArH); 8.06 (d, 1H, J=7.89, ArH); 8.18 (s, 1H, CH); 10.67 (s, 1H, NH); 12.57 (s, 1H, NH).
5f	2.23 (s, 6H, CH_3); 2.25 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 4.33 (s, 2H, CH_2); 7.21 (m, 1H, ArH); 7.25 (m, 2H, ArH); 7.69 (m, 1H, ArH); 7.70 (m, 2H, ArH); 8.00 (m, 1H, ArH); 8.18 (m, 1H, ArH); 8.31 (s, 1H, CH); 10.76 (s, 1H, NH); 12.44 (s, 1H, NH).
5g	2.26 (s, 3H, CH_3); 2.30 (s, 3H, CH_3); 4.38 (s, 2H, CH_2); 7.36 (t, 1H, J = 7.20, ArH); 7.44 (m, 3H, ArH); 7.51 (d, 1H, J=7.96, ArH); 7.76 (m, 1H, ArH); 7.88 (d, 1H, J=7.91, ArH); 7,99 (d, 1H, J=7.90, ArH); 8.12 (s, 1H, CH); 11.00 (s, 1H, NH); 12.49 (s, 1H, NH).
5h	2.31 (s, 3H, CH_3); 2.35 (s, 3H, CH_3); 4.09 (s, 2H, CH_2); 6.60 (d, 2H, J = 7.80, ArH); 7.06 (s, 1H, ArH); 7.65 (s, 1H, ArH); 8.24 (m, 2H, ArH); 12.28 (s, 1H, NH); 12.31 (s, 1H, NH)
6e	4.30 (s, 2H, CH_2); 7.19 (t, 1H, J = 7.39, ArH); 7.36 (m, 5H, ArH); 7.50 (d, 1H, J=7.94, ArH); 7.60 (m, 3H, ArH); 8.01 (d, 1H, J=7.89, ArH); 8.04 (d, 1H, J=7.92, ArH); 8.20 (s, 1H, CH); 10.79 (s, 1H, NH); 12.60(s, 1H, NH).
6f	2.27 (s, 3H, CH_3); 2.29 (s, 3H, CH_3); 4.19 (s, 2H, CH_2); 7.23 (m, 1H, ArH); 7.26 (m, 4H, ArH); 7.62 (m, 1H, ArH); 7.65 (m, 3H, ArH); 8.13 (m, 1H, ArH); 8.15 (s, 1H, CH); 11.02 (s, 1H, NH); 12.79 (s, 1H, NH).
6g	4.33 (s, 2H, CH_2); 7.26 (t, 1H, J = 7.22, ArH); 7.40 (m, 3H, ArH); 7.51 (d, 1H, J=7.96, ArH); 7.59 (m, 3H, ArH); 7.88 (d, 1H, J=7.91, ArH); 8.04 (d, 1H, J=7.93, ArH); 8.10 (s, 1H, CH); 10.99 (s, 1H, NH); 12.55 (s, 1H, NH).
7b	2.31 (s, 3H, CH_3); 2.32 (s, 3H, CH_3); 4.14 (s, 2H, CH_2); 5.28 (s, 2H, NH_2); 6.93 (m, 3H, ArH); 7.54 (m, 3H, ArH); 12.39 (s, 1H, NH).
7d	1.30 (t, 3H, J=7.06, CH_3); 2.30 (s, 3H, CH_3); 2.35 (s, 3H, CH_3); 4.21 (m, 4H, CH_2); 7.30 (t, 2H, J=7.70, ArH); 7.40 (t, 1H, J=8.40, ArH); 7.52 (t, 1H, J=7.47, ArH); 7.68 (d, 1H, J=8.50, ArH); 7.71 (t, 1H, J=7.52, ArH); 10.61 (s, 1H, NH); 12.41 (s, 1H, NH); 12.71 (s, 1H, NH).
7e	2.29 (s, 3H, CH_3); 2.33 (s, 3H, CH_3); 4.25 (s, 2H, CH_2); 7.19 (t, 2H, J = 7.39, ArH); 7.36 (m, 3H, ArH); 7.50 (d, 1H, J=7.94, ArH); 7.60 (m, 4H, ArH); 8.66 (s, 1H, CH); 10.32 (s, 1H, NH); 10.79 (s, 1H, NH); 12.60 (s, 1H, NH).
7f	2.27 (s, 6H, CH_3); 2.30 (s, 3H, CH_3); 2.34 (s, 3H, CH_3); 4.25 (s, 2H, CH_2); 7.36 (m, 4H, ArH); 7.60 (m, 4H, ArH); 8.66 (s, 1H, CH); 10.32 (s, 1H, NH); 10.79 (s, 1H, NH); 12.60 (s, 1H, NH).
7g	2.29 (s, 3H, CH_3); 2.31 (s, 3H, CH_3); 4.28 (s, 2H, CH_2); 7.27 (m, 2H, ArH); 7.36 (m, 3H, ArH;, 7.58 (d, 1H, J=7.94, ArH); 7.63 (m, 2H, ArH); 8.73 (s, 1H, CH); 10.39 (s, 1H, NH); 10.82 (s, 1H, NH); 12.65 (s, 1H, NH).
7h	2.32 (s, 3H, CH_3); 2.3 (s, 3H, CH_3); 4.32 (s, 2H, CH_2); 7.30 (d, 1H, J=7.70, ArH); 7.40 (d, 1H, J=8.40, ArH); 7.52 (d, 1H, J=7.47, ArH); 7.68 (d, 2H, J=8.50, ArH); 7.71 (d, 1H, J=7.52, ArH); 12.41(s, 1H, NH); 12.71(s, 1H, NH).

Table 3. IR spectra of compounds **1-7**

Compound	IR spectrum
1d	3225, 3062, 2983, 2940, 2213, 1772, 1752, 1654, 1488, 1444, 1394, 1284, 1197, 1093, 1025, 925, 863, 757, 669, 605, 578, 497, 431
1h	3328, 3197, 3143, 3075, 2964, 2923, 2240, 1716, 1660, 1631, 1571, 1494, 1450, 1392, 1332, 1292, 1251, 1189, 1106, 1054, 1020, 875, 804, 767, 719, 624, 590, 528, 472, 422
2e	3030, 1672, 1600, 1547, 1498, 1449, 1288, 1206, 1156, 1081, 857, 762, 691
2f	3033, 2880, 1718, 1665, 1555, 1503, 1444, 1270, 1235, 1138, 1090, 905, 760, 666
2g	1668, 1607, 1567, 1465, 1376, 1183, 899, 758, 595
3b	3478, 3336, 3205, 2921, 2858, 1710, 1656, 1604, 1523, 1471, 1282, 1180, 1024, 881, 592, 536, 451
3c	3245, 3176, 3068, 2929, 2858, 1692, 1656, 1598, 1525, 1407, 1324, 1280, 1180, 1008, 854, 806, 760, 669, 590, 526, 460
3d	3190, 2985, 2899, 2215, 1770, 1704, 1660, 1600, 1540, 1488, 1377, 1270, 1000, 855, 660
3e	3053, 2980, 2889, 1719, 1663, 1570, 1523, 1444, 1293, 1245, 1138, 1100, 905, 767
3f	2918, 2869, 1659, 1623, 1560, 1487, 1395, 1253, 1178, 990, 904, 866, 592
3g	3000, 2969, 1675, 1635, 1599, 1567, 1445, 1300, 1283, 999, 770, 590
3h	3030, 2990, 2244, 1710, 1650, 1604, 1540, 1401, 1325, 1189, 1090, 755, 600, 535
4e	3251, 3196, 3151, 3074, 2879, 1661, 1611, 1534, 1451, 1393, 1326, 1180, 1152, 976, 905, 843, 745, 593
4f	3030, 1672, 1600, 1547, 1498, 1449, 1288, 1206, 1156, 1081, 857, 762, 691
4g	3033, 2880, 1718, 1665, 1555, 1503, 1444, 1270, 1235, 1138, 1090, 905, 760, 666
5a	3160, 2946, 2919, 2869, 1658, 1554, 1523, 1442, 1398, 1336, 1263, 1164, 1137, 1024, 890, 862, 796, 730, 671, 592, 514, 428
5b	3420, 3149, 3064, 2971, 2861, 1698, 1604, 1525, 1483, 1396, 1313, 1286, 1170, 1091, 1006, 881, 846, 773, 669, 597, 518, 458
5d	3285, 2967, 2215, 1770, 1740, 1664, 1631, 1579, 1490, 1373, 1276, 1176, 1093, 1024, 983, 755, 682, 597, 503, 431
5e	3043, 2980, 2880, 1720, 1660, 1573, 1523, 1444, 1293, 1245, 1138, 1100, 905, 767
5f	2918, 2869, 1659, 1623, 1560, 1487, 1395, 1253, 1178, 990, 904, 866, 592
5g	3000, 2969, 1675, 1635, 1599, 1567, 1445, 1300, 1283, 999, 770, 590
5h	3108, 2911, 2220, 1697, 1632, 1600, 1577, 1400, 1325, 1100, 1000, 755, 600
6e	3251, 3196, 3151, 3074, 2879, 1661, 1611, 1534, 1451, 1393, 1326, 1180, 1152, 976, 905, 843, 745, 593
6f	3030, 1672, 1600, 1547, 1498, 1449, 1288, 1206, 1156, 1081, 857, 762, 691
6g	3029, 2880, 1718, 1665, 1585, 1503, 1444, 1270, 1235, 1138, 1090, 905, 760, 666
7b	3440, 3325, 3154, 3099, 3054, 3000, 2967, 1684, 1507, 1437, 1429, 1262, 1000, 812, 709, 632, 582
7d	3226, 3188, 3050, 2989, 2900, 2213, 1768, 1699, 1650, 1609, 1544, 1480, 1268, 1011, 920, 770, 667
7e	3055, 2989, 2878, 1739, 1662, 1569, 1523, 1444, 1280, 1239, 1138, 1090, 900, 770
7f	3312, 2920, 2879, 1667, 1633, 1552, 1487, 1300, 1247, 1189, 999, 900, 876, 590
7g	3120, 2979, 1669, 1600, 1599, 1577, 1459, 1299, 1200, 999, 767, 583
7h	3100, 3069, 3023, 2220, 1730, 1665, 1599, 1519, 999, 693, 648