Tetrazole Compounds. 10 [1]. Novel Tetrazolylindoles by Fischer Indolization of Substituted Tetrazolylacetaldehyde Phenylhydrazones

Gerhard W. Fischer

Institut für Organische Chemie, Universität Leipzig, Aussenstelle,
Permoserstrasse 15, 04303 Leipzig, Germany

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The acid-catalyzed reaction of substituted phenylhydrazines **1** with 1-aryl-5-(2-dimethylaminovinyl)-1*H*-tetrazoles **2** afforded (1-aryl-1*H*-tetrazol-5-yl)acetaldehyde phenylhydrazones **3** which on heating in acetic acid/perchloric acid underwent a Fischer indolization to give substituted 3-(1-aryl-1*H*-tetrazol-5-yl)-indoles **4a-k**. Indoles of this type are also formed on subjecting **1** and **2** directly to indolization conditions; thus, starting from phenylhydrazine the tetrazolylindoles **4l-s** were obtained by a one-pot procedure. Indolization of corresponding N_α-methylphenylhydrazones **5** resulted in 1-methyl-3-(1-aryl-1*H*-tetrazol-5-yl)indoles **6**.

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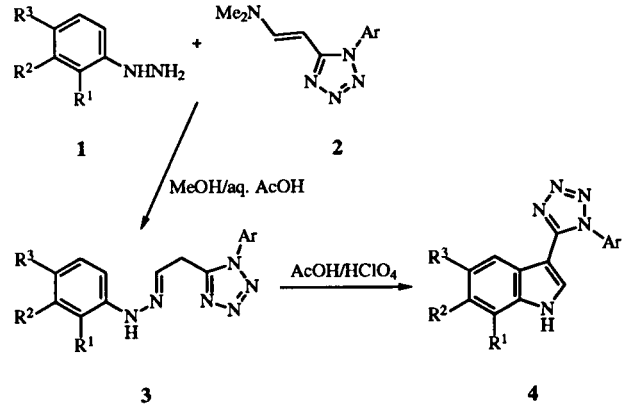
The continuing interest in the chemistry of indoles comes largely from the potent biological activity of many indole derivatives [2]. In the class of tetrazolyl-substituted indoles a number of compounds were reported to possess antiinflammatory [3], CNS antidepressant [4], 5-HT_4 antagonist [5] and aldose reductase inhibitory activity [6]. These and other tetrazolylindoles and indolyltetrazolium salts described in the literature [7-9] were synthesized exclusively through a tetrazole ring-closure reaction starting from appropriate indole derivatives. However, so far no examples were known for the reverse order, *i.e.* for indole ring-closure reactions starting from suitably substituted tetrazole derivatives. The present communication describes the first time an approach for preparing tetrazolylindoles in the last-mentioned way.

The idea of this study arose from the observation that the easily accessible 1-aryl-5-(2-dimethylaminovinyl)-1*H*-tetrazoles **2** [10] under acidic conditions smoothly react with various carbonyl reagents to give stable derivatives (*e.g.*, arylhydrazones, thiosemicarbazones, *etc.*) of (1-aryl-1*H*-tetrazol-5-yl)acetaldehydes, whereas the free aldehydes theirself, if generated from **2** by acid-catalyzed hydrolysis, proved to be unstable [11]. The simple entry to tetrazolylacetaldehyde arylhydrazones suggested their transformation into tetrazolylindoles by the Fischer indole synthesis [12].

In order to test this possibility a series of substituted phenylhydrazines **1** were reacted (mostly in form of their hydrochlorides) with enamines of type **2** in aqueous methanolic acetic acid to give the (1-aryl-1*H*-tetrazol-5-yl)-acetaldehyde phenylhydrazones **3a-k** in 72-98% yields. First attempts to effect the Fischer indolization of these arylhydrazones showed that they are stable in boiling acetic acid, whereas heating with alcoholic mineral acids mainly leads to other products rather than indoles [13]. However, the expected indolization could be achieved using a boiling mixture of acetic acid and 70% perchloric acid [14] as the reaction medium. Under these conditions **3a-k** were transformed into the substituted 3-(1-aryl-1*H*-tetrazol-5-yl)-indoles **4a-k** in 41-88% yields. In case of the 3,4-disubstituted phenylhydrazones **3j** and **3k**, as expected [12], the indolization resulted in mixtures of two regioisomeric indoles; recrystallization of the crude products afforded the predominating isomers **4j** and **4k** in pure state.



1 **2** **3** **4**

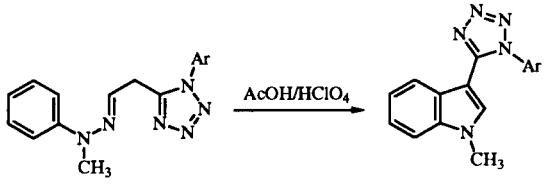
3	4	R^1	R^2	R^3	Ar
a	**a**	H	H	Me	Ph
b	**b**	H	H	F	Ph
c	**c**	Cl	H	H	Ph
d	**d**	H	H	Cl	Ph
e	**e**	Me	Me	H	Ph
f	**f**	Me	H	Me	Ph
g	**g**	F	H	F	Ph
h	**h**	Cl	H	Cl	Ph
i	**i**	H	H	Me	4-Cl-C_6H_4
j	**j**	H	Cl	F	Ph
k	**k**	H	Cl	Cl	Ph
	l	H	H	H	Ph
	m	H	H	H	4-Me-C_6H_4
	n	H	H	H	4-Et-C_6H_4
	o	H	H	H	4-MeO-C_6H_4
	p	H	H	H	4-F-C_6H_4
	q	H	H	H	4-Cl-C_6H_4
	r	H	H	H	4-Br-C_6H_4
	s	H	H	H	4-Ph-C_6H_4

All the indoles **4a-k** can also be prepared by subjecting equimolar mixtures of **1** and **2** directly to indolization conditions, only the yields are mostly some lower. However, the one-pot procedure is favorable when the arylhydrazones **3** are difficult to isolate due to low melting points or low tendency to crystallize. Starting from phenylhydrazine (**1**, $R^1 = R^2 = R^3 = H$) in this way the 3-(1-aryl-1*H*-tetrazol-5-yl)indoles **4l-s** were obtained in 26-51% yields. In view of the fact that the indolization of aldehyde arylhydrazones frequently affords low yields of the desired 3-substituted indoles [12] the moderate yields of **4a-s** may be regarded as reasonable.

In case of phenylhydrazines with halogen substituents in certain positions, *e.g.*, 2,5-difluoro- or 3,5-dichlorophenylhydrazine, the indolization of the corresponding phenylhydrazones failed and the reaction afforded other products [13].

Heterocycles of type **4** represent a novel type of 3-substituted tetrazolylindoles, differing from hitherto described compounds of this class [3-5,7-9] by another substitution pattern of the tetrazole moiety. Moreover, the reaction **1** + **2** → **4** demonstrates that also enamines successfully may function as protected aldehydes in the Fischer synthesis of 2-unsubstituted indoles; so far labile aldehydes were mainly used in form of their acetals [12,15-22], aminals [23] or bisulfite addition products [24].

Structure proof for all newly synthesized compounds rests on elemental analyses as well as on ^1H nmr spectroscopic data (Tables 1 and 2). To exclude a possible migration of the 3-substituent to position 2 of the indole moiety, a reaction often observed in 2-unsubstituted indoles under indolization conditions [12], special attention was directed to the assignment of the indole five-membered ring proton of **4a-s**. The ^1H nmr signal of this proton appears throughout as a characteristic doublet (J ~ 2.9 Hz) at δ 6.85-7.15 ppm indicating a proton located at C-2 [25]. Further confirmation of this assignment was obtained from NOE experiments with the 1-methyl derivatives **6**, synthesized in the same manner by indolization of corresponding N_α-methylphenylhydrazones **5**. Irradiation of the 1-methyl signal caused a strong NOE in the indole five-membered ring hydrogen, proving vicinity of the latter to the 1-methyl group.



5 **6**

5, 6	Ar
a	4-Me-C_6H_4
b	4-MeO-C_6H_4
c	4-Cl-C_6H_4

EXPERIMENTAL

Melting points were determined on a "Boetius" hot-stage apparatus and are uncorrected. The ^1H nmr spectra were recorded with a Varian G 200 instrument (200 MHz) at ambient temperature using DMSO-d_6 as the deuterated solvent and TMS as the internal reference. The preparation of the 1-aryl-5-(2-dimethylaminovinyl)-1*H*-tetrazoles **2** is described in [10].

General Procedure for the Preparation of Substituted (1-Aryl-1*H*-tetrazol-5-yl)acetaldehyde Phenylhydrazones **3a-k**.

A solution of 10 mmoles of the 1-aryl-5-(2-dimethylaminovinyl)-1*H*-tetrazole **2** in methanol (10 ml) was added to a hot solution of 10 mmoles of a substituted phenylhydrazine **1** or its hydrochloride in a mixture of methanol (10 ml), acetic acid (1.5 ml) and water (1.5 ml). After refluxing for 5 minutes the solvent was partially distilled off (10-15 ml). On cooling the products **3a-k** precipitated as colorless crystals.

Data on the prepared compounds are listed in Table 1.

Synthesis of the Substituted 3-(1-Aryl-1*H*-tetrazol-5-yl)indoles **4a-k**. General Procedure.

To a stirred solution of 10 mmoles of the respective (1-aryl-1*H*-tetrazol-5-yl)acetaldehyde phenylhydrazone **3** in hot acetic acid (4 ml) 70% perchloric acid (2 ml) was added and the reaction mixture heated under reflux for 15 minutes. After adding some drops of water the products **4a-k** precipitated slowly on standing overnight at room temperature. They were filtered off, washed with cold ethanol and recrystallized from the solvents given in Table 2.

General Procedure for the Preparation of 3-(1-Aryl-1*H*-tetrazol-5-yl)indoles **4l-s** by a One-Pot Reaction.

To a stirred solution of phenylhydrazine (1.08 g, 10 mmoles) in hot acetic acid (4 ml) 10 mmoles of the respective 1-aryl-5-(2-dimethylaminovinyl)-1*H*-tetrazole **2** were added in small portions followed by addition of 70% perchloric acid (2 ml). After refluxing for 15 minutes the mixture was worked up as described above for **4a-k**.

Characteristics of the obtained compounds **4l-s** are shown in Table 2.

[1-(4-Methylphenyl)-1*H*-tetrazol-5-yl]acetaldehyde N_α-Methylphenylhydrazone (**5a**).

Using the procedure employed for **3a-k**, compound **5a** was obtained from N_α-methylphenylhydrazine and **2** (Ar = 4-CH_3-C_6H_4) in 88% yield as colorless crystals, mp 118-119° (methanol); ^1H nmr: δ 2.38 (s, 3H, CH_3), 3.16 (s, 3H, NCH_3), 4.05 (d, 2H, CH_2), 6.82 (t, 1H, C_6H_5), 6.94 (t, 1H, N=CH), 7.04 (d, 2H, C_6H_5), 7.22 (t, 2H, C_6H_5), 7.41/7.56 (2d, 4H, C_6H_4).

Anal. Calcd. for $C_{17}H_{18}N_6$: C, 66.65; H, 5.92; N, 27.43. Found: C, 65.57; H, 5.98; N, 27.36.

[1-(4-Methoxyphenyl)-1*H*-tetrazol-5-yl]acetaldehyde N_α-Methylphenylhydrazone (**5b**).

Table 1

Substituted (1-Aryl-1*H*-tetrazol-5-yl)acetaldehyde Phenylhydrazones **3a-k**

Compound	Yield %	Mp °C	^{1}H NMR [a] δ, ppm	Molecular Formula	Analyses % Calcd./Found C	H	N
3a	98	137-138 [b]	2.18 (s, 3H, CH_3), 3.99 (d, 2H, CH_2), 6.70/6.96 (2d, 4H, C_6H_4), 7.24 (t, 1H, N=CH), 7.63-7.70 (m, 5H, C_6H_5), 9.87 (s, 1H, NH)	$C_{16}H_{16}N_6$	65.74 65.55	5.52 5.69	28.75 28.48
3b	98	109-110 [b]	4.00 (d, 2H, CH_2), 6.76-7.07 (m, 4H, C_6H_4), 7.26 (t, 1H, N=CH), 7.63-7.75 (m, 5H, C_6H_5), 9.98 (s, 1H, NH)	$C_{15}H_{13}FN_6$	60.80 60.71	4.42 4.35	28.36 28.50
3c	72	75-76 [c]	4.06 (d, 2H, CH_2), 6.75 (t, 1H, C_6H_4Cl), 7.06-7.31 (m, 3H, N=CH, C_6H_4Cl), 7.63-7.76 (m, 6H, C_6H_4Cl, C_6H_5), 9.69 (s, 1H, NH)	$C_{15}H_{13}ClN_6$	57.60 57.71	4.19 4.25	26.87 26.75
3d	98	137-138 [b]	4.01 (d, 2H, CH_2), 6.77/7.18 (2d, 4H, C_6H_4Cl), 7.28 (t, 1H, N=CH), 7.63-7.74 (m, 5H, C_6H_5), 10.15 (s, 1H, NH)	$C_{15}H_{13}ClN_6$	57.60 57.48	4.19 4.10	26.87 26.95
3e	85	144-145 [d]	2.10 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 4.01 (d, 2H, CH_2), 6.82-6.90 (m, 3H, $C_6H_3Me_2$), 7.50 (t, 1H, N=CH), 7.63-7.75 (m, 5H, C_6H_5), 9.16 (s, 1H, NH)	$C_{17}H_{18}N_6$	66.65 66.50	5.92 6.03	27.43 27.31
3f	76	123-124 [b]	2.10 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 4.01 (d, 2H, CH_2), 6.83-6.90 (m, 3H, $C_6H_3Me_2$), 7.50 (t, 1H, N=CH), 7.63-7.75 (m, 5H, C_6H_5), 9.16 (s, 1H, NH)	$C_{17}H_{18}N_6$	66.65 66.73	5.92 5.85	27.43 27.50
3g	96	123-124 [b]	4.03 (d, 2H, CH_2), 6.87-7.21 (m, 3H, $C_6H_3F_2$), 7.52 (t, 1H, N=CH), 7.63-7.75 (m, 5H, C_6H_5), 9.91 (s, 1H, NH)	$C_{15}H_{12}F_2N_6$	57.32 57.21	3.85 3.69	26.74 26.65
3h	94	121-122 [b]	4.05 (d, 2H, CH_2), 7.05 (d, 1H, $C_6H_3Cl_2$), 7.24 (d, 1H, $C_6H_3Cl_2$), 7.41 (s, 1H, $C_6H_3Cl_2$), 7.61-7.75 (m, 6H, N=CH, C_6H_5), 9.83 (s, 1H, NH)	$C_{15}H_{12}Cl_2N_6$	51.89 51.70	3.48 3.35	24.20 24.33
3i	80	129-130 [b]	2.18 (s, 3H, CH_3), 4.00 (d, 2H, CH_2), 6.68/6.96 (2d, 4H, C_6H_4Me), 7.21 (t, 1H, N=CH), 7.76/7.73 (2d, 4H, C_6H_4Cl), 9.87 (s, 1H, NH)	$C_{16}H_{15}ClN_6$	58.81 58.96	4.63 4.75	25.72 25.56
3j	97	124-125 [b]	4.03 (d, 2H, CH_2), 6.66-6.74 (m, 1H, C_6H_3ClF), 6.86 (d, 1H, C_6H_3ClF), 7.20 (t, 1H, C_6H_3ClF), 7.29 (t, 1H, N=CH), 7.63-7.75 (m, 5H, C_6H_5), 10.17 (s, 1H, NH)	$C_{15}H_{12}ClFN_6$	54.47 54.29	3.66 3.71	25.41 25.35
3k	91	161-162 [d]	4.04 (d, 2H, CH_2), 6.74 (d, 1H, $C_6H_3Cl_2$), 6.94 (s, 1H, $C_6H_3Cl_2$), 7.31 (t, 1H, N=CH), 7.36 (d, 1H, $C_6H_3Cl_2$), 7.63-7.75 (m, 5H, C_6H_5), 10.34 (s, 1H, NH)	$C_{15}H_{12}Cl_2N_6$	51.89 51.75	3.48 3.39	24.20 24.09

[a] Multiplicity data refer to vicinal couplings only, *i.e.* fine splitting due to long-range coupling was left out of consideration. [b] Methanol. [c] Diethylether. [d] Ethanol.

Product **5b** was prepared in 94% yield in analogy to **5a** starting from **2** (Ar = 4-CH_3O-C_6H_4). Recrystallization from methanol gave colorless needles, mp 87-88°; ^{1}H nmr: δ 3.16 (s, 3H, NCH_3), 3.81 (s, 3H, OCH_3), 4.03 (d, 2H, CH_2), 6.83 (t, 1H, C_6H_5), 6.93 (t, 1H, N=CH), 7.05 (d, 2H, C_6H_5), 7.14 (d, 2H, C_6H_4), 7.21 (t, 2H, C_6H_5), 7.60 (d, 2H, C_6H_4).

Anal. Calcd. for $C_{17}H_{18}N_6O$: C, 63.34; H, 5.63; N, 26.07. Found: C, 63.55; H, 5.71; N, 25.95.

[1-(4-Chlorophenyl)-1*H*-tetrazol-5-yl]acetaldehyde N_α-Methylphenylhydrazone (**5c**).

This compound was obtained in 96% yield in analogy to **5a** starting from **2** (Ar = 4-Cl-C_6H_4). Recrystallization from methanol afforded colorless needles, mp 122-123°, ^{1}H nmr: δ 3.16 (s, 3H, NCH_3), 4.09 (d, 2H, CH_2), 6.83 (t, 1H, C_6H_5), 6.93 (t, 1H, N=CH), 7.02 (d, 2H, C_6H_5), 7.21 (t, 2H, C_6H_5), 7.70/7.74 (2d, 4H, C_6H_4Cl).

Anal. Calcd. for $C_{16}H_{15}ClN_6$: C, 58.81; H, 4.63; N, 25.72. Found: C, 58.77; H, 4.48; N, 25.80.

1-Methyl-3-[1-(4-methylphenyl)-1*H*-tetrazol-5-yl]indole (**6a**).

The indolization of **5a** according to the procedure described for **4a-k** afforded the indole **6a** in 46% yield as colorless needles, mp 239-240° (acetonitrile); ^{1}H nmr: δ 2.48 (s, 3H, CH_3), 3.77 (s, 3H, NCH_3), 7.12 (s, 1H, H-2), 7.24 (t, 1H, H-6), 7.33 (t, 1H, H-5), 7.47-7.58 (m, 5H, H-7, C_6H_4), 8.11 (d, 1H, H-4).

Anal. Calcd. for $C_{17}H_{15}N_5$: C, 70.57; H, 5.23; N, 24.20. Found: C, 70.69; H, 5.29; N, 24.13.

1-Methyl-3-[1-(4-methoxyphenyl)-1*H*-tetrazol-5-yl]indole (**6b**).

This compound was obtained in 54% yield in analogy to **4a-k** starting from **5b**. Recrystallization from acetonitrile afforded

Table 2

Substituted 3-(1-Aryl-1*H*-tetrazol-5-yl)indoles **4a-s**

Compound	Yield %	Mp °C	^{1}H NMR [a] δ, ppm	Molecular Formula	Analyses % Calcd./Found C	H	N
4a	43	202-203 [b]	2.44 (s, 3H, CH_3), 6.93 (d, 1H, H-2), 7.09 (d, 1H, H-6), 7.40 (d, 1H, H-7), 7.67-7.73 (m, 5H, C_6H_5), 7.95 (s, 1H, H-4), 11.64 (s, 1H, NH)	$C_{16}H_{13}N_5$	69.80 69.68	4.76 4.81	25.44 25.35
4b	85	208-209 [b]	7.05 (d, 1H, H-2), 7.12 (t, 1H, H-6), 7.55 (dd, 1H, H-7), 7.72 (s, 5H, C_6H_5), 7.83 (d, 1H, H-4), 11.86 (s, 1H, NH)	$C_{15}H_{10}FN_5$	64.51 64.60	3.61 3.52	25.08 24.95
4c	49	216-217 [b]	6.99 (d, 1H, H-2), 7.23 (t, 1H, H-5), 7.36 (d, 1H, H-6), 7.22 (s, 5H, C_6H_5), 8.11 (d, 1H, H-4), 12.19 (s, 1H, NH)	$C_{15}H_{10}ClN_5$	60.92 61.05	3.41 3.52	23.68 23.50
4d	88	201-202 [b]	7.06 (d, 1H, H-2), 7.27 (d, 1H, H-6), 7.55 (d, 1H, H-7), 7.72 (s, 5H, C_6H_5), 8.17 (s, 1H, H-4), 11.92 (s, 1H, NH)	$C_{15}H_{10}ClN_5$	60.92 60.85	3.41 3.36	23.68 23.78
4e	56	277-278 [b]	2.35 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 6.85 (d, 1H, H-2), 7.02 (d, 1H, H-5), 7.66-7.73 (m, 5H, C_6H_5), 7.81 (d, 1H, H-4), 11.60 (s, 1H, NH)	$C_{17}H_{15}N_5$	70.57 70.49	5.23 5.15	24.20 24.09
4f	38	246-247 [b]	2.40 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 6.87 (d, 1H, H-2), 6.89 (s, 1H, H-6), 7.67-7.73 (m, 5H, C_6H_5), 7.75 (s, 1H, H-4), 11.66 (s, 1H, NH)	$C_{17}H_{15}N_5$	70.57 70.65	5.23 5.31	24.20 24.27
4g	42	267-268 [b]	7.05 (d, 1H, H-2), 7.21 (m, 1H, H-6), 7.67 (d, 1H, H-4), 7.72 (s, 5H, C_6H_5), 12.50 (s, 1H, NH)	$C_{15}H_9F_2N_5$	60.61 60.80	3.05 2.97	23.56 23.45
4h	51	262-263 [c]	7.01 (d, 1H, H-2), 7.44 (s, 1H, H-6), 7.73 (s, 5H, C_6H_5), 8.08 (s, 1H, H-4), 12.41 (s, 1H, NH)	$C_{15}H_9Cl_2N_5$	54.57 54.66	2.75 2.70	21.21 20.98
4i	63	241-242 [b]	2.44 (s, 3H, CH_3), 7.05 (d, 1H, H-2), 7.09 (d, 1H, H-6), 7.41 (d, 1H, H-7), 7.76 (s, 4H, C_6H_4), 7.92 (s, 1H, H-4), 11.63 (s, 1H, NH)	$C_{16}H_{12}ClN_5$	62.04 61.95	3.90 3.87	22.61 22.72
4j	41	264-265 [b]	7.10 (d, 1H, H-2), 7.69-7.75 (m, 6H, H-7, C_6H_5), 7.96 (d, 1H, H-4), 11.90 (s, 1H, NH)	$C_{15}H_9ClFN_5$	57.43 57.57	2.89 2.81	22.32 22.19
4k	52	282-283 [b]	7.11 (d, 1H, H-2), 7.72 (s, 5H, C_6H_5), 7.79 (s, 1H, H-7), 8.27 (s, 1H, H-4), 11.95 (s, 1H, NH)	$C_{15}H_9Cl_2N_5$	54.57 54.45	2.75 2.83	21.21 21.28
4l	32	226-227 [b]	6.97 (d, 1H, H-2), 7.17-7.28 (m, 2H, H-5, H-6), 7.50 (d, 1H, H-7), 7.67-7.76 (m, 5H, C_6H_5), 8.13 (d, 1H, H-4), 11.75 (s, 1H, NH)	$C_{15}H_{11}N_5$	68.95 69.07	4.24 4.19	26.80 26.72
4m	31	242-243 [b]	2.46 (s, 3H, CH_3), 6.98 (d, 1H, H-2), 7.18-7.29 (m, 2H, H-5, H-6), 7.48-7.58 (m, 5H, H-7, C_6H_4), 8.18 (d, 1H, H-4), 11.72 (s, 1H, NH)	$C_{16}H_{13}N_5$	69.80 69.86	4.76 4.59	25.44 25.55
4n	25	189-190 [b]	1.28 (t, 3H, CH_3), 2.78 (q, 2H, CH_2), 6.99 (d, 1H, H-2), 7.18-7.30 (m, 2H, H-5, H-6), 7.50-7.62 (m, 5H, H-7, C_6H_4), 8.17 (d, 1H, H-4), 11.74 (s, 1H, NH)	$C_{17}H_{15}N_5$	70.57 70.42	5.23 5.15	24.20 24.09
4o	44	241-242 [b]	3.88 (s, 3H, CH_3O), 6.96 (d, 1H, H-2), 7.21 (d, 2H, C_6H_4), 7.21-7.28 (m, 2H, H-5, H-6), 7.51 (d, 1H, H-7), 7.60 (d, 2H, C_6H_4), 8.20 (d, 1H, H-4), 11.70 (s, 1H, NH)	$C_{16}H_{13}N_5O$	65.97 66.05	4.50 4.43	24.04 23.90
4p	32	253-254 [b]	7.06 (d, 1H, H-2), 7.19-7.31 (m, 2H, H-5, H-6), 7.51-7.84 (m, 5H, H-7, C_6H_4), 8.17 (d, 1H, H-4), 11.76 (s, 1H, NH)	$C_{15}H_{10}FN_5$	64.51 64.38	3.61 3.55	25.08 25.13
4q	30	266-267 [b]	7.11 (d, 1H, H-2), 7.17-7.29 (m, 2H, H-5, H-6), 7.52 (d, 1H, H-7), 7.75 (s, 4H, C_6H_4), 8.11 (d, 1H, H-4), 11.74 (s, 1H, NH)	$C_{15}H_{10}ClN_5$	60.92 60.80	3.41 3.35	23.68 23.83
4r	28	268-269 [b]	7.13 (d, 1H, H-2), 7.18-7.31 (m, 2H, H-5, H-6), 7.54 (d, 1H, H-7), 7.69/7.91 (2d, 4H, C_6H_4), 8.13 (d, 1H, H-4), 11.76 (s, 1H, NH)	$C_{15}H_{10}BrN_5$	52.96 53.05	2.96 2.88	20.59 20.71

Table 2 (continued)

Compound	Yield %	Mp °C	^{1}H NMR [a] δ, ppm	Molecular Formula	Analyses % Calcd./Found C	H	N
4s	26	240-241 [b]	7.14 (d, 1H, H-2), 7.20-7.32 (m, 2H, H-5, H-6), 7.42-7.59 (m, 4H, H-7, C_6H_5), 7.78/7.99 (2d, 4H, C_6H_4), 7.80-7.85 (m, 2H, C_6H_5), 8.21 (d, 1H, H-4), 11.78 (s, 1H, NH)	$C_{21}H_{15}N_5$	74.76 74.60	4.48 4.55	20.76 20.63

[a] Multiplicity data refer to vicinal couplings only, *i.e.* fine splitting due to longe-range coupling was left out of consideration. The vicinal coupling constant $^3J_{H\text{-}1,H\text{-}2}$ of the H-2 doublet averages 2.9 Hz. [b] Acetonitrile. [c] Acetic acid.

colorless crystals, mp 252-253°; ^{1}H nmr: δ 3.77 (s, 3H, NCH_3), 3.90 (s, 3H, OCH_3), 7.08 (s, 1H, H-2), 7.21 (d, 2H, C_6H_4), 7.25 (t, 1H, H-6), 7.33 (t, 1H, H-5), 7.56 (d, 1H, H-7), 7.60 (d, 2H, C_6H_4), 8.16 (d, 1H, H-4).

Anal. Calcd. for $C_{17}H_{15}N_5O$: C, 66.87; H, 4.95; N, 22.94. Found: C, 66.71; H, 5.03; N, 23.07.

1-Methyl-3-[1-(4-chlorophenyl)-1*H*-tetrazol-5-yl]indole (**6c**).

Indole **6c** was prepared from **5c** in 42% yield using the procedure decribed for **4a-k**. Recrystallization from acetonitrile gave colorless crystals, mp 212-213°; ^{1}H nmr: δ 3.79 (s, 3H, NCH_3), 7.21 (t, 1H, H-6), 7.24 (s, 1H, H-2), 7.33 (t, 1H, H-5), 7.56 (d, 1H, H-7), 7.75 (s, 4H, C_6H_4Cl), 8.10 (d, 1H, H-4).

Anal. Calcd. for $C_{16}H_{12}ClN_5$: C, 62.04; H, 3.90; N, 22.61. Found: C, 62.11; H, 3.98; N, 22.53.

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