Tetrazole Compounds. 9 [1]. A New Approach to Tetrazolyl-substituted Quinoline Derivatives

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The acid-catalyzed reaction of 1-aryl-5-(2-dimethylaminovinyl)-1*H*-tetrazoles **2** with arylamines suitably functionalized in the *ortho*-position resulted in *Z*-configurated transamination products which were cyclized to novel 3-tetrazolylquinolines by the action of sodium ethoxide. Thus, on reacting **2** with 2-aminoacetophenone or 2-aminobenzophenone, respectively, the 2-[2-(1-aryl-1*H*-tetrazol-5-yl)vinylamino]aryl ketones **3a-g** were obtained, the cyclization of which gave 4-substituted 3-(1-aryl-1*H*-tetrazol-5-yl)quinolines **4**. In the case of the transamination products **3h-l**, prepared from **2** and methyl anthranilate, the ring closure afforded 3-(1-aryl-1*H*-tetrazol-5-yl)-1*H*-quinolin-4-ones **5**. Starting from **2** and anthranilonitrile 4-amino-3-(1-aryl-1*H*-tetrazol-5-yl)quinolines **10** were obtained *via* the corresponding intermediates **9**.

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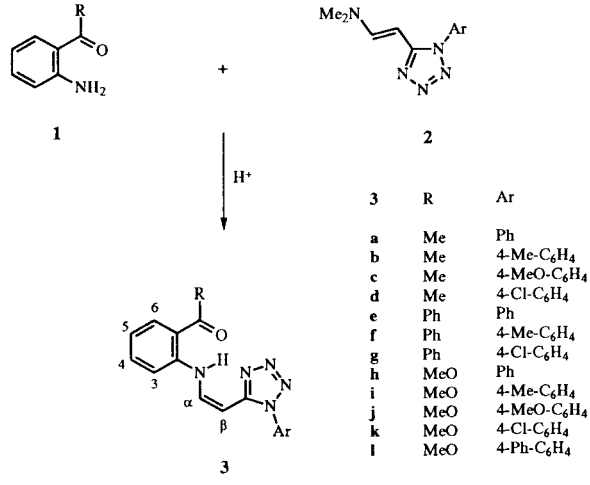
3-Hetarylquinolines were represented until several years ago only by few examples [2], among them the unsubstituted 3-(1*H*-tetrazol-5-yl)quinoline [3]. Recently derivatives of the latter have resulted in increasing interest in connection with pharmacological studies [4-6]. Their synthesis occurs either starting from appropriate quinoline derivatives and formation of the tetrazole ring [3,5,6] or inversely by a quinoline ring closure using suitable tetrazole building blocks [4]. The present communication describes a new approach for preparing substituted 3-(1*H*-tetrazol-5-yl)quinolines in the last-mentioned way.

As reported in a previous paper [7], the acid-catalyzed transamination of 1-aryl-5-(2-dimethylaminovinyl)-1*H*-tetrazoles **2** [8] with various primary and secondary amines proved to be a simple route to specially *N*-substituted enamines of this type not otherwise accessible. Starting from arylamines with suitable functional groups in the *ortho*-position, the transamination of **2** should lead to potential precursors for quinoline ring-closure reactions.

Thus, on reacting **2** in methanolic solution with 2-aminoacetophenone (**1**, R = Me) or 2-aminobenzophenone (**1**, R = Ph) in the presence of aqueous hydrochloric acid the 2-[2-(1-aryl-1*H*-tetrazol-5-yl)vinylamino]acetophenones **3a-d** and benzophenones **3e-g**, respectively, were obtained in 76-86% yields. Under the same conditions, reaction of **2** with anthranilic acid methyl ester (**1**, R = MeO) gave the transamination products **3h-l**, likewise in good yields (86-95%).

As indicated by the vicinal coupling constants of the vinylic protons (J = 8.7-9.1 Hz) all the compounds of type **3** possess the *Z*-configuration [9], which is most probably favored by a partial hydrogen bonding of the amino proton to the tetrazole N-4 atom. The large downfield shift (δ 11.44-12.19 ppm) of the NH proton, however, is mainly due to a strong intramolecular hydrogen bonding to the *ortho*-oriented carbonyl group in **3a-l**.

When heated in an ethanolic solution of sodium ethoxide, the *N*-substituted 2-aminoacetophenones **3a-d** and 2-aminobenzophenones **3e-g** smoothly underwent a cyclization to afford 3-(1-aryl-1*H*-tetrazol-5-yl)quinolines

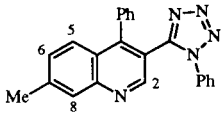


3	R	Ar
a	Me	Ph
b	Me	4-Me-C_6H_4
c	Me	4-MeO-C_6H_4
d	Me	4-Cl-C_6H_4
e	Ph	Ph
f	Ph	4-Me-C_6H_4
g	Ph	4-Cl-C_6H_4
h	MeO	Ph
i	MeO	4-Me-C_6H_4
j	MeO	4-MeO-C_6H_4
k	MeO	4-Cl-C_6H_4
l	MeO	4-Ph-C_6H_4

4	R	Ar
a	Me	Ph
b	Me	4-Me-C_6H_4
c	Me	4-MeO-C_6H_4
d	Me	4-Cl-C_6H_4
e	Ph	Ph
f	Ph	4-Me-C_6H_4
g	Ph	4-Cl-C_6H_4

5	Ar
a	Ph
b	4-Me-C_6H_4
c	4-MeO-C_6H_4
d	4-Cl-C_6H_4
e	4-Ph-C_6H_4

4a-g in 68-96% yields. Due to the base catalysis of this reaction involving charge delocalization in the aminovinyl moiety the initial *Z*-configuration of the educts **3a-g** has not any unfavorable influence. The ring closure can also be achieved under acidic conditions, *e.g.* on heating **3a-g** in concentrated sulfuric acid, but in this case yields and purity of the products leaves to be desired.



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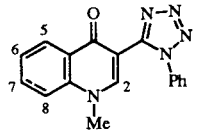

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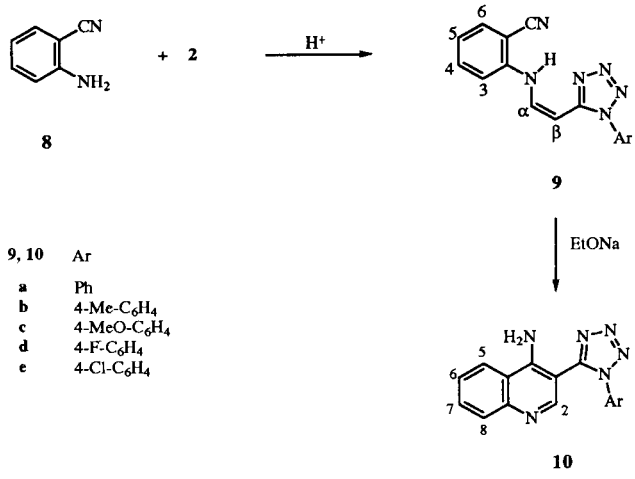
The sequence **1** + **2** → **3** → **4** may be regarded as a modified two-step Friedländer quinoline synthesis [10], in which the α-methylene carbonyl component is replaced by a corresponding enamine. For the preparation of 3-aryl- or 3-hetarylquinolines unsubstituted in position 2 the classic Friedländer reaction normally requires aryl- or hetarylacetaldehydes [11,12], which are known to be mostly unstable or non-existent. Therefore, when enamines of such aldehydes are accessible in other ways, as for instance **2** [8,13], the method described here is a useful extension of the classic approach. Furthermore, it offers the advantage of isolating well-defined intermediates and their cyclization under optimal conditions. Thus, *e.g.*, the base-initiated reaction **3** → **4** succeeds even in case of R = Ph (**3/4e-g**), whereas 2-aminobenzophenone itself as a rule fails to undergo the base-catalyzed Friedländer condensation [10].

Unlike **3a-g**, the cyclization of which proceeds *via* splitting off water, the *N*-substituted anthranilic acid methyl esters **3h-l** reacted on treatment with ethanolic



8 **9** **10**

9, 10	Ar
a	Ph
b	4-Me-C_6H_4
c	4-MeO-C_6H_4
d	4-F-C_6H_4
e	4-Cl-C_6H_4

sodium ethoxide under elimination of methanol to give isolable sodium salts of the corresponding 4-hydroxy-

Table 1

2-(1-Aryl-1*H*-tetrazol-5-yl)vinylamino Derivatives **3a-l**, 4-Substituted 3-(1-Aryl-1*H*-tetrazol-5-yl)quinolines **4a-g** and 3-(1-Aryl-1*H*-tetrazol-5-yl)-1*H*-quinolin-4-ones **5a-e**

Compound	Yield %	Mp °C	^{1}H NMR δ, ppm	Molecular Formula	Analyses % Calcd./Found C	H	N
3a	76	168-169 [a]	2.68 (s, 3H, CH_3CO), 5.27 (d, J = 9.0 Hz, 1H, H-β), 7.09 (t, 1H, H-5), 7.51-7.77 (m, 8H, C_6H_5, H-α, H-3, H-4), 8.05 (d, 1H, H-6), 12.19 (d, J = 12.8 Hz, 1H, NH)	$C_{17}H_{15}N_5O$	66.87 66.59	4.95 4.81	22.94 23.03
3b	83	191-192 [a]	2.44 (s, 3H, CH_3), 2.68 (s, 3H, CH_3CO), 5.25 (d, J = 9.0 Hz, 1H, H-β), 7.08 (t, 1H, H-5), 7.46-7.67 (m, 6H, C_6H_4, H-3, H-4), 7.71 (dd, J = 9.0/12.5 Hz, 1H, H-α), 8.05 (d, 1H, H-6), 12.17 (d, J = 12.5 Hz, 1H, NH)	$C_{18}H_{17}N_5O$	67.70 67.84	5.37 5.41	21.93 21.70
3c	86	179-180 [b]	2.68 (s, 3H, CH_3CO), 3.87 (s, 3H, CH_3O), 5.21 (d, J = 9.1 Hz, 1H, H-β), 7.08 (t, 1H, H-5), 7.20/7.58 (2d, 4H, C_6H_4), 7.50-7.63 (m, 2H, H-3, H-4), 7.70 (dd, J = 9.1/12.6 Hz, 1H, H-α), 8.05 (d, 1H, H-6), 12.15 (d, J = 12.6 Hz, 1H, NH)	$C_{18}H_{17}N_5O_2$	64.47 64.39	5.11 4.98	20.88 20.71
3d	76	205-206 [c]	2.68 (s, 3H, CH_3CO), 5.28 (d, J = 9.0 Hz, 1H, H-β), 7.08 (t, 1H, H-5), 7.51-7.78 (m, 7H, C_6H_4, H-3, H-4, H-α), 8.05 (d, 1H, H-6), 12.17 (d, J = 12.8 Hz, 1H, NH)	$C_{17}H_{14}ClN_5O$	60.09 59.96	4.15 4.08	20.61 20.44
3e	84	167-168 [a]	5.30 (d, J = 8.7 Hz, 1H, H-β), 7.09 (t, 1H, H-5), 7.49-7.80 (m, 14H, 2 x C_6H_5, H-3, H-4, H-6, H-α), 11.51 (d, J = 12.7 Hz, 1H, NH)	$C_{22}H_{17}N_5O$	71.92 71.85	4.66 4.50	19.06 18.94

Table 1 (continued)

Compound	Yield %	Mp °C	^{1}H NMR δ, ppm	Molecular Formula	Analyses % Calcd./Found C	H	N
3f	78	176-177 [c]	2.43 (s, 3H, CH_3), 5.27 (d, J = 8.8 Hz, 1H, H-β), 7.08 (t, 1H, H-5), 7.45-7.61 (m, 13H, C_6H_4, C_6H_5, H-3, H-4, H-6, H-α), 11.44 (d, J = 12.8 Hz, 1H, NH)	$C_{23}H_{19}N_5O$	72.42 72.49	5.02 4.95	18.36 18.22
3g	84	185-186 [c]	5.30 (d, J = 8.8 Hz, 1H, H-β), 7.09 (t, 1H, H-5), 7.49-7.77 (m, 13H, C_6H_4, C_6H_5, H-3, H-4, H-6, H-α), 11.48 (d, J = 12.5 Hz, 1H, NH)	$C_{22}H_{18}ClN_5O$	65.43 65.56	4.49 4.37	17.34 17.43
3h	87	118-119 [a]	4.03 (s, 3H, CH_3O), 5.30 (d, J = 9.0 Hz, 1H, H-β), 7.06 (t, 1H, H-5), 7.51-7.69 (m, 7H, C_6H_5, H-3, H-4), 7.73 (dd, J = 9.0/12.5 Hz, 1H, H-α), 7.98 (d, 1H, H-6), 11.61 (d, J = 12.5 Hz, 1H, NH)	$C_{17}H_{15}N_5O_2$	63.54 63.39	4.71 4.55	21.79 21.61
3i	83	138-139 [a]	2.44 (s, 3H, CH_3), 4.02 (s, 3H, CH_3OCO), 5.26 (d, J = 8.8 Hz, 1H, H-β), 7.06 (t, 1H, H-5), 7.46-7.64 (m, 6H, C_6H_4, H-3, H-4), 7.73 (dd, J = 9.0/12.5 Hz, 1H, H-α), 7.98 (d, 1H, H-6), 11.59 (d, J = 12.5 Hz, 1H, NH)	$C_{18}H_{17}N_5O_2$	64.47 64.56	5.11 5.02	20.88 20.71
3j	95	120-121 [a]	3.87 (s, 3H, CH_3O), 4.02 (s, 3H, CH_3OCO), 5.23 (d, J = 8.8 Hz, 1H, H-β), 7.06 (t, 1H, H-5), 7.20/7.57 (2d, 4H, C_6H_4), 7.50-7.64 (m, 2H, H-3, H-4), 7.70 (dd, J = 8.8/12.5 Hz, 1H, H-α), 7.98 (d, 1H, H-6), 11.53 (d, J = 12.5 Hz, 1H, NH,)	$C_{18}H_{17}N_5O_3$	61.53 61.40	4.88 4.69	19.93 19.78
3k	88	169-170 [c]	4.01 (s, 3H, CH_3O), 5,30 (d, J = 8.7 Hz, 1H H-β), 7,08 (t, 1H, H-5), 7.53-7.79 (m, 7H, C_6H_4, H-3, H-4, H-α), 7.98 (d, 1H, H-6), 11.58 (d, J = 12.5 Hz, 1H, NH)	$C_{17}H_{14}ClN_5O_2$	57.39 57.22	3.97 4.05	19.68 19.57
3l	96	146-147 [d]	4.03 (s, 3H, CH_3O), 5.37 (d, J = 8.8 Hz, 1H, H-β), 7,08 (t, 1H, H-5), 7.45-8.02 (m, 13H, C_6H_5, C_6H_4, H-3, H-4, H-6, H-α), 11.62 (d, J = 12.7 Hz, 1H, NH)	$C_{23}H_{19}N_5O_2$	69.51 69.45	4.82 4.60	17.62 17.49
4a	79	160-161 [a]	2.54 (s, 3H, 4-CH_3), 7.51-7.58 (m, 5H, C_6H_5), 7.73 (t, 1H, H-6), 7.89 (t, 1H, H-7), 8.07 (d, 1H, H-8), 8.23 (d, 1H, H-5), 8.81 (s, 1H, H-2)	$C_{17}H_{13}N_5$	71.07 70.96	4.56 4.49	24.37 24.40
4b	96	177-178 [a]	2.31 (s, 3H, $CH_3C_6H_4$), 2.53 (s, 3H, 4-CH_3), 7.30/7.42 (2d, 4H, C_6H_4), 7.73 (t, 1H, H-6), 7.89 (t, 1H, H-7), 8.06 (d, 1H, H-8), 8.23 (d, 1H, H-5), 8.78 (s, 1H, H-2)	$C_{18}H_{15}N_5$	71.74 71.80	5.02 4.95	23.24 23.16
4c	94	149-150 [a]	2.53 (s, 3H, 4-CH_3), 3.76 (s, 3H, CH_3O), 7.04/7.48 (2d, 4H, C_6H_4), 7.73 (t, 1H, H-6), 7.89 (t, 1H, H-7), 8.06 (d, 1H, H-8), 8.23 (d, 1H, H-5), 8.79 (s, 1H, H-2)	$C_{18}H_{15}N_5O$	68.13 67.98	4.76 4.65	22.07 21.95
4d	96	204-205 [c]	2.55 (s, 3H, 4-CH_3), 7.61 (s, 4H, C_6H_4), 7.74 (t, 1H, H-6), 7.90 (t, 1H, H-7), 8.08 (d, 1H, H-8), 8.24 (d, 1H, H-5), 8.79 (s, 1H, H-2)	$C_{17}H_{12}ClN_5$	63.46 63.60	3.76 3.59	21.76 21.66
4e	89	138-139 [a]	6.77 (d, 2H, Ph), 6.99 (d, 2H, Ph), 7.25-7.49 (m, 6H, Ph), 7.62-7.65 (m, 2H, H-5, H-6), 7.94 (t, 1H, H-7), 8.22 (d, 1H, H-8), 9.23 (s, 1H, H-2)	$C_{22}H_{15}N_5$	75.63 75.48	4.33 4.20	20.04 19.89
4f	68	137-138 [a]	2.30 (s, 3H, CH_3), 6.79-7.44 (m, 9H, C_6H_4, C_6H_5), 7.59-7.68 (m, 2H, H-5, H-6), 7.93 (t, 1H, H-7), 8.21 (d, 1H, H-8), 9.19 (s, 1H, H-2)	$C_{23}H_{17}N_5$	76.01 75.89	4.71 4.66	19.27 19.15
4g	77	149-150 [a]	6.78-7.46 (m, 9H, C_6H_4, C_6H_5), 7.65 (m, 2H, H-5, H-6), 7.95 (br, 1H, H-7), 8.23 (d, 1H, H-8), 9.23 (s, 1H, H-2)	$C_{22}H_{14}ClN_5$	68.84 68.75	3.68 3.77	18.25 18.03
5a	94	267-268 [a],[e] [f]	7.39 (t, 1H, H-6), 7.47-7.60 (m, 5H, C_6H_5), 7.66 (d, 1H, H-8), 7.74 (t, 1H, H-7), 7.99 (d, 1H, H-5), 8.56 (s, 1H, H-2), 12.63 (s, 1H, NH)	$C_{16}H_{11}N_5O$	66.43 66.59	3.83 3.76	24.21 24.33

Table 1 (continued)

Compound	Yield %	Mp °C	^{1}H NMR δ, ppm	Molecular Formula	Analyses % Calcd./Found C	H	N
5b	89	265-267 [a],[e] [g]	2.31 (s, 3H, CH_3), 7.28/7.44 (2d, 4H, C_6H_4), 7.39 (t, 1H, H-6), 7.64 (d, 1H, H-8), 7.74 (t, 1H, H-7), 7.99 (d, 1H, H-5), 8.52 (s, 1H, H-2), 12.58 (s, 1H, NH)	$C_{17}H_{13}N_5O$	67.32 67.20	4.32 4.43	23.09 22.97
5c	82	249-250 [b],[h]	3.76 (s, 3H, CH_3O), 7.02/7.48 (2d, 4H, C_6H_4), 7.39 (t, 1H, H-6), 7.64 (d, 1H, H-8), 7.73 (t, 1H, H-7), 8.02 (d, 1H, H-5), 8.47 (s, 1H, H-2), 12.48 (s, 1H, NH)	$C_{17}H_{13}N_5O_2$	63.94 64.08	4.10 4.02	21.93 22.05
5d	69	282-283 [b],[i]	7.41 (t, 1H, H-6), 7.58/7.61 (2d, 4H, C_6H_4), 7.67 (d, 1H, H-8), 7.77 (t, 1H, H-7), 8.00 (d, 1H, H-5), 8.57 (s, 1H, H-2), 12.65 (s, 1H, NH)	$C_{16}H_{10}ClN_5O$	59.36 59.30	3.11 3.03	21.63 21.81
5e	63	269-270 [a],[j]	7.36-7.83 (m, 12H, C_6H_4, C_6H_5, H-6, H-7, H-8), 8.02 (d, 1H, H-5), 8.58 (s, 1H, H-2), 12.64 (s, 1H, NH)	$C_{22}H_{15}N_5O$	72.32 72.15	4.14 4.08	19.19 19.11

[a] Methanol. [b] Ethanol. [c] Acetonitrile. [d] Ethyl acetate. [e] Decomposition. [f] Ir: ν CO 1625 cm^{-1}. [g] Ir: ν CO 1628 cm^{-1}. [h] Ir:ν CO 1626 cm^{-1}. [i] Ir: ν CO 1627 cm^{-1}. [j] Ir: ν CO 1625 cm^{-1}.

Table 2

N-[2-(1-Aryl-1*H*-tetrazol-5-yl)vinyl]anthranilonitriles **9a-e** und 4-Amino-3-(1-aryl-1*H*-tetrazol-5-yl)quinolines **10a-e**

Compound	Yield %	Mp °C	^{1}H NMR δ, ppm	Molecular Formula	Analyses % Calcd./Found C	H	N
9a	83	174-175 [a]	5.42 (d, J = 8.5 Hz, 1H, H-β), 7.14 (t, 1H, H-5), 7.57-7.86 (m, 9H, C_6H_5, H-α, H-3, H-4, H-6), 10.29 (d, J = 12.3 Hz, 1H, NH)	$C_{16}H_{12}N_6$	66.66 66.50	4.20 4.13	29.15 29.24
9b	85	175-176 [a]	2.45 (s, 3H, CH_3), 5.39 (d, J = 8.5 Hz, 1H, H-β), 7.13 (t, 1H, H-5), 7.49/7.56 (2d, 4H, C_6H_4), 7.59 (d, 1H, H-3), 7.68 (t, 1H, H-4), 7.76-7.84 (m, 2H, H-6, H-α), 10.29 (d, J = 12.3 Hz, 1H, NH)	$C_{17}H_{14}N_6$	67.54 67.63	4.67 4.55	27.80 27.68
9c	92	185-186 [a]	3.88 (s, 3H, CH_3O), 5.35 (d, J = 8.5 Hz, 1H, H-β), 7.13 (t, 1H, H-5), 7.22/7.60 (2d, 4H, C_6H_4), 7.58 (d, 1H, H-3), 7.68 (t, 1H, H-4), 7.74-7.82 (m, 2H, H-6, H-α), 10.26 (d, J = 12.3 Hz, 1H, NH)	$C_{17}H_{14}N_6O$	64.14 64.03	4.43 4.35	26.40 26.54
9d	90	234-235 [a]	5.40 (d, J = 8.6 Hz, 1H, H-β), 7.19 (t, 1H, H-5), 7.56-7.87 (m, 8H, C_6H_4, H-α, H-3, H-4, H-6), 10.28 (d, J = 12.1 Hz, 1H, NH)	$C_{16}H_{11}FN_6$	62.74 62.90	3.62 3.57	27.44 27.38
9e	79	260-261 [a],[b]	5.42 (d, J = 8.3 Hz, 1H, H-β), 7.14 (t, 1H, H-5), 7.57-7.83 (m, 8H, C_6H_4, H-α, H-3, H-4, H-6), 10.27 (d, J = 12.5 Hz, 1H, NH)	$C_{16}H_{11}ClN_6$	59.54 59.50	3.44 3.29	26.04 25.89
10a	68	269-270 [a]	7.47 (br, 2H, NH_2), 7.50 (t, 1H, H-7), 7.57 (s, 5H, C_6H_5), 7.68-7.78 (m, 2H, H-5, H-6), 8.16 (s, 1H, H-2), 8.32 (d, 1H, H-8)	$C_{16}H_{12}N_6$	66.66 66.81	4.20 4.33	29.15 29.09
10b	67	243-244 [a]	2.36 (s, 3H, CH_3), 7.35/7.45 (2d, 4H, C_6H_4), 7.45-7.53 (m, 3H, NH_2, H-7), 7.67-7.78 (m, 2H, H-5, H-6), 8.14 (s, 1H, H-2), 8.31 (d, 1H, H-8)	$C_{17}H_{14}N_6$	67.54 67.37	4.67 4.73	27.80 27.71
10c	82	262-263 [c]	3.80 (s, 3H, CH_3O), 7.08/7.51 (2d, 4H, C_6H_4), 7.46-7.54 (m, 3H, NH_2, H-7), 7.66-7.78 (m, 2H, H-5, H-6), 8.15 (s, 1H, H-2), 8.31 (d, 1H, H-8)	$C_{17}H_{14}N_6O$	64.14 64.27	4.43 4.40	26.40 26.29
10d	55	284-285 [a],[b]	7 38-7.79 (m, 8H, C_6H_4, NH_2, H-5, H-6), 8.18 (s, 1H, H-2), 8.30 (d, 1H, H-8)	$C_{16}H_{11}FN_6$	62.74 62.60	3.62 3.75	27.44 27.61

Table 2 (continued)

Compound	Yield %	Mp °C	^{1}H NMR δ, ppm	Molecular Formula	Analyses % Calcd./Found C	H	N
10e	56	283-284 [b],[c]	7.36 (s, 2H, NH_2), 7.49 (t, 1H, H-7), 7.58-7.80 (m, 6H, C_6H_4, H-5, H-6), 8.19 (s, 1H, H-2), 8.29 (d, 1H, H-8)	$C_{16}H_{11}ClN_6$	59.54 59.39	3.44 3.51	26.04 25.78

[a] Acetonitrile. [b] Decomposition. [c] Dioxane.

quinolines; acidification of their aqueous solutions afforded then the 3-(1-aryl-1*H*-tetrazol-5-yl)-1*H*-quinolin-4-ones **5a-g** as colorless solids in 63-94% yields. An analogue ring closure was already used for preparing 1*H*-quinolin-4-one 2,3-dicarboxylic acid esters [14]. Reactions of this type are formally related to the Niementowski quinolinone synthesis [15].

The assignment of the signals in the ^{1}H nmr spectra of **4** and **5** was established by NOE difference and decoupling experiments. Thus, *e.g.*, the closely adjacent doublets of H-5 and H-8 in **4a-d** could be assigned by irradiation of the 4-methyl signal resulting in a strong NOE in H-5. In case of the 4-phenylquinolines **4e-g** the corresponding 7-methyl derivative **6**, synthesized in the same manner, was used as an aid for assigning the benzene-ring bonded protons of the quinoline system. Similarly, assignments for the quinlinones **5a-e** were supported by NOE and decoupling experiments with the 1-methyl derivative **7**, which was obtained on reacting the **5a** sodium salt with dimethyl sulfate.

In accordance with the quinolinone structure, the ir spectra of **5a-e** displayed a strong carbonyl band at 1625-1628 cm^{-1}, in the case of **7** at 1637 cm^{-1}. Physical, spectral and analytical data of the new compounds **3-5** are summarized in Table 1.

Certain *N*-vinylanthranilonitriles are known to cyclize under basic conditions to give 4-aminoquinolines [16]. To test the behaviour of the corresponding *N*-tetrazolylvinyl-substituted anthranilonitriles, compounds **9a-e** were prepared in 79-93% yields by acid-catalyzed transamination of **2** with anthranilonitrile (**8**) in analogy to reaction **1** + **2** → **3**. According to their ^{1}H nmr spectra they exist as pure *Z*-isomers ($J_{H\text{-}\alpha,\ H\text{-}\beta}$ = 8.3-8.6 Hz). On refluxing in ethanolic sodium ethoxide **9a-e** underwent in fact a smooth cyclization to give the expected 4-amino-3-(1-aryl-1*H*-tetrazol-5-yl)quinolines **10a-e**. Detailed data of the compounds **9** and **10** are given in Table 2.

In conclusion, reactions of type **3** → **4**, **3** → **5** and **9** → **10** show that the cyclization of *N*-(2-tetrazolylvinyl)arylamines suitably functionalized in the *ortho*-position provides a new convenient route to 3-tetrazolyl-substituted quinoline derivatives.

EXPERIMENTAL

Melting points were determined on a "Boetius" hot-stage apparatus and are uncorrected. The ir spectra were obtained on a Perkin-Elmer spectrometer 2000 FT IR in solid phase potassium bromide. The ^{1}H nmr spectra were recorded with a Bruker AM 250 instrument (250 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 [13].

General Procedure for the Preparation of 2-(1-Aryl-1*H*-tetrazol-5-yl)vinylamino Derivatives **3a-l** and **9a-e**.

To a hot solution of 10 mmoles of a 1-aryl-5-(2-dimethylaminovinyl)-1*H*-tetrazole **2** and 20 mmoles of an arylamine **1** (R = Me, Ph, or MeO) or anthranilonitrile (**8**), respectively, in methanol (10 ml) 25% hydrochloric acid (2.5 ml) was added. After cooling, the crystalline reaction products were filtered off, washed with cold methanol and recrystallized from the solvents given in Tables 1 and 2, respectively.

Synthesis of 4-Substituted 3-(1-Aryl-1*H*-tetrazol-5-yl)quinolines **4a-g**. General Procedure.

To a suspension of 5 mmoles of the respective 2-[2-(1-aryl-1*H*-tetrazol-5-yl)vinylamino]acetophenone or benzophenone **3** (R = Me, Ph) in absolute ethanol (15 ml) a 1 *M* ethanolic solution of sodium ethoxide (3 ml, 3 mmoles) was added. After refluxing for 1 hour, the solvent was partially distilled off (5-10 ml). On cooling or if necessary by dropwise addition of water the products **4a-g** precipitated as colorless crystals.

Data on the prepared compounds are listed in Table 1.

Synthesis of 3-(1-Aryl-1*H*-tetrazol-5-yl)-1*H*-quinolin-4-ones **5a-e**. General Procedure.

A mixture of the respective *N*-[2-(1-aryl-1*H*-tetrazol-5-yl)vinyl]anthranilic acid methyl ester **3** (R = MeO) (10 mmoles) and 1 *M* ethanolic solution of sodium ethoxide (10 ml, 10 mmoles) was refluxed for 1 hour and then evaporated until the sodium salt of the reaction product begun to precipitate. After cooling diethyl ether was added, the sodium salt filtered off, washed with ether and after drying dissolved in water (20-30 ml). Acidification with 2 *N* hydrochloric acid afforded **5a-e** as colorless solids.

Characteristics of the compounds thus prepared are shown in Table 1.

7-Methyl-4-phenyl-3-(1-phenyl-1*H*-tetrazol-5-yl)quinoline (**6**).

To a hot solution of 2-amino-4-methylbenzophenone (2.11 g,

10 mmoles) and 5-(2-dimethylaminoviny1)-1-phenyl-1*H*-tetrazole (**2**, Ar = Ph) (2.15 g, 10 mmoles) in methanol (10 ml) 25% hydrochloric acid (2.5 ml) was added. The resulting 4-methyl-2-[2-(1-phenyl-1*H*-tetrazol-5yl)vinylamino]benzophenone (2.95 g, 77%), mp 162-163° (acetonitrile) was then cyclized in the same way as described for **4a-g** to afford **6** in 90% yield as colorless crystals (methanol), mp 180-181; ^{1}H nmr: δ 2.55 (s, 3H, CH_3), 6.75 (d, 2H, Ph), 6.98 (d, 2H, Ph), 7.24-7.52 (m, 8H, Ph, H-5, H-6), 8.00 (s, 1H, H-8), 9.17 (s, 1H, H-2).

Anal. Calcd. for $C_{23}H_{17}N_5$: C, 76.01; H, 4.71; N, 19.27. Found: C, 75.91; H, 4.85; N, 19.21.

1-Methyl-3-(1-phenyl-1*H*-tetrazol-5-yl)-1*H*-quinolin-4-one (**7**).

A mixture of the **5a** sodium salt (see the general procedure for **5a-e**) (2.53 g, 8.14 mmoles) and dimethyl sulfate (1.26 g, 10 mmoles) in absolute acetonitrile (15 ml) was refluxed for 30 minutes and then the solvent partially distilled off (*ca.* 10 ml). On cooling the reaction product precipitated as colorless crystals (1.19 g, 48%), which were recrystallized from acetonitrile, mp 254-256° (decomposition); ir: ν CO 1637 cm^{-1}; ^{1}H nmr: δ 3.97 (s, 3H, CH_3), 7.42-7.60 (m, 6H, C_6H_5, H-6), 7.77 (d, 1H, H-8), 7.83 (t, 1H, H-7), 8.10 (d, 1H, H-5), 8.68 (s, 1H, H-2).

Anal. Calcd. for $C_{17}H_{13}N_5O$: C, 67.32; H, 4.32; N, 23.09. Found: C, 67.50; H, 4.25; N, 23.18.

Synthesis of 4-Amino-3-(1-aryl-1*H*-tetrazol-5-yl)quinolines **10a-e**. General Procedure.

A mixture of the respective *N*-[2-(1-aryl-1*H*-tetrazol-5-yl)vinyl]anthranilonitrile **9** (10 mmoles) and 1 *M* ethanolic solution of sodium ethoxide (20 ml, 20 mmoles) was refluxed for 1 hour. After cooling the products formed were filtered off, washed with methanol and recrystallized from the solvents given in Table 2.

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