Structure and Dynamics of Hydrogen Chelates

Part 1

NMR-Spectroscopic Studies in the Quinazoline-2-acetonitrile Series

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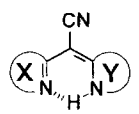
To get informations on both the structure and dynamics of hydrogen chelates **1** of heteroaromatic systems, a great variety of quinazoline-2-acetonitrile chelates were synthesized (see **2**–**4**). Similarly to the situation of the corresponding H-chelates in the pyrimidine-2-acetonitrile series, the investigation of these new derivatives **2**–**4** by NMR spectroscopic methods (DNMR, COSY, NOESY, ROESY, EXSY, HMQC, HMBC) confirms the presence of an equilibrium of the two possible H-chelate structures (two 'rotamers' **I** and **II**, *i.e.*, (*E*)/(*Z*) isomers; see *Scheme*). The corresponding equilibria **I** ⇌ **II** were determined by complete ^{1}H-NMR signal assignment at low temperatures (after freezing the rotational processes). In addition, the tautomer equilibria **A** ⇌ **B** (relative energies of the two minima of the nonsymmetrical double-well potential) for both 'rotamers' are ascertained by H,H and C,H couplings. The results are an important basis for the interpretation of both the UV/VIS absorptions and the dependence of fluorescence and fluorescence quantum yields on temperature.

Introduction. – Studies of H-bonds are of actual interest, both regarding the understanding of the nature of chemical bond as well as its effects on molecular structures [1–4]. Interested in systematic studies on the shape of the potential-energy surfaces of H-chelates, we synthesized a large variety of compounds of the general structure **1**. Having solved the problem of single- *vs.* double-well potential in favour of a double-well potential for all cases **1** with X = Y [5][6], for these cases the problem of the dependance of the double-well potential barrier on the nature of X remains. For the cases **1** with X ≠ Y, the position of the tautomer equilibrium is of particular interest, especially regarding the UV/VIS spectra.



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X,Y = N-heteroaromatic systems

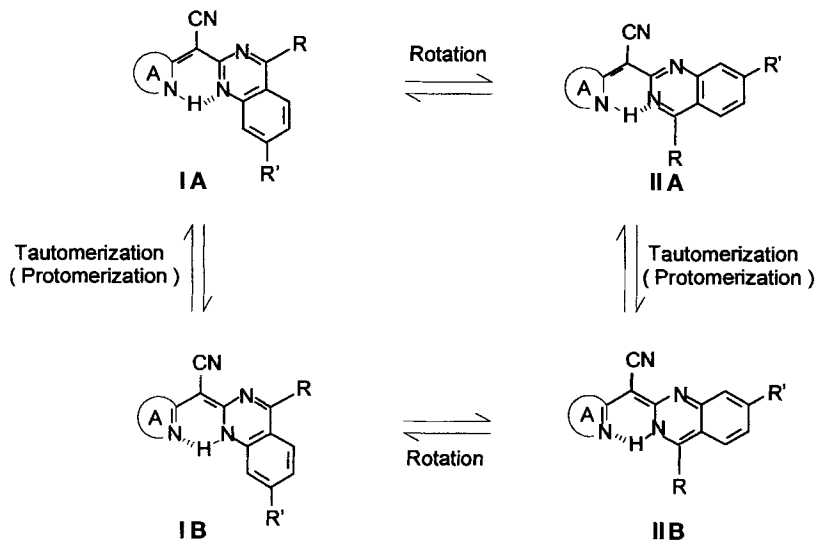
From the temperature dependance of both the UV/VIS absorption and emission, we derived a high innermolecular mobility for compounds **1** in solution at room temperature, in spite of π-electron conjugation and additional stabilization of the system's coplanarity by the intramolecular H-bridge (δ(NH) between 13 and 20 ppm!). To determine this postulated dynamics, we synthesized a variety of pyrimidine-2-acetonitrile chelates **1** (X = pyrimidine, Y = any N-heteroaromatic system). Due to the rotational

symmetry of the pyrimidin-2-yl moiety, these chelates permit an easy NMR spectroscopic determination of the rotational barrier of the pyrimidine system: Depending on the residue Y, the barriers $\Delta G^{\ddagger}$ are 50–60 kJ · mol^{-1} and the room-temperature rotational frequencies of the pyrimidine ring within the magnitude of 10^3 s^{-1} [7].

An analogous NMR spectroscopic determination of the kinetic parameters of the molecular dynamics of the chelates **1** of N-heteroaromatic systems is only possible for cases, where the N-heteroaromate has an additional N-atom in position 3. In this case only, there is a realistic chance that the rotamer formed after a 180° rotation lies energetically not too far from the thermodynamically preferred chelate. A detectable amount of this second minimum conformer can only be expected when a second H-chelate structure exists. For any other case, all rotamers beyond the H-chelate structure, due to steric effects, are energetically so unfavoured that their contribution to the equilibrium must be negligible. Then, even for frozen rotation, no NMR-detectable amount of conformers apart from the most stable one can be expected.

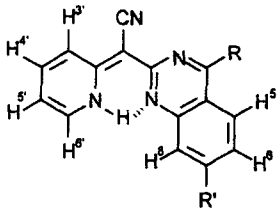
In this paper, we report on the determination of both the rotamer (= (*E*)/(*Z*) isomerization) and tautomer equilibria (**I** ⇌ **II** and **A** ⇌ **B**, resp.) of new H-chelates of the quinazoline-2-acetonitrile series (*Scheme*).

Scheme. *Possible Rotamers/Tautomers of Quinazoline-2-acetonitrile H-Chelates*

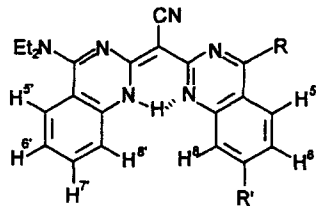


Results and Discussion. – To examine the equilibrium structures and their dependance on substituents, the dyes **2**–**4** were synthesized by condensation of heteroarene-2-acetonitriles and 2-chloroquinazolines under basic conditions.

Whereas the rotation **I** ⇌ **II** of the quinazoline moiety takes place at rates detectable by ^{1}H-NMR, the tautomerization **A** ⇌ **B** is fast compared with the NMR time scale. Thus, it is only possible to measure mean values.



	R	R′
2a	Ph	MeO
b	Et	MeO
c	4-MeO–C_6H_4	MeO
d	Ph	BuO
e	4-Me–C_6H_4	MeO
f	4-MeO–C_6H_4	BuO
g	4-(*t*-Bu)–C_6H_4	MeO
h	Et_2N	H
i	EtO	H
j	Ph	H



	R	R′
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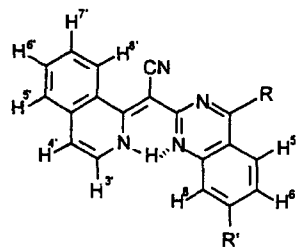
f	4-MeO–C_6H_4	BuO
g	4-(*t*-Bu)–C_6H_4	MeO
h	Et_2N	H
i	Ph	H



	R	R′
4a	Ph	MeO
b	Et	MeO
c	4-MeO–C_6H_4	MeO
d	Ph	BuO
e	4-Me–C_6H_4	MeO
f	4-MeO–C_6H_4	BuO
g	4-(*t*-Bu)–C_6H_4	MeO
h	Et_2N	H
i	EtO	H

Rotation **I** ⇌ **II**. The low-temperature NMR spectra of all dyes, except **2h**, **i** and **4h**, **i**, show two sets of peaks, each belonging to one of the isomers **I** and **II**; as an example, the low-temperature ^{1}H-NMR spectra of **3b** are given in *Fig. 1*. The rotation of the quinazoline moiety is slow enough to get sharp separated signals for the quinazoline derivatives **3** at 263 K and for the pyridine derivatives **2** at 253 K. Whereas for the

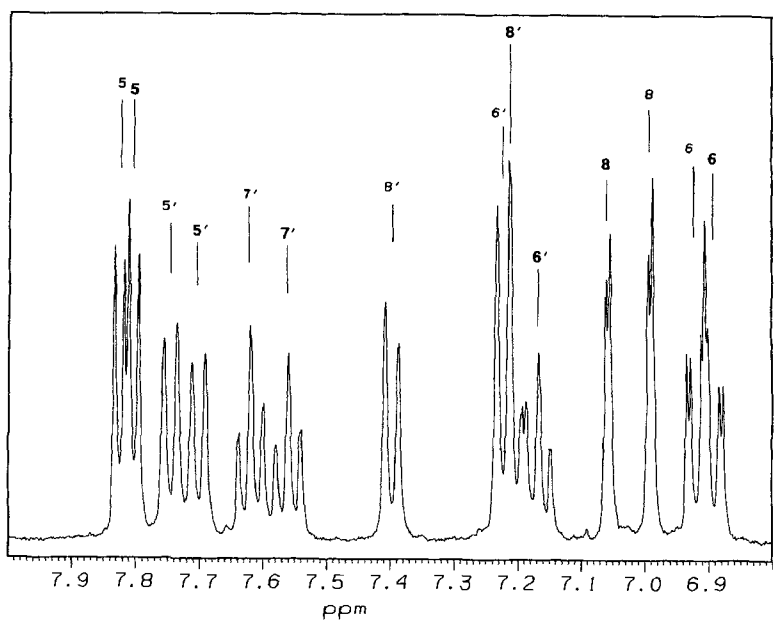


Fig. 1. *^{1}H-NMR Spectrum of* **3b** *at 263 K* (CD_2Cl_2, 400 MHz). The signals of isomer **II** are indicated in boldface.

isoquinoline derivatives **4**, a much lower temperature of 203 K is needed to freeze the rotation. For a given temperature, the rotation of the quinazoline moiety for isoquinoline dyes **4** is obviously much faster than for the pyridine or quinazoline dyes. This has to be attributed to the non-planarity of the derivatives **4** due to steric hindrance. The rotational frequencies lie in a range detectable by NMR techniques such as line-shape analyses or two-dimensional exchange spectroscopy (see *Fig. 2*). The rotational barriers will be reported elsewhere.

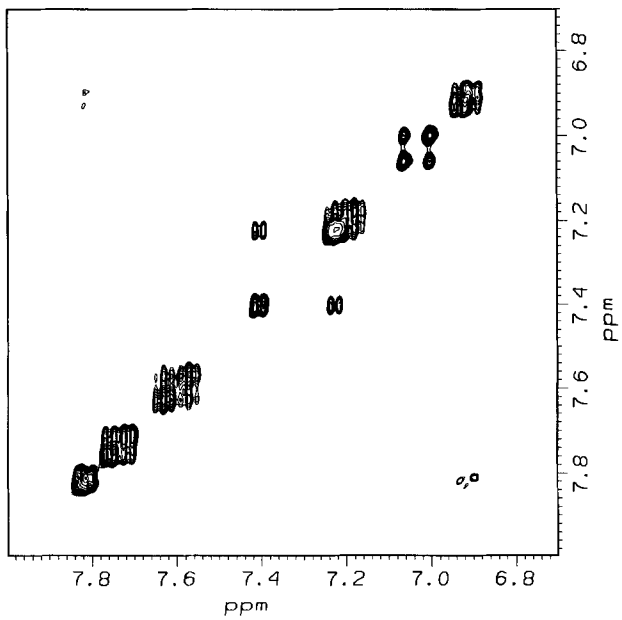


Fig. 2. *EXSY Spectrum of* **3b** *at 273 K* (CD_2Cl_2, 400 MHz, mixing time 100 ms)

Total signal assignments were done by two-dimensional NMR techniques such as COSY, NOESY, and ROESY. As the total signal assignments are important for the discrimination between the rotamers **I** and **II** and the determination of the rotational barriers, the procedure for **3a** is detailed below as an example (see *Figs. 3* and *4*). The assignments of the ^{1}H-NMR chemical shifts and the relative amounts of the rotamers for **2a**–**j**, **3a**–**i**, and **4a**–**i** are summarized in *Tables 5*–*7* in the *Exper. Part.* The determination of the structure of the rotamers **I** and **II** was made by the use of nuclear *Overhauser* effects (NOEs) between the proton of the H-bridge and other protons of the system.

For the pyridine dyes **2**, the NOESY and ROESY spectra show NOEs between the chelate proton and H–C(6′) as well as H–C(8) for rotamer **I**. For isomer **II**, in addition to the NOE to H–C(6′), additional NOEs to protons of the substituent R are observed. In the case of the quinazoline derivatives **3**, for isomer **I**, NOEs between the chelate proton and H–C(8′) and H–C(8), and for isomer **II**, NOEs between the chelate proton and H–C(8′) as well as to the substituent R are detected. The isoquinoline dyes **4** show NOEs between the chelate proton and H–C(3′) and H–C(8) for isomer **I**, and H–C(3′) and R for isomer **II**.

The ^{1}H-NMR signals of **3a** at 7.10 and 7.22 ppm are easily assigned to H–C(8) just because of their appearance (*d*, showing only a splitting of 2.4 Hz, due to a ^4J coupling to H–C(6)), each signal belonging to one

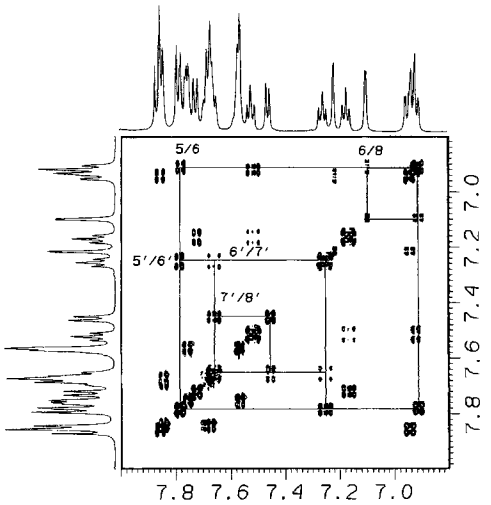


Fig. 3. *Aromatic part of the DQF-COSY spectrum* (CD_2Cl_2, 400 MHz) *of* **3a** *at 263 K.* The rectangles show the signal assignment of the aromatic protons of rotamer **I**.

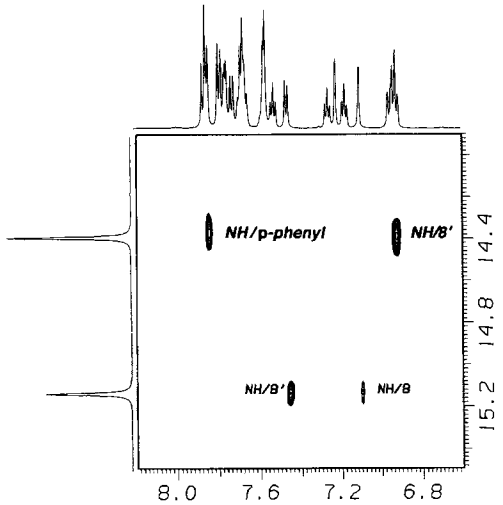


Fig. 4. *Part of the ROESY spectrum* (CD_2Cl_2, 600 MHz) *of* **3a** *at 263 K, showing the nuclear* Overhauser *effects, used for the differentiation of the rotamers* **I** *and* **II**. Signals whose annotations are indicated in boldface belong to rotamer **II**.

of the two rotamers **I** and **II**. The DQF-COSY spectra (*Fig. 3*) reveal couplings between H–C(8) at 7.10 and H–C(6) at 6.91 ppm and between H–C(8) at 7.22 and H–C(6) at 6.94 ppm. The signals of H–C(6) show couplings to H–C(5) at 7.78 and 7.86 ppm, resp. The ROESY spectra of **3a** establish NOEs between the Et_2N group and H–C(5') at 7.78 and 7.72 ppm, respectively. With the DQF-COSY (*Fig. 3*), it is possible to assign the signals of H–C(6'), H–C(7'), and H–C(8'): Starting with the signal of H–C(5') at 7.78 ppm, we find a coupling to H–C(6') at 7.25 ppm. The H–C(6') signal exhibits cross-peaks with the H–C(7') signal at 7.66 ppm; H–C(7') at 7.66 ppm couples with H–C(8') at 7.45 ppm. The signals of the second rotamer can be assigned in the same way. The ^{1}H-NMR signals of **3a** not yet assigned belong to the Ph substituent. For one of the rotamers, these are the signals at 7.76 ppm (H_o of Ph) and at 7.56 ppm (H_m and H_p of Ph) and for the other rotamer at 7.85 ppm (H_o) and at 7.67 ppm (H_m and H_p). Now we have three different spin systems, each containing two sets of signals because of the two rotamers. The next step is to assign these sets to the corresponding structure: The ROESY spectra (*Fig. 4*) show NOEs between the chelate proton at 15.13 ppm and the protons H–C(8') at 7.45 ppm and H–C(8) at 7.10 ppm. Therefore, these protons must belong to structure **I**. The chelate proton at 14.38 ppm exhibits NOEs to 6.92 ppm (H–C(8')) and 7.85 ppm (H_o of Ph). Therefore, this rotamer has the structure **II**.

The relative amounts of the two rotamers **I** and **II** follow from the signal integrals. These values were refined by spectra simulation made for line-shape analyses to determine the activation barriers. The accuracy of the values of the deduced equilibrium constants K = [**II**]/[**I**] (see *Table 1*) is better than 10%. The variation of R has only small effects on K except for R = EtO (**2i** and **4i**) or R = Et_2N (**2h**, **3h**, and **4h**), where only (in case of **3h** almost only) isomer **I** is found. For **4b** with R = Et, the contribution of isomer **II** is doubled compared with the other isoquinoline dyes with R = aryl. The effect of R' is more important; for **2j** and **3i**, where R' = H instead of R' = alkoxy, the amount of isomer **II** is reduced to half the value. The largest effect is observed for a variation of the heterocycle A. Whereas the pyridine as well as the isoquinoline dyes with R = phenyl and R' = alkoxy (**2a**, **2c–g**, **4d**, **f**, **g**) show equilibrium constants K of *ca.* 0.1, the quinazoline dyes with R = aryl and R' = alkoxy (**3a**, **3c–g**) show K's of *ca.* 1. Thus, the dyes **2–4** –

Table 1. *Equilibrium Constants* K = [II]/[I] *for the (E)/(Z)-Isomerization* **I** ⇌ **II** *in* CD_2Cl_2

	$K_{253\,K}$		$K_{263\,K}$		$K_{203\,K}$
2a	0.11	**3a**	1.08	**4a**	[a])
b	0.12	**b**	0.96	**b**	0.37
c	0.11	**c**	1.13	**c**	[a])
d	0.10	**d**	1.08	**d**	0.12
e	0.11	**e**	1.27	**e**	[a])
f	0.09	**f**	1.13	**f**	0.12
g	0.09	**g**	0.82	**g**	0.14
h	0	**h**	0.05	**h**	0
i	0	**i**	0.33	**i**	0
j	0.04				

[a]) The solubility of these dyes at 203 K is not sufficient for measuring the NMR spectra.

apart from the pyrimidine chelates mentioned (**1** with X = pyrimidine, Y = arbitrary N-heteroaromatic system) – are additional systems for the study of the dynamics of H-chelates.

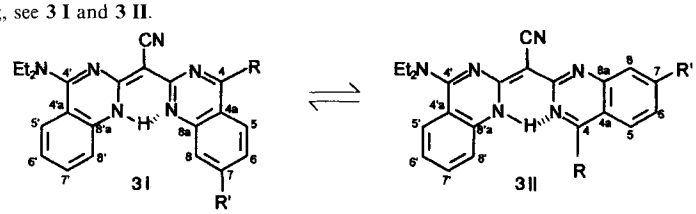
Tautomerization **A** ⇌ **B**. The tautomerization process is fast compared with the NMR time scale. Therefore, the observable chemical shifts and coupling constants are averaged values (both tautomers). The coupling constant between the chelate proton and H–C(6′) of the pyridine dyes **2** or H–C(3′) of the isoquinoline dyes **4**, however, can be used to determine the tautomer equilibrium. This coupling constant is given by $^3J_m = x_A \cdot {}^3J_A^0 + x_B \cdot {}^3J_B^0$, where ^3J_m is the measured coupling constant between the chelate proton and the *ortho*-proton of the heterocyclic system A; x_A and x_B are the molar fractions and $^3J_A^0$ and $^3J_B^0$ the coupling constants of the tautomers **A** and **B**, respectively. In tautomer **B**, there is no coupling observable between the chelate proton and H–C(6′) of compounds **2** or H–C(3′) of compounds **4**. Therefore, $^3J_B^0$ is zero, and the amount of tautomer **A** can be calculated directly from the ratio between the measured coupling constant ^3J_m and the coupling constant $^3J_A^0$ of tautomer **A**. The values of $^3J_A^0$ for the pyridine dyes **2a–g** are between 6.0 and 6.3 Hz, and for the isoquinoline dyes **4b, d, f, g** between 5.2 and 5.6 Hz. These values were taken from the signals of rotamer **II**, where only tautomer **A** occurs. Tautomer **B** of rotamer **II** is energetically very unfavourable due to its *o*-quinoid structure: an interpretation that is supported by AM1 calculations, showing energy differences of *ca.* 50 kJ/mol between the tautomers **IIA** and **IIB**. The coupling constants ^3J_m were taken from the one-dimensional spectra after *Lorentz-Gauss* transformation.

In the case of the pyridine dyes **2**, the coupling constants for rotamer **I** were taken from the signal of H–C(6′) in spectra where H–C(4′) is decoupled so that only the couplings with H–C(5′) and with the chelate proton are active. The signal of H–C(6′) of rotamer **II** of the pyridine dyes is covered so that the couplings were taken from the NH signal. This was only possible by lowering the temperature down to 203 K making the splitting in the NH signal observable. For the pyridine dyes **2a–g, j** the coupling constant ^3J_m of the rotamer **I** at 253 K amounts to 1.9–2.3 Hz; thus, in these cases, the relative amount of tautomer **A** is 30–40%. The dyes **2h, i** show no coupling between NH and H–C(6′); these dyes obviously exist only in the rotamer **I** and the tautomer **B**, *i.e.* **IB**.

In the case of the isoquinoline dyes **4**, the coupling constants ^3J_m of both rotamers **I** and **II** were also taken from the signal of the chelate proton, which shows a splitting at 203 K (the signal of H–C(3′) of rotamer **I** is covered). All measured coupling constants ^3J_m are *ca.* 5.5 Hz, thus the rotamers **I** also exist only as tautomer **A**, where the chelate proton is bound to the isoquinoline system.

The quinazoline dyes **3** possess no proton that can show a larger coupling to the chelate proton, thus the previously mentioned method for the determination of the tautomer equilibrium cannot be applied. Measuring the $^{15}N,^1H$-coupling constants is not possible because of insufficient solubility of these dyes. Even for measuring the coupling constants with more sensitive methods such as INEPT or inverse methods, the low-temperature solubilities proved to be too low. To get informations about the tautomeric situation in these dyes, the couplings of the NH proton to ^{13}C-nuclei were examined for the fairly soluble dyes **3d**, **f**, **g**. The ^{13}C-NMR signals were assigned by HMQC [8] and HMBC [9] spectra (see *Table 2*). The HMBC spectra show couplings between the chelate proton and the nuclei C(4′a), C(8′a), and C(8′) for both rotamers **I** and **II**. There are no couplings to C-atoms of the second quinazoline system. Therefore, both rotamers only (or at least mainly) exist in the tautomer **A**.

Table 2. *^{13}C-NMR Chemical Shifts* (CD_2Cl_2) *of the Quinazoline Dyes* **3d**, **f**, **g** *at 263 K for the Rotamers* **I** *and* **II**. For numbering, see **3 I** and **3 II**.



		C(4′)	C(4′a)	C(5′)	C(6′)	C(7′)	C(8′)	C(8′a)	C(4)	C(4a)	C(5)	C(6)	C(7)	C(8)	C(8a)
3d	**I**	158.09	111.04	126.01	122.41	133.29	117.64	141.19	166.94	113.66	128.74	116.39	163.31	104.07	151.59
	II	158.91	110.63	126.04	122.73	133.39	116.75	141.08	164.16	113.40	128.44	116.90	163.68	105.23	155.13
3f	**I**	159.24	111.29	126.16	122.77	133.35	117.84	141.57	166.48	113.75	128.60	116.25	163.72	104.28	151.68
	II	159.12	110.85	126.14	122.46	133.52	116.88	141.33	163.91	113.56	128.95	117.84	163.35	105.25	155.25
3g	**I**	159.32	111.32	126.20	122.86	133.44	117.83	141.60	167.23	114.06	129.11	116.13	163.40	103.86	151.75
	II	159.24	110.98	126.24	122.59	133.55	116.97	141.42	164.37	113.81	128.84	117.70	163.90	105.02	155.20

The position of the tautomerization equilibria can be explained for the quinazoline derivatives **3** and the isoquinoline derivatives **4** just by comparing the basicity of the heterocyclic systems. The chelate proton is bound to the ring with the highest electron density at the N-atom involved in the H-bond. For the case of the isoquinoline dyes **4**, this is the isoquinoline moiety, for the quinazoline dyes **3**, it is the Et_2N-substituted quinazoline moiety, in which the electron density is raised by the Et_2N group. For the pyridine dyes **2**, the situation is more difficult. Contrary to the observation, one would expect the more basic pyridine ring to carry the H-atom and not the less basic quinazoline system. From *Table 3* follows that the enthalpical preference of

Table 3. *Temperature Dependance of the Tautomer Equilibrium* **A** ⇌ **B** *of Compounds* **2** *in* CD_2Cl_2 *and Resulting Enthalpies and Entropies for the Tautomerization Process*[a]). Equilibrium Constant $K = [\mathbf{A}]/[\mathbf{B}]$.

	2c	**2d**	**2e**	**2f**	**2g**	**2j**
$K_{263\ K}$	0.39	0.54	0.49	0.39	0.49	0.53
$K_{243\ K}$	0.54	0.59	0.59	0.49	0.59	0.61
$K_{223\ K}$	0.61	0.67	0.67	0.59	0.72	0.72
$K_{203\ K}$	0.75	0.82	0.82	0.67	0.82	0.92
$K_{183\ K}$	0.82	0.92	0.92	0.75	0.92	1.13
ΔH^0 [kJ/mol][b])	-3.7 ± 0.9	-2.8 ± 0.9	-3.2 ± 0.9	-3.3 ± 0.9	-3.3 ± 0.9	-3.8 ± 0.9
ΔS^0 [J/mol K][b])	-20.8 ± 4.3	-15.8 ± 4.1	-17.9 ± 4.1	-19.6 ± 4.3	-18.0 ± 4.1	-19.4 ± 4.3

[a]) The solubility of **2a** at low temperatures is not sufficiently high, **2h** and **2i** show no measurable amounts of tautomer **A**; **2b** shows no temperature dependance, the equilibrium constant is *ca.* 0.5. [b]) For the linear regression $\ln K$ *vs.* $1/T$, the errors in K and T were considered. The accuracy of the coupling constants ^3J from which the equilibrium constants are calculated is *ca.* ± 0.2 Hz. The temperature was measured with a standard sample of MeOH, the accuracy is ± 1 K.

tautomers **A** is (obviously) overcompensated by the significantly higher entropy of the tautomers **B**. We ascribe this effect to a more flexible structure of tautomer **B**. In this tautomer, the π-bond between the pyridine ring and the acetonitrile part has a significantly lower C=C bond character (π-bond order 0.45, according to SCF-CI calculations/PPP approximation) than in tautomer **A** (π-bond order 0.65). Therefore, a rotation or torsional vibration of the smaller and more moveable pyridine ring (compared with the quinazoline ring) can take place much easier in tautomer **B** than in tautomer **A**.

The acquisition of HMBC and HMQC spectra by Dr. *A. Geyer* is thankfully acknowledged.

Experimental Part

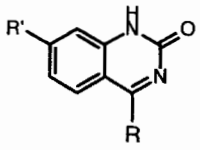
1. *General.* Commercially available reagents and solvents were used without further purification. DMF was destilled from CaH_2. NMR Spectra: *JEOL-GX-400* spectrometer; heteronuclear experiments on a *Bruker-DRX-600* spectrometer; spectra transfer to an external workstation and exploitation with the program Felix 95.0 from *Biosym*; δ in ppm rel. to internal $SiMe_4$ (= 0 ppm).

2. *Educt Syntheses. Quinazolin-2(1H)-ones* **5a**–**11a**: The quinazolinones were prepared according to *Budesinsky* and *Lederer* [10] from 3-methoxy- or 3-butoxyphenyl isocyanate [11] and amides to give 1-acylureas which were cyclized to the quinazolinones in polyphosphoric acid without purification. The quinazolinones were crystallized from EtOH. Yields are given in *Table 4*.

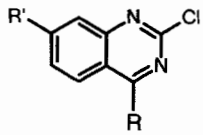
2-Chloroquinazolines **5b**–**11b**: The quinazolin-2(1*H*)-ones **5a**–**11a** were refluxed with phosphorous oxychloride ($POCl_3$; 10 ml per g quinazolinone) for 30 min, then poured into ice-water, neutralized with NaOH, and extracted with $CHCl_3$. After evaporation the residue was crystallized from EtOH. Yields are given in *Table 4*. An alternative method for the synthesis of 4-substituted 2-chloroquinazolines could be the reaction of 2,4-dichloroquinazoline with trialkylalanes under Pd-catalysis, see [12].

tert-Butyl α-Cyano-4-(diethylamino)quinazoline-2-acetate (**12**). To a suspension of NaH (450 mg, 19 mmol) in 1-methylpyrrolidin-2-one (10 ml) a soln. of *tert*-butyl cyanoacetate (2.7 g, 19 mmol) in 1-methylpyrrolidin-2-one (10 ml) was added dropwise under N_2. After the evolution of H_2 had finished, a soln. of 2-chloro-4-(diethylamino)quinazoline [13] (1.5 g, 6.38 mmol) in 1-methylpyrrolidin-2-one (20 ml) was added. The soln. was heated to 100° for 18 h. Then the cooled soln. was poured into H_2O (200 ml). After addition of a few drops of ammonia, a yellow precipitate separated, which was filtered off and crystallized from MeOH: 1.35 g (62%). ^{1}H-NMR ($CDCl_3$): 12.52 (br., 1 H); 7.73 (*d*, 1 H); 7.57 (*dd*, 1 H); 7.25 (*d*, 1 H); 7.21 (*dd*, 1 H); 3.81 (*q*, 4 H); 1.55 (*s*, 9 H); 1.44 (*t*, 6 H).

Table 4. *Yields of the Quinazolin-2(1H)-ones* **5a**–**11a** *and Yields and* ^{1}*H-NMR Data* ($CDCl_3$, 298 K) *of the Chloroquinazolines* **5b**–**11b**

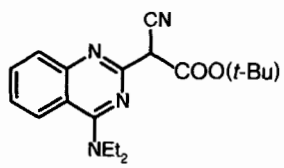


5a–11a

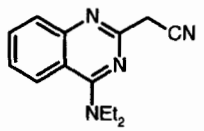


5b–11b

	R	R′	Yield	δ [ppm]
5	Ph	MeO	**a**: 56%	
			b: 93%	7.99 (*d*, H–C(5)); 7.33 (*d*, H–C(8)); 7.21 (*dd*, H–C(6)); 7.75 (*m*, 2 H); 7.56 (*m*, 3 H); 3.99 (*s*, 3 H)
6	Et	MeO	**a**: 30%	
			b: 83%	7.99 (*d*, H–C(5)); 7.23 (*m*, H–C(8), H–C(6)); 3.22 (*q*, 2 H); 1.43 (*t*, 3 H); 3.96 (*s*, 3 H)
7	4-$MeOC_6H_4$	MeO	**a**: 26%	
			b: 67%	8.01 (*d*, H–C(5)); 7.26 (*d*, H–C(8)); 7.18 (*dd*, H–C(6)); 7.74 (*m*, 2 H); 7.05 (*m*, 2 H); 3.96 (*s*, 3 H); 3.89 (*s*, 3 H)
8	4-MeC_6H_4	MeO	**a**: 50%	
			b: 80%	8.01 (*d*, H–C(5)); 7.31 (*d*, H–C(8)); 7.19 (*dd*, H–C(6)); 7.34 (*m*, 2 H); 7.16 (*m*, 2 H); 3.98 (*s*, 3 H); 2.47 (*s*, 3 H)
9	4-(*t*-Bu)C_6H_4	MeO	**a**: 30%	
		MeO	**b**: 70%	8.05 (*d*, H–C(5)); 7.31 (*d*, H–C(8)); 7.20 (*dd*, H–C(6)); 7.71 (*m*, 2 H); 7.58 (*m*, 2 H); 3.98 (*s*, 3 H); 1.39 (*s*, 9 H)
10	Ph	BuO	**a**: 17%	
			b: 65%	7.95 (*d*, H–C(5)); 7.27 (*d*, H–C(8)); 7.17 (*dd*, H–C(6)); 7.72 (*m*, 2 H); 7.55 (*m*, 3 H); 4.13 (*t*, 2 H); 1.84 (*m*, 2 H); 1.52 (*m*, 2 H); 0.98 (*t*, 3 H)
11	4-$MeOC_6H_4$	BuO	**a**: 12%	
			b: 90%	8.00 (*d*, H–C(5)); 7.26 (*d*, H–C(8)); 7.17 (*dd*, H–C(6)); 7.74 (*m*, 2 H); 7.05 (*m*, 2 H); 3.89 (*s*, 3 H); 4.13 (*t*, 2 H); 1.83 (*m*, 2 H); 1.52 (*m*, 2 H); 0.99 (*t*, 3 H)



12



13

4-(Diethylamino)quinazoline-2-acetonitrile (**13**). The ester **12** was stirred in HCOOH (20 ml) at 60° for 30 min. The clear soln. was diluted with H_2O (20 ml), neutralized with ammonia, and extracted with CH_2Cl_2. Evaporation and crystallization of the residue from petroleum ether gave **13** (85%). ^{1}H-NMR ($CDCl_3$): 7.91 (*d*, 1 H); 7.78 (*d*, 1 H); 7.69 (*dd*, 1 H); 7.39 (*dd*, 1 H); 3.94 (*s*, 2 H); 3.79 (*q*, 4 H); 1.43 (*t*, 6 H).

3. *Dye Syntheses. General Procedure.* NaH was suspended in dry DMF (2 mmol of NaH in 5 ml of DMF per 1 mmol of chloroquinazoline) and cooled to 0° under N_2. The acetonitrile derivative, dissolved in a minimum of DMF, was added dropwise. The soln. was stirred until the evolution of H_2 had finished. Then, the 2-chloroquinazoline, dissolved in a minimum of DMF, was added. Temp. and reaction time were adjusted by TLC monitoring. When all the chloroquinazoline had reacted, the soln. was poured into 100 ml of ice-water acidified by AcOH (5 ml). The separating precipitate was filtered off and crystallized from MeCN. Spectral data of **2**–**4**, see *Tables 5–7*.

7-Methoxy-4-phenyl-α-(pyridin-2(1H)-ylidene)quinazoline-2-acetonitrile (**2a**). From pyridine-2-acetonitrile [14] (230 mg) and 2-chloro-7-methoxy-4-phenylquinazoline (**5b**; 500 mg), 1 h at 25°: 450 mg (71%) of **2a**. Anal. calc. for $C_{22}H_{16}N_4O$: C 74.98, H 4.58, N 15.90; found: C 74.98, H 4.67, N 15.64.

4-Ethyl-7-methoxy-α-(pyridin-2(1H)-ylidene)quinazoline-2-acetonitrile (**2b**). From pyridine-2-acetonitrile (200 mg) and 2-chloro-4-ethyl-7-methoxyquinazoline (**6b**; 340 mg), 3 h at 25°: 130 mg (28%) of **2b**. Anal. calc. for $C_{18}H_{16}N_4O$: C 71.03, H 5.30, N 18.41; found: C 71.03, H 5.43, N 18.48.

7-Methoxy-4-(4-methoxyphenyl)-α-(pyridin-2(1H)-ylidene)quinazoline-2-acetonitrile (**2c**). From pyridine-2-acetonitrile (200 mg) and 2-chloro-7-methoxy-4-(4-methoxyphenyl)quinazoline (**7b**; 500 mg), 2 h at 25°: 470 mg (74%) of **2c**. Anal. calc. for $C_{23}H_{18}N_4O_2$: C 72.24, H 4.74, N 14.65; found: C 71.66, H 4.86, N 14.63.

7-Butoxy-4-phenyl-α-(pyridin-2(1H)-ylidene)quinazoline-2-acetonitrile (**2d**). From pyridine-2-acetonitrile (160 mg) and 7-butoxy-2-chloro-4-phenylquinazoline (**10b**; 400 mg), 0.5 h at 25°: 335 mg (66%) of **2d**. Anal. calc. for $C_{25}H_{24}N_4O$: C 75.73, H 6.10, N 14.13; found: C 75.98, H 5.80, N 14.13.

7-Methoxy-4-(4-methylphenyl)-α-(pyridin-2(1H)-ylidene)quinazoline-2-acetonitrile (**2e**). From pyridine-2-acetonitrile (220 mg) and 2-chloro-7-methoxy-4-(4-methylphenyl)quinazoline (**8b**; 500 mg), 1.5 h at 25°: 405 mg (63%) of **2e**. Anal. calc. for $C_{23}H_{18}N_4O$: C 75.39, H 4.95, N 15.29; found: C 75.27, H 5.00, N 15.09.

7-Butoxy-4-(4-methoxyphenyl)-α-(pyridin-2(1H)-ylidene)quinazoline-2-acetonitrile (**2f**). From pyridine-2-acetonitrile (200 mg) and 7-butoxy-2-chloro-4-(4-methoxyphenyl)quinazoline (**11b**; 630 mg), 0.75 h at 25°: 265 mg (42%) of **2f**. Anal. calc. for $C_{26}H_{24}N_4O_2$: C 73.56, H 5.70, N 13.21; found: C 73.39, H 5.79, N 13.08.

*4-[4(*tert*-Butyl)phenyl]-7-methoxy-α-(pyridin-2(1H)-ylidene)quinazoline-2-acetonitrile* (**2g**). From pyridine-2-acetonitrile (190 mg) and 4-[4-(*tert*-butyl)phenyl]-2-chloro-7-methoxyquinazoline (**9b**; 500 mg), 0.75 h at 25°: 500 mg (80%) of **2g**. Anal. calc. for $C_{26}H_{24}N_4O$: C 76.45, H 5.92, N 13.71; found: C 77.29, H 6.04, N 13.76.

4-(Diethylamino)-α-(pyridin-2(1H)-ylidene)quinazoline-2-acetonitrile (**2h**). From pyridine-2-acetonitrile (270 mg) and 2-chloro-4-(diethylamino)quinazoline [13] (500 mg) 30 h at 25°: 420 mg (64%) of **2h** after crystallization from MeOH. Anal. calc. for $C_{19}H_{19}N_5$: C 71.90, H 6.03, N 22.07; found: C 71.92, H 6.09, N 21.62.

4-Ethoxy-α-(pyridin-2(1H)-ylidene)quinazoline-2-acetonitrile (**2i**). From pyridine-2-acetonitrile (400 mg) and 2-chloro-4-ethoxyquinazoline [15] (700 mg), 1 h at 25°: 200 mg (21%) of **2i**, after chromatography (silica gel, toluol/AcOEt 3:2). The main product resulted from substitution of the EtO group: Anal. calc. for $C_{17}H_{14}N_4O$: C 70.33, H 4.86, N 19.30; found: C 70.81, H 4.95, N 19.15.

7-Methoxy-4-phenyl-α-(pyridin-2(1H)-ylidene)quinazoline-2-acetonitrile (**2j**). From pyridine-2-acetonitrile (590 mg) and 2-chloro-4-phenylquinazoline [16] (1.35 g), 0.75 h at 25°: 1.1 g (71%) of **2j**. Anal. calc. for $C_{21}H_{14}N_4$: C 78.24, H4.38, N 17.38; found: C 78.46, H 4.40, N 17.41.

α-[4-(Diethylamino)quinazolin-2(1H)-ylidene]-7-methoxy-4-phenylquinazoline-2-acetonitrile (**3a**). From **13** (400 mg) and **5b** (450 mg); 5 h at 50°: 270 mg (34%) of **3a**. Anal. calc. for $C_{29}H_{26}N_6O$: C 73.40, H 5.52, N 17.71; found: C 73.02, H 5.56, N 17.41.

α-[4-(Diethylamino)quinazolin-2(1H)-ylidene]-4-ethyl-7-methoxyquinazoline-2-acetonitrile (**3b**). From **13** (300 mg) and **6b** (260 mg), 23 h at 25°: 150 mg (30%) of **3b**. Anal. calc. for $C_{25}H_{26}N_6O$: C 70.40, H 6.14, N 19.70; found: C 70.51, H 6.18, N 19.13.

α-[4-(Diethylamino)quinazolin-2(1H)-ylidene]-7-methoxy-4-(4-methoxyphenyl)quinazoline-2-acetonitrile (**3c**). From **13** (250 mg) and **7b** (270 mg), 20 h at 25°: 270 mg (60%) of **3c**. Anal. calc. for $C_{30}H_{23}N_6O_2$: C 71.41, H 5.59, N 16.66; found: C 71.71, H 5.69, N 16.48.

7-Butoxy-α-[4-(diethylamino)quinazolin-2(1H)-ylidene]-4-phenylquinazoline-2-acetonitrile (**3d**). From **13** (220 mg) and **10b** (250 mg), 20 h at 40°: 200 mg (49%) of **3d**. Anal. calc. for $C_{32}H_{32}N_6O$: C 74.39, H 6.24, N 16.27; found: C 74.47, H 6.20, N 16.26.

α-[4-(Diethylamino)quinazolin-2(1H)-ylidene]-7-methoxy-4-(4-methylphenyl)quinazoline-2-acetonitrile (**3e**). From **13** (200 mg) and **8b** (230 mg), 20 h at 25°: 93 mg (24%) of **3e**. Anal. calc. for $C_{30}H_{28}N_6O$: C 73.75, H 5.78, N 17.20; found: C 74.22, H 5.82, N 17.20.

Table 5. *^{1}H-NMR Chemical Shifts and Rotamer Equilibria of the Pyridine Dyes* **2**, *at 253 K in CD_2Cl_2*

	Rotamer [%]	δ [ppm] H–C(3′)	H–C(4′)	H–C(5′)	H–C(6′)	H–C(5)	H–C(6)	H–C(8)	NH	R	R′
2a	**I** 90	7.55	7.64	6.87	8.25	7.72	6.83	6.92	15.88	7.75, 7.57	3.96
	II 10	7.42	7.48	6.48	7.49	7.82	6.95	7.21	15.56	*ca.* 7.7, *ca.* 7.6	3.96
2b	**I** 89	7.51	7.63	6.88	8.29	7.74	6.83	6.78	15.64	3.07, 1.37	3.93
	II 11	7.36	7.45	6.50	7.61	7.82	6.95	7.08	15.88	3.25, 1.46	3.91
2c	**I** 90	7.53	7.64	6.87	8.27	7.77	6.83	6.88	15.78	7.75, 7.06, 3.88	3.95
	II 10	7.41	7.49	6.50	7.52	7.85	6.95	7.21	15.56	7.73, 7.11, *ca.* 3.9	*ca.* 3.9
2d	**I** 91	7.53	7.65	6.87	8.26	7.70	6.82	6.89	15.85	7.75, 7.56	4.10, 1.81, 1.50, 0.98
	II 9	7.43	7.56	6.47	7.52	7.82	6.94	7.17	15.58	7.75, 7.61	4.07, 1.81, 1.50, 0.98
2e	**I** 90	7.55	7.65	6.87	8.29	7.75	6.83	6.90	15.83	7.66, 7.37, 2.45	3.96
	II 10	7.45	7.47	6.48	7.49	7.84	6.95	7.20	15.67	7.67, 7.42, 2.48	3.97
2f	**I** 92	7.52	7.63	6.87	8.28	7.75	6.81	6.84	15.74	7.74, 7.06, 3.88	4.08, 1.80, 1.50, 0.98
	II 8	7.38	7.46	6.47	7.50	7.84	6.93	7.14	15.73	7.72, 7.11, 3.90	4.09, 1.80, 1.50, 0.98
2g	**I** 92	7.53	7.63	6.86	8.26	7.77	6.82	6.89	15.78	7.70, 7.58, 1.38	3.95
	II 8	7.41	7.46	6.47	7.52	7.86	6.95	7.19	15.62	*ca.* 7.7, *ca.* 7.6, 1.40	3.96
2h	**I** 100	7.44	7.58	6.81	8.34	7.72	7.16	7.27	14.83	3.77, 1.44	7.55
	II 0[a])										
2i	**I** 100	7.53	7.65	6.92	8.33	7.91	7.22	7.32	15.27	4.68, 1.52	7.64
	II 0[a])										
2j	**I** 96	7.57	7.67	6.89	8.24	7.83	7.26	7.58	15.85	7.79, 7.58	7.73
	II 4	7.50	7.50	6.50	7.51	7.94	7.37	7.92	15.33	*ca.* 7.8, *ca.* 7.6	*ca.* 7.8

[a]) Even at 203 K, no detectable amount of the second rotamer could be observed; values were taken at 298 K.

Table 6. *^{1}H-NMR Chemical Shifts and Rotamer Equilibria of the Quinazoline Dyes* **3**, *at 263 K in CD_2Cl_2*[a])

	Rotamer [%]	δ[ppm] H–C(5′)	H–C(6′)	H–C(7′)	H–C(8′)	H–C(5)	H–C(6)	H–C(8)	NH	R	R′
3a	**I** 48	7.78	7.25	7.66	7.45	7.78	6.91	7.10	15.13	7.76, 7.56	4.02
	II 52	7.72	7.17	7.52	6.92	7.86	6.94	7.22	14.38	*ca.* 7.85, 7.67	3.98
3b	**I** 51	7.75	7.23	7.63	7.40	7.82	6.93	7.00	15.19	3.12, 1.42	4.00
	II 49	7.70	7.18	7.57	7.22	7.80	6.88	7.04	14.03	3.31, 1.58	3.90
3c	**I** 47	7.76	7.23	7.63	7.42	7.80	6.90	7.06	15.15	7.75, 7.08, 3.95	4.01
	II 53	7.71	7.16	7.53	6.96	7.87	6.94	7.18	14.43	7.81, 7.18, 3.93	3.96
3d	**I** 48	7.78	7.25	7.65	7.46	7.75	6.91	7.08	15.15	7.76, 7.56	4.18, 1.84, 1.55, 1.01
	II 52	7.72	7.16	7.51	6.92	7.85	6.94	7.19	14.39	7.85, 7.68	4.16, 1.83, 1.50, 0.99
3e	**I** 44	7.77	7.24	7.65	7.43	7.80	6.90	7.08	15.15	7.66, 7.37, 2.46	4.01
	II 56	7.72	7.17	7.54	6.96	7.87	6.93	7.20	14.42	7.74, 7.48, 2.53	3.97
3f	**I** 47	7.78	7.25	7.66	7.46	7.85	6.91	7.07	15.17	7.76, 7.08, 3.89	4.17, 1.85, 1.55, 1.00
	II 53	7.72	7.17	7.54	6.97	7.88	6.94	7.18	14.46	7.81, 7.19, 3.94	4.15, 1.83, 1.50, 0.98
3g	**I** 55	7.76	7.23	7.64	7.42	7.82	6.90	7.07	15.12	7.69, 7.58, 1.39	4.02
	II 45	7.72	7.17	7.53	6.97	7.89	6.94	7.22	14.39	7.80, 7.70, 1.44	3.97
3h	**I** 95	7.75	7.18	7.59	7.48	7.75	7.18	7.48	15.54	3.74, 1.41	7.59
	II 5								13.35		
3i	**I** 75	7.80	7.26	7.66	7.46	7.91	7.32	*ca.* 7.8	15.18	*ca.* 7.8, 7.58	*ca.* 7.8
	II 25	7.73	7.18	7.53	6.93	7.99	7.36	*ca.* 7.88	14.17	*ca.* 7.88, *ca.* 7.7	*ca.* 7.8

[a]) Chemical shifts of the Et_2N protons: 3.80 and 1.46 ppm for the rotamers **I** and 3.79 and 1.45 ppm for the rotamers **II**.

Table 7. *^{1}H-NMR-Chemical Shifts and Rotamer Equilibria of the Isoquinoline Dyes* **4**, *at 203 K in CD_2Cl_2*

	Rotamer [%]	δ[ppm] H–C(3′)	H–C(4′)	H–C(5′)	H–C(6′)	H–C(7′)	H–C(8′)	H–C(5)	H–C(6)	H–C(8)	NH	R	R′
4a	[a])	7.53	6.85	*ca.* 7.6	7.70	*ca.* 7.6	9.65	7.90	7.02	7.21	16.72	7.84, *ca.* 7.6	4.01
4b	**I** 73	*ca.* 7.5	6.77	7.55	7.62	7.50	9.49	7.82	6.89	6.99	16.88	3.14, 1.39	3.91
	II 27	7.20	6.57	7.42	7.55	7.43	9.41	7.67	6.86	6.99	16.34	3.14, 1.39	3.88
4c	[a])	7.53	6.88	7.64	7.71	7.61	9.67	7.98	7.05	7.22	16.78	7.85, 7.13, 3.93	4.01
4d	**I** 89	7.59	6.83	*ca.* 7.55	*ca.* 7.6	7.51	9.53	7.78	6.88	7.04	16.86	7.76, *ca.* 7.55	4.05, 1.77, 1.48, 0.96
	II 11	7.18	6.71	*ca.* 7.55	*ca.* 7.6	*ca.* 7.5	9.47	7.89	6.95	7.14	16.13	7.78, *ca.* 7.55	4.05, 1.77, 1.48, 0.96
4e	[a])	7.58	6.87	7.64	7.72	7.62	9.67	7.95	7.05	7.23	16.76	7.75, 7.57, 2.50	4.02
4f	**I** 89	7.64	6.88	7.60	7.67	7.56	9.57	7.89	6.93	7.10	16.94	7.79, 7.07, 3.87	4.07, 1.79, 1.48, 0.96
	II 11	7.25	6.74	*ca.* 7.6	*ca.* 7.6	7.50	9.50	7.93	7.00	7.15	16.31	7.79, 7.11, 3.89	4.07, 1.79, 1.48, 0.96
4g	**I** 88	7.62	6.86	*ca.* 7.6	7.66	7.55	9.57	7.89	6.94	7.12	16.88	7.74, 7.58, 1.36	3.95
	II 12	7.31	6.75	*ca.* 7.6	*ca.* 7.6	7.55	9.53	7.96	7.02	7.23	16.29	7.76, *ca.* 7.6, 1.36	3.95
4h	**I** 100	7.62	6.84	*ca.* 7.6	*ca.* 7.65	7.56	9.56	7.86	7.27	*ca.* 7.6	17.04	3.82, 1.46	7.64
	II 0[b])												
4i	**I** 100	7.61	6.92	*ca.* 7.7	*ca.* 7.7	7.62	9.63	8.09	7.40	*ca.* 7.7	17.16	4.76, 1.59	7.77
	II 0[b])												

[a]) At 203 K, the solubility is not sufficient for measuring NMR spectra; therefore, these spectra were measured at 298 K where the rotation of the quinazoline ring is fast with respect to the NMR time scale. [b]) Even at 203 K, no detectable amount of the second rotamer was observable; values were taken at 298 K.

7-Butoxy-α-[4-(diethylamino)quinazolin-2(1H)-ylidene]-4-(4-methoxyphenyl)quinazoline-2-acetonitrile (**3f**). From **13** (60 mg) and **11b** (50 mg), 20 h at 40°: 17 mg (21%) of **3f**. Anal. calc. for $C_{33}H_{34}N_6O_2$: C 72.50, H 6.27, N 15.37; found: C 72.31, H 6.48, N 14.88.

*4-[4-(*tert*-Butyl)phenyl]-α-[4-(diethylamino)quinazolin-2(1H)-ylidene]-7-methoxyquinazoline-2-acetonitrile* (**3g**). From **13** (160 mg) and **9b** (210 mg), 20 h at 25°: 170 mg (50%) of **3g**. Anal. calc. for $C_{33}H_{34}N_6O$: C 74.69, H 6.46, N 15.84; found: C 74.19, H 6.48, N 15.75.

4-(Diethylamino)-α-[4-(diethylamino)quinazolin-2(1H)-ylidene]quinazoline-2-acetonitrile (**3h**). From **13** (250 mg) and 2-chloro-4-(diethylamino)quinazoline [13] (240 mg), 20 h at 80°: 195 mg (45%) of **3h**, after crystallization from MeOH. Anal. calc. for $C_{26}H_{29}N_7$: C 71.04, H 6.65, N 22.31; found: C 70.74, H 6.65, N 22.45.

α-[4-(Diethylamino)quinazolin-2(1H)-ylidene]-4-phenylquinazoline-2-acetonitrile (**3i**). From **13** (500 mg) and 2-chloro-4-phenylquinazoline [16] (500 mg), 17 h at 40°: 530 mg (57%) of **3i**. Anal. calc. for $C_{28}H_{24}N_6$: C 75.65, H 5.44, N 18.91; found: C 75.77, H 5.54, N 19.07.

α-(Isoquinolin-1(2H)-ylidene)-7-methoxy-4-phenylquinazoline-2-acetonitrile (**4a**). From isoquinoline-1-acetonitrile [17] (250 mg) and **5b** (350 mg), 20 h at 25°: 315 mg (60%) of **4a**. Anal. calc. for $C_{26}H_{18}N_4O$: C 77.59, H 4.51, N 13.92; found: C 77.59, H 4.67, N 13.78.

4-Ethyl-α-(isoquinolin-1-(2H)-ylidene)-7-methoxyquinazoline-2-acetonitrile (**4b**). From isoquinoline-1-acetonitrile (250 mg) and **6b** (270 mg), 7 h at 25°: 130 mg (30%) of **4b**. Anal. calc. for $C_{22}H_{18}N_4O$: C 74.56, H 5.12, N 15.81; found: C 74.51, H 5.36, N 15.73.

α-(Isoquinolin-1(2H)-ylidene)-7-methoxy-4-(4-methoxyphenyl)quinazoline-2-acetonitrile (**4c**). From isoquinoline-1-acetonitrile (200 mg) and **7b** (350 mg), 4 h at 40°: 175 mg (35%) of **4c**. Anal. calc. for $C_{27}H_{20}N_4O_2$: C 74.98, H 4.66, N 12.96; found: C 75.06, H 4.80, N 12.95.

7-Butoxy-α-(isoquinolin-1(2H)-ylidene)-4-phenylquinazoline-2-acetonitrile (**4d**). From isoquinoline-1-acetonitrile (100 mg) and **10b** (120 mg), 18 h at 25°: 120 mg (715%) of **4d**. Anal. calc. for $C_{29}H_{24}N_4O$: C 78.36, H 5.44, N 12.60; found: C 78.73, H 5.53, N 12.28.

α-(Isoquinolin-1(2H)-ylidene)-7-methoxy-4-(4-methylphenyl)quinazoline-2-acetonitrile (**4e**). From isoquinoline-1-acetonitrile (200 mg) and **8b** (310 mg), 4 h at 40°: 205 mg (45%) of **4e**. Anal. calc. for $C_{26}H_{20}N_4O$: C 77.21, H 4.98, N 13.85; found: C 77.85, H 4.90, N 13.23.

7-Butoxy-α-(isoquinolin-1(2H)-ylidene)-4-(4-methoxyphenyl)quinazoline-2-acetonitrile (**4f**). From isoquinoline-1-acetonitrile (90 mg) and **11b** (100 mg), 16 h at 25°: 65 mg (44%) of **4f**. Anal. calc. for $C_{30}H_{26}N_4O_2$: C 75.93, H 5.52, N 11.81; found: C 75.32, H 5.81, N 11.44.

*4-[4-(*tert*-Butyl)phenyl]-α-(isoquinolin-1(2H)-ylidene)-7-methoxyquinazoline-2-acetonitrile* (**4g**). From isoquinoline-1-acetonitrile (200 mg) and **9b** (380 mg), 3 h at 25°: 300 mg (57%) of 4g. Anal. calc. for $C_{30}H_{26}N_4O$: C 78.58, H 5.71, N 12.22; found: C 78.29, H 5.85, N 12.02.

4-(Diethylamino)-α-(isoquinolin-1(2H)-ylidene)quinazoline-2-acetonitrile (**4h**). From isoquinoline-1-acetonitrile (250 mg) and 2-chloro-4-(diethylamino)quinazoline [13] (310 mg), 20 h at 80°: 170 mg (36%) of **4h**, after crystallization from MeOH. Anal. calc. for $C_{23}H_{21}N_5$: C 75.18, H 5.76, N 19.06; found: C 75.12, H 5.95, N 19.05.

4-Ethoxy-α-(isoquinolin-1(2H)-ylidene)quinazoline-2-acetonitrile (**4i**). From isoquinoline-1-acetonitrile (250 mg) and 2-chloro-4-ethoxyquinazoline [15] (270 mg), 7 h at 25°: 145 mg (33%) of **4i**, after crystallization from MeOH. Anal. calc. for $C_{21}H_{16}N_4O$: C 74.10, H 4.74, N 16.46; found: C 74.09, H 4.89, N 16.67.

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