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DETERMINATION OF THE *R* ⇄ *S* ENANTIOMERIZATION BARRIER IN 5,6-DIHYDROBENZOIMIDAZO[1,2-*c*]QUINAZOLINES

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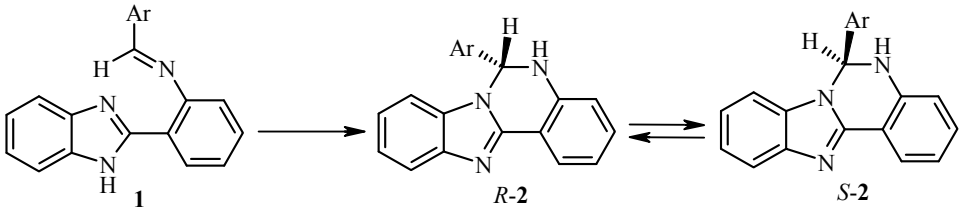
Chiral imidazoquinazolines undergoing thermally induced reversible R ⇄ S enantiomerization have been synthesized by the interaction of 2-(o-aminophenyl)benzimidazoles with aldehydes and ketones. The benzimidazole fragment has been used for the first time as an indicator group in temperature-dependent ^{1}H NMR spectra for determining the energy barrier of this rearrangement. The effects of nearby substituents on the kinetic and activation parameters, and on the recyclization mechanism have been investigated.

Keywords: benzimidazole, quinazoline, enantiomerization, rearrangement, dynamic ^{1}H NMR.

It is known that azomethines of type **1**, formed on interacting 2-(*o*-aminophenyl)benzimidazole with aromatic aldehydes, are spontaneously cyclized into chiral imidazoquinazolines of type **2** [1].



If the energy barrier of intramolecular conversion (such as *R*-**2** ⇄ *S*-**2**) falls into the time scale of ^{1}H NMR ($\Delta G^{\neq}_{298}$ 30-125 kJ/mol) and is accompanied by a change in configuration of the chiral center, then it is possible to determine it without a prior separation of the *R*- and *S*-enantiomers. For this, it is necessary to introduce a diastereotopic label, such as a benzyl or isopropyl group, into the near environment of the stereogenic center and to follow the evolution of its signal in temperature-dependent NMR spectra. Similar methods of studying stereoconversions, proceeding through dissociation–recombination of bonds formed by the stereogenic center, have been successfully used for carbon and other elements [2, 3]. However, the introduction of a diastereotopic label is synthetically difficult and/or affects the kinetics and mechanism of the intramolecular reaction being studied.

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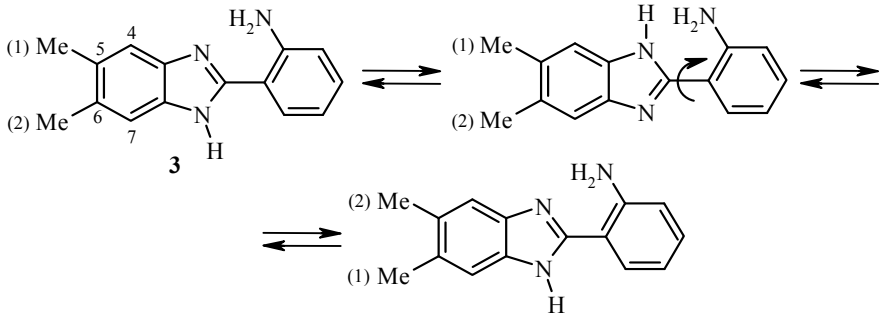
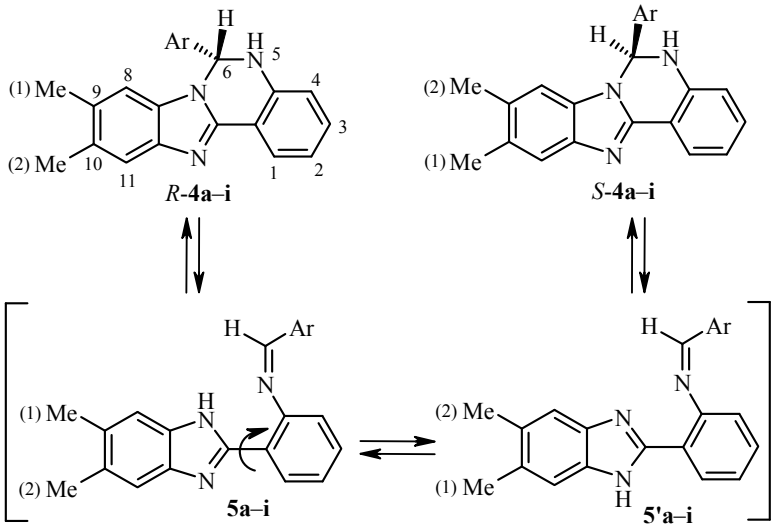
The aim of our work was the investigation of the kinetic stability and the mechanism of cleavage–formation of the C–N bond in the quinazoline ring by using a benzimidazole fragment as indicator group. On interacting 2-(2-aminophenyl)-5,6-dimethylbenzimidazole (**3**), synthesized by us, with aldehydes the 9,10-dimethyl substituted analogs of quinazolines of type **2** are formed. We introduced two indicator methyl groups, in order to simplify the appearance of the benzimidazole fragment signals and to facilitate analysis of the dynamic NMR spectra. It is necessary to emphasize that in the ^{1}H NMR spectrum of the starting benzimidazole **3**, the H-4 and H-7 proton signals are displayed as a two-proton singlet, while the methyl group signals appear as a six-proton singlet [3].



The methyl groups (and also the H-4 and H-7 protons) undergo rapid positional exchange, caused by N-1 ⇄ N-3 transfer of a proton and rotation around the benzimidazolyl–phenyl bond. In the ^{1}H NMR spectra of the obtained dimethylimidazoquinazolines **4a-i**, the signals of the methyl groups at room temperature are anisochronous and are displayed as two three-proton singlets in the 2.1-2.3 ppm region. On heating solutions of compounds **4a-i** in deuterated nitrobenzene, positional exchange of the methyl groups was observed in a series of cases, reflecting the thermally induced reversible recyclization of the pyrimidine ring. The signals of the methyl groups were broadened, then coalesced and were transformed into a broad six-proton singlet, narrowing on further increasing of the ampoule temperature in the NMR spectrometer. Cleavage of the quinazoline ring C–N bond was accompanied by a rotation of the benzimidazole fragment in the "open" intermediate state of type **5** and by *R* ⇄ *S* inversion of the chiral spiro carbon configuration. The kinetic and activation parameters of these rearrangements are given in Table 1.



a Ar = Ph, **b** Ar = 4-$Me_2NC_6H_4$, **c** Ar = 4-$MeOC_6H_4$, **d** Ar = 3,4-$(MeO)_2C_6H_3$,
e Ar = 3,4,5-$(MeO)_3C_6H_2$, **f** Ar = 4-ClC_6H_4, **g** Ar = 4-$O_2NC_6H_4$, **h** Ar = 2-furyl, **i** Ar = 2-thienyl

TABLE 1. Kinetic and Activation Parameters of the *R* ⇄ *S* Rearrangement of 5,6-Dihydrobenzoimidazo[1,2-*c*]quinazolines **4a-i**

Compound	Ar	$\Delta G^{\neq}_{298}$, kJ/mol	$\Delta H^{\neq}$, kJ/mol	$\Delta S^{\neq}$, J/mol·K	k_{298}, sec^{-1}
4a	Ph	>125	—	—	$<1\cdot10^{-9}$
4b	4-$Me_2NC_6H_4$	78.2	48	-103	$1.1\cdot10^{-1}$
4c	4-$MeOC_6H_4$	83.3	66	-59	$1.4\cdot10^{-2}$
4d	3,4-$(MeO)_2C_6H_3$	77.8	55	-77	$1.4\cdot10^{-1}$
4e	3,4,5-$(MeO)_3C_6H_2$	>125	—	—	$<1\cdot10^{-9}$
4f	4-ClC_6H_4	>125	—	—	$<1\cdot10^{-9}$
4g	4-$O_2NC_6H_4$	>125	—	—	$<1\cdot10^{-9}$
4h	2-Furyl	80.3	43	-125	$5.2\cdot10^{-2}$
4i	2-Thienyl	>125	—	—	$<1\cdot10^{-9}$

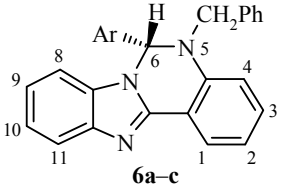
It follows from the data of Table 1, that the phenyl substituent and its derivatives containing electron-withdrawing groups (compounds **4a,f,g**) sharply increase the activation barrier, moving it beyond the limits of determination by the NMR method. The most probable explanation of such a substituent effect seems to be the following. The rate of the *R*-**4** ⇄ *S*-**4** rearrangement is determined by the stability of the intermediate of type **5**. Electron-donating substituents reduce the electron deficit on the azomethine carbon atom and stabilize the open structure **5**, but electron-withdrawing substituents destabilize it.

The activation barrier is significantly reduced for derivatives of π-electron-rich aldehydes (compounds **4b-d,h**). The greatest effect is shown by the dimethylamino group and two methoxy groups. It should be noted that the introduction of a third methoxy group (compound **4e**) already sharply increases $\Delta G^{\neq}$. This is linked to the fact that as a result of steric crowding, the lone pair of the *p*-methoxy group oxygen atom is not effectively conjugated with the π-system of the benzene ring and the C=N bond, and the electron-withdrawing inductive effect of the three methoxy groups thus predominates.

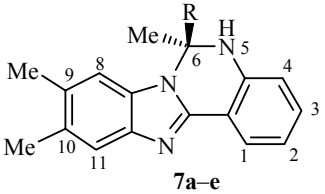
It is known, that by their ability of stabilizing electron-deficient centers, heteroatoms are arranged in the sequence –NH– > –O– > –Te– ≈ –Se- > –S– [4]. This explains the higher kinetic mobility of the furan derivative **4h** in comparison with the thiophene derivative **4i**.

The recyclization *R*-**4** ⇄ *S*-**4** is apparently accompanied by proton transfer from the amino group to the benzimidazole group and the formation of intermediate structures of type **5**, and is not simply a case of a reversible heterolysis of the C–N bond. To verify this hypothesis we synthesized *N*-alkylated quinazolines of type **6**. The introduction of a diastereotopic benzyl group into the near environment of the chiral center allows, apart from clarifying the role of the N–H fragment, the use of an additional indicator group for studying the stereodynamics in quinazolines of type **6**. However imidazoquinazolines **6a-c**, even containing electron-donating substituents, unlike those type **4** compounds lacking an *N*-alkyl group, were not recyclized upon heating in deuterated nitrobenzene solutions up to 180°C ($\Delta G^{\neq}_{298}$ > 125 kJ/mol). The signals of the H-8,11 and H-9,10 protons of the benzimidazole moiety remained anisochronous and were not broadened, but the methylene group signal was retained as an AB quartet.

In difference from *N*-alkylation sharply increasing the activation barrier of recyclization, *C*-alkylation of the chiral center predictably reduces the activation barrier as a result of the electron-donating effect of the methyl group (compounds **4c** and **7b**, Tables 1 and 2).



6a–c



7a–e

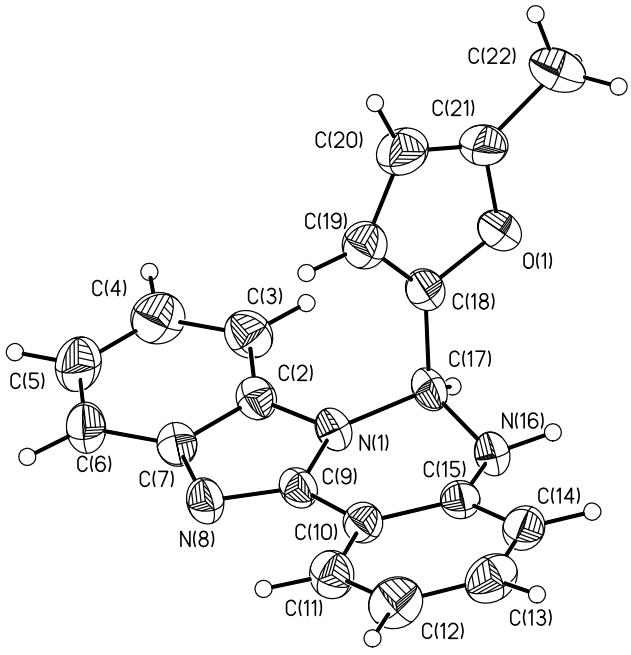
6 a Ar = 4-$MeOC_6H_4$, **b** Ar = 4-$Me_2NC_6H_4$, **c** Ar = 2-furyl;
7 a R = Ph, **b** R = 4-$MeOC_6H_4$, **c** R = Me, **d** R = Et, **e** R = Pr

TABLE 2. Kinetics and Activation Parameters of the Rearrangements of 5,6-Dihydrobenzoimidazo[1,2-*c*]quinazolines **7a-e**

Compound	R	$\Delta G^{\neq}_{298}$, kJ/mol	$\Delta H^{\neq}$, kJ/mol	$\Delta S^{\neq}$, J/mol·K	k_{298}, sec^{-1}
7a	Ph	>125	—	—	$<1\cdot10^{-9}$
7b	4-$MeOC_6H_4$	78.2	72	-22	$1.2\cdot10^{-1}$
7c	Me	117.5	153	119	$1.5\cdot10^{-8}$
7d	Et	93.3	77	-53	$2.7\cdot10^{-4}$
7e	Pr	87.4	64	-78	$2.6\cdot10^{-3}$

In the series of derivatives **7c-e** synthesized from benzimidazole **3** and the corresponding ketones, the activation barrier of thermally induced recyclization is also progressively reduced (Table 2).

Introduction of methyl groups into the benzimidazole fragment simplified spectral investigation of compounds of types **4** and **7**, but hindered the preparation of monocrystals suitable for investigation by X-ray structural analysis. We successfully grew a monocrystal of the unmethylated benzimidazole derivative – quinazoline **8**. According to the data of X-ray structural analysis (Fig. 1) molecules of compound **8** were packed in the crystal as racemate (space group *P*) due to an intermolecular hydrogen bond N(16)–H···N-8 between the *R*- and *S*-enantiomers.



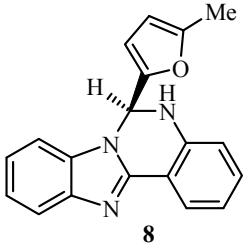


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Fig. 1. Molecular structure of the quinazoline **8** with atoms represented by thermal vibrations ellipsoids with 50% probability.

In conclusion, it is necessary to mention that the new approach proposed by us using a benzimidazole fragment as an indicator label enables processes of bond cleavage–formation to be investigated even for achiral structures, for which known approaches using a diastereotopic label are not applicable in principle. Thus, the kinetic stability of any interaction (covalent, coordination, hydrogen bonding), affecting azole or azine nitrogen atoms in a benzimidazole fragment and inhibiting free rotation as a result, may be investigated.

TABLE 3. Physicochemical Characteristics of the Synthesized Compounds **4a-i, 6a-c, 7a-e** and **8**

Compound	Empirical formula	Found, % / Calculated, %			Mp, °C	Yield, %
		C	H	N		
4a	$C_{22}H_{19}N_3$	81.23 / 81.20	5.97 / 5.89	12.99 / 12.91	260-262	61
4b	$C_{24}H_{24}N_4$	78.36 / 78.23	6.70 / 6.57	15.31 / 15.20	226-228	84
4c	$C_{23}H_{21}N_3O$	77.85 / 77.72	6.04 / 5.96	11.91 / 11.82	224-226	66
4d	$C_{24}H_{23}N_3O_2$	74.90 / 74.78	6.11 / 6.01	10.12 / 10.90	212-214	95
4e	$C_{25}H_{25}N_3O_3$	72.40 / 72.27	6.16 / 6.06	10.20 / 10.11	196-198	86
4f	$C_{22}H_{18}ClN_3$	73.55 / 73.43	5.16 / 5.04	11.80 / 11.68	264-266	73
4g	$C_{22}H_{18}N_4O_2$	71.47 / 71.34	5.01 / 4.90	15.22 / 15.13	314-316	96
4h	$C_{20}H_{17}N_3O$	76.30 / 76.17	5.55 / 5.43	13.45 / 13.32	220-222	63
4i	$C_{20}H_{17}N_3S$	72.62 / 72.48	5.28 / 5.17	12.80 / 12.68	238-240	62
6a	$C_{28}H_{23}N_3O$	80.71 / 80.55	5.66 / 5.55	10.17 / 10.06	162-164	85
6b	$C_{29}H_{26}N_4$	81.16 / 80.90	6.20 / 6.09	13.13 / 13.01	220-222	80
6c	$C_{25}H_{19}N_3O$	79.70 / 79.55	5.13 / 5.06	11.20 / 11.13	170-172	50
7a	$C_{23}H_{21}N_3$	81.53 / 81.39	6.45 / 6.24	12.48 / 12.38	210-212	56
7b	$C_{24}H_{23}N_3O$	78.15 / 78.02	6.37 / 6.27	11.48 / 11.37	232-234	63
7c	$C_{18}H_{19}N_3$	78.11 / 77.95	7.01 / 6.90	15.27 / 15.15	202-204	63
7d	$C_{19}H_{21}N_3$	78.48 / 78.32	7.37 / 7.26	14.52 / 14.42	218-220	49
7e	$C_{20}H_{23}N_3$	78.82 / 78.65	7.70 / 7.59	13.84 / 13.76	206-208	70
8	$C_{19}H_{15}N_3O$	75.96 / 75.73	5.28 / 5.02	13.80 / 13.94	150-152	55

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker DPX-250 (250 MHz) instrument in $CDCl_3$ (for compound **4g** in DMSO-d_6), temperature-dependent spectra were recorded in $C_6D_5NO_2$, internal standard was TMS. Computer modelling of spectra and calculation of rate constants were carried out with the aid of program gNMR 5.1 [5]. Values of the Gibbs free energy ($\Delta G^{\neq}$) were calculated according to the Arrhenius equation for each rate constant. Enthalpies ($\Delta H^{\neq}$) and entropies ($\Delta S^{\neq}$) of activation with a correlation coefficient of at least 0.98 were found by linearization using the least squares method.

Physicochemical characteristics of the synthesized compounds **4a-i, 6a-c. 7a-e** and **8** are given in Table 3, and the ^{1}H NMR spectroscopy data are in Table 4.

9,10-Dimethyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazolines 4a-i, 6-(5-Methylfuran-2-yl)-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline (8) (General Method). An aldehyde (1.27 mmol) and AcOH (0.01 ml) were added to a solution of 2-(2-aminophenyl)benzimidazole (1.27 mmol) or its 5,6-dimethyl derivative **3** [6] (1.27 mmol) in MeOH (5 ml). The reaction mixture was refluxed for 2 h and left overnight for complete precipitation of solid. The solid was filtered off, washed with cold MeOH, and air-dried at 50°C.

TABLE 4. ^{1}H NMR Spectra of the Synthesized Imidazoquinazolines **4a-i, 6a-c, 7a-e** and **8**

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)
1	2
4a	2.15 (3H, s) and 2.28 (3H, s, 9,10-CH_3); 4.94 (1H, br. s, NH); 6.30 (1H, s) and 7.50 (1H, s, H-8,11); 6.55 (1H, s, H-6); 6.66 (1H, d, *J* = 8.1, H-4); 6.91 (1H, dd, *J* = 7.3, *J* = 7.7, H-2); 7.19 (1H, dd, *J* = 7.3, *J* = 8.1, H-3); 7.27-7.43 (5H, m, H Ph); 8.15 (1H, d, *J* = 7.7, H-1)
4b	2.15 (3H, s) and 2.28 (3H, s, 9,10-CH_3); 2.93 (6H, s, $N(CH_3)_2$); 4.64 (1H, s, NH); 6.28 (1H, s) and 7.50 (1H, s, H-8,11); 6.43 (1H, s, H-6); 6.59-6.69 (3H, m, H-4,3',5'); 6.90 (1H, dd, *J* = 7.3, *J* = 7.7, H-2); 7.18 (1H, dd, *J* = 7.3, *J* = 8.0, H-3); 7.25 (2H, d, *J* = 8.7, H-2',6'); 8.16 (1H, d, *J* = 7.7, H-1)
4c	2.15 (3H, s) and 2.28 (3H, s, 9,10-CH_3); 3.76 (3H, s, OCH_3); 4.85 (1H, s, NH); 6.27 (1H, s) and 7.49 (1H, s, H-8,11); 6.48 (1H, s, H-6); 6.66 (1H, d, *J* = 8.0, H-4); 6.84 (2H, d, *J* = 8.7, H Ar); 7.30 (2H, d, *J* = 8.7, H Ar); 6.91 (1H, dd, *J* = 7.4, *J* = 7.8, H-2); 7.19 (1H, dd, *J* = 7.4, *J* = 8.0, H-3); 8.15 (1H, d, *J* = 7.8, H-1)
4d	2.13 (3H, s) and 2.28 (3H, s, 9,10-CH_3); 3.72 (3H, s) and 3.88 (3H, s, 3',4'-OCH_3); 4.66 (1H, s, NH); 6.20 (1H, s) and 7.50 (1H, s, H-8,11); 6.47 (1H, s, H-6); 6.69 (1H, d, *J* = 8.6, H-4); 6.80-7.03 (4H, m, H-2,2',5',6'); 7.22 (1H, dd, *J* = 7.6, *J* = 8.6, H-3); 8.16 (1H, d, *J* = 7.7, H-1)
4e	2.14 (3H, s) and 2.28 (3H, s, 9,10-CH_3); 3.68 (6H, s, 3',5'-OCH_3); 3.82 (3H, s, 4'-OCH_3); 5.02 (1H, s, NH); 6.22 (1H, s) and 7.49 (1H, s, H-8,11); 6.38 (1H, s, H-6); 6.61 (2H, s, H-2',6'); 6.74 (1H, d, *J* = 7.9, H-4); 6.92 (1H, dd, *J* = 7.6, *J* = 7.8, H-2); 7.22 (1H, dd, *J* = 7.6, *J* = 7.9, H-3); 8.14 (1H, d, *J* = 7.8, H-1)
4f	2.19 (3H, s) and 2.30 (3H, s, 9,10-CH_3); 4.77 (1H, s, NH); 6.39 (1H, s) and 7.51 (1H, s, H-8,11); 6.58 (1H, s, H-6); 6.69 (1H, d, *J* = 7.3, H-4); 6.94 (1H, dd, *J* = 7.6, *J* = 7.6, H-2); 7.17-7.34 (5H, m, H-3, H Ar); 8.15 (1H, d, *J* = 7.6, H-1)
4g	2.24 (3H, s) and 2.29 (3H, s, 9,10-CH_3); 6.78-6.89 (2H, m, H-2,4); 7.16 (1H, s) and 7.47 (1H, s, H-8,11); 7.18-7.29 (2H, m, H-3,6); 7.39 (2H, d, *J* = 8.7, H-2',6'); 7.73 (1H, s, NH); 7.95 (1H, d, *J* = 8.1, H-1); 8.16 (2H, d, *J* = 8.7, H-3',5')
4h	2.30 (3H, s) and 2.33 (3H, s, 9,10-CH_3); 5.23 (1H, s, NH); 6.00 (1H, d, *J* = 3.4, H-3'); 6.18 (1H, dd, *J* = 1.8, *J* = 3.2, H-4'); 6.68 (1H, d, *J* = 1.8, H-6); 6.74 (1H, d, *J* = 8.3, H-4); 6.80 (1H, s) and 7.52 (1H, s, H-8,11); 6.92 (1H, dd, *J* = 7.6, *J* = 7.9, H-2); 7.20 (1H, dd, *J* = 7.6, *J* = 8.3, H-3); 7.28 (1H, d, *J* = 1.8, H-5'); 8.11 (1H, d, *J* = 7.9, H-1)
4i	2.25 (3H, s) and 2.31 (3H, s, 9,10-CH_3); 4.99 (1H, s, NH); 6.62 (1H, s) and 7.50 (1H, s, H-8,11); 6.74 (1H, d, *J* = 8.3, H-4); 6.86-6.92 (2H, m, H-6,4'); 6.95 (1H, dd, *J* = 7.3, *J* = 7.6, H-2); 7.04 (1H, d, *J* = 3.4, H-3'); 7.18-7.28 (2H, m, H-3,5'); 8.14 (1H, d, *J* = 7.6, H-1)
6a	3.68 (3H, s, OCH_3); 4.28 (1H, d, *J* = 15.6) and 4.64 (1H, d, *J* = 15.6, CH_2); 6.51 (1H, s, H-6); 6.71 (2H, d, *J* = 8.5, H-3',5'); 6.80 (1H, d, *J* = 8.5, H-4); 6.91-7.44 (12H, m, H Ar); 7.80 (1H, d, *J* = 8.1, H-11); 8.31 (1H, d, *J* = 7.7, H-1)
6b	2.84 (6H, s, $N(CH_3)_2$); 4.28 (1H, d, *J* = 16.0) and 4.64 (1H, d, *J* = 16.0, CH_2); 6.45-6.54 (3H, m, H-6,3',5'); 6.75 (1H, d, *J* = 8.4, H-4); 6.92-7.38 (12H, m, H Ar); 7.78 (1H, d, *J* = 8.1, H-11); 8.30 (1H, d, *J* = 7.7, H-1)
6c	4.46 (1H, d, *J* = 15.4) and 4.80 (1H, d, *J* = 15.4, CH_2); 5.89 (1H, d, *J* = 3.7, H-3'); 6.13 (1H, dd, *J* = 1.8, *J* = 3.7, H-4'); 6.59 (1H, s, H-6); 6.86 (1H, d, *J* = 8.4, H-4); 7.02 (1H, dd, *J* = 7.3, *J* = 7.7, H-2); 7.14-7.40 (10H, m, H Ar); 7.81 (1H, d, *J* = 8.1, H-11); 8.27 (1H, d, *J* = 7.7, H-1)
7a	2.10 (3H, s), 2.12 (3H, s) and 2.28 (3H, s, 6,9,10-CH_3); 4.64 (1H, s, NH); 6.11 (1H, s) and 7.50 (1H, s, H-8,11); 6.67 (1H, d, *J* = 8.1, H-4); 6.91 (1H, dd, *J* = 7.3, *J* = 7.7, H-2); 7.21 (1H, dd, *J* = 7.3, *J* = 8.1, H-3); 7.33-7.44 (3H, m, H-3',4',5'); 7.54-7.66 (2H, m, H-2',6'); 8.16 (1H, d, *J* = 7.7, H-1)
7b	2.06 (3H, s, 6-CH_3); 2.12 (3H, s) and 2.26 (3H, s, 9,10-CH_3); 3.80 (3H, s, OCH_3); 4.63 (1H, s, NH); 6.12 (1H, s) and 7.49 (1H, s, H-8,11); 6.67 (1H, d, *J* = 8.1, H-4); 6.83-6.94 (3H, m, H-2,3',5'); 7.20 (1H, dd, *J* = 7.7, *J* = 8.1, H-3); 7.55 (2H, d, *J* = 8.5, H-2',6'); 8.15 (1H, d, *J* = 7.7, H-1)
7c	1.88 (6H, s, 6-$C(CH_3)_2$); 2.35 (3H, s) and 2.38 (3H, s, 9,10-CH_3); 4.60 (1H, s, NH); 6.71 (1H, d, *J* = 8.1, H-4); 6.89 (1H, dd, *J* = 7.3, *J* = 7.7, H-2); 7.20 (1H, dd, *J* = 7.3, *J* = 8.1, H-3); 7.30 (1H, s) and 7.56 (1H, s, H-8,11); 8.13 (1H, d, *J* = 7.7, H-1)

TABLE 4 (continued)

1	2
7d	0.93 (3H, t, *J* = 7.3, $CH_2C\underline{H}_3$); 1.89 (3H, s, 6-CH_3); 2.28-2.52 (8H, m, $C\underline{H}_2CH_3$, 9,10-CH_3); 4.24 (1H, s, NH); 6.67 (1H, d, *J* = 8.1, H-4); 6.83 (1H, dd, *J* = 7.3, *J* = 7.7, H-2); 7.18 (1H, dd, *J* = 7.3, *J* = 8.1, H-3); 7.24 (1H, s) and 7.54 (1H, s, H-8,11); 8.09 (1H, d, *J* = 7.7, H-1)
7e	0.82 (3H, t, *J* = 7.3, $CH_2CH_2C\underline{H}_3$); 1.13-1.37 (1H, m) and 1.39-1.63 (1H, m, $CH_2C\underline{H}_2CH_3$); 1.74-1.96 (4H, m, 6-CH_3, $C\underline{H}_2CH_2CH_3$); 2.23-2.51 (7H, m, 9,10-CH_3, $C\underline{H}_2CH_2CH_3$); 4.40 (1H, s, NH); 6.67 (1H, d, *J* = 8.1, H-4); 6.84 (1H, dd, *J* = 7.3, *J* = 7.7, H-2); 7.18 (1H, dd, *J* = 7.3, *J* = 8.1, H-3); 7.23 (1H, s) and 7.54 (1H, s, H-8,11); 8.09 (1H, d, *J* = 7.7, H-1)
8	2.13 (3H, s, CH_3); 5.13 (1H, s, NH); 5.70 (1H, d, *J* = 3.4, H-4'); 5.76 (1H, d, *J* = 3.4, H-3'); 6.54 (1H, s, H-6); 6.83 (1H, d, *J* = 8.4, H-4); 6.98 (1H, dd, *J* = 7.4, *J* = 7.6, H-2); 7.14-7.38 (4H, m, H Ar); 7.80 (1H, d, *J* = 7.6, H-11); 8.25 (1H, d, *J* = 7.6, H-1)

TABLE 5. Basic Bond Lengths (l) in the Molecule of Imidazoquinazoline **8**

Bond	*l*, Å	Bond	*l*, Å
O(1)–C(18)	1.3688(14)	C(10)–C(11)	1.3977(18)
O(1)–(21)	1.3806(16)	C(10)–C(15)	1.4079(16)
N(1)–C(9)	1.3716(15)	C(11)–C(12)	1.381(2)
N(1)–C(2)	1.3878(16)	C(12)–C(13)	1.388(2)
N(1)–C(17)	1.4549(14)	C(13)–C(14)	1.377(2)
C(2)–C(3)	1.3851(19)	C(14)–C(15)	1.4000(18)
C(2)–C(7)	1.4017(17)	C(15)–N(16)	1.3862(16)
C(3)–C(4)	1.381(2)	N(16)–C(17)	1.4536(16)
C(4)–C(5)	1.395(2)	C(17)–C(18)	1.5030(17)
C(6)–C(7)	1.3929(18)	C(18)–C(19)	1.3347(18)
C(7)–N(8)	1.3982(16)	C(19)–C(20)	1.425(2)
N(8)–C(9)	1.3208(15)	C(20)–C(21)	1.339(2)
C(9)–C(10)	1.4451(17)	C(21)–C(22)	1.485(2)

TABLE 6. Basic Valence Angles (ω) in the Molecule of Imidazoquinazoline **8**

Bond	ω, deg.	Bond	ω, deg.
C(18)–O(1)–C(21)	106.34(10)	N(8)–C(9)–C(10)	128.46(11)
C(9)–N(1)–C(2)	107.16(10)	N(1)–C(9)–C(10)	118.69(10)
C(9)–N(1)–C(17)	124.50(10)	C(11)–C(10)–C(15)	120.14(12)
C(2)–N(1)–C(17)	126.52(10)	C(11)–C(10)–C(9)	122.52(11)
C(3)–C(2)–N(1)	132.39(12)	C(15)–C(10)–C(9)	117.30(11)
C(3)–C(2)–C(7)	122.62(12)	C(12)–C(11)–C(10)	120.44(13)
N(1)–C(2)–C(7)	104.96(11)	C(11)–C(12)–C(13)	119.22(14)
C(4)–C(3)–C(2)	116.50(13)	C(14)–C(13)–C(12)	121.39(14)
C(3)–C(4)–C(5)	121.53(15)	C(13)–C(14)–C(15)	120.23(13)
C(6)–C(5)–C(4)	121.91(14)	N(16)–(15)–C(14)	121.25(11)
C(5)–C(6)–C(7)	117.40(13)	N(16)–C(15)–C(10)	120.11(11)
C(6)–C(7)–N(8)	129.77(12)	C(14)–C(15)–C(10)	118.56(12)
C(6)–C(7)–C(2)	120.04(12)	C(15)–N(16)–C(17)	120.15(10)
N(8)–C(7)–C(2)	110.16(10)	N(16)–C(17)–N(1)	108.44(10)
C(9)–N(8)–C(7)	104.86(10)	N(16)–C(17)–C(18)	114.10(10)
N(8)–C(9)–N(1)	112.76(11)	N(1)–C(17)–C(18)	108.50(10)

5,6-Dihydrobenzoimidazo[1,2-*c*]quinazolines 6a-c, 7a,b,d,e (General Method). A solution of the corresponding 2-(2-aminophenyl)benzimidazole (4.2 mmol) or its *N*-benzyl derivative [6] (4.2 mmol), carbonyl compound (8.4 mmol) and *p*-toluenesulfonic acid (5 mg) in butanol (5 ml) was refluxed for 21 h. The solid was filtered off, washed first with a butanol–petroleum ether 1:2 mixture (5 ml), then with petroleum ether (10 ml), and air-dried at 80°C.

6,6,9,10-Tetramethyl-5,6-dihydrobenzoimidazo[1,2-*c*]quinazoline (7c). 2-(2-Aminophenyl)-5,6-dimethylbenzimidazole (1 g, 4.2 mmol) was dissolved with heating in acetone (10 ml). AcOH (0.1 ml) was added to the obtained solution, and the mixture was refluxed for 14 h. The precipitated solid was filtered off and washed with acetone (5 ml).

X-Ray Structural Investigation of Compound 8. Monocrystals of quinazoline **8** were obtained from methyl alcohol. The crystals of compound **8** ($C_{19}H_{15}N_3O_3$, *M* 301.34) were monoclinic, space group *P* at 293 K: *a* 8.9393(18), *b* 12.798(3), *c* 13.361(3) Å; β 92.90(3)°; *V* 1526.6(5) Å^3; *Z* 4 (*Z*' 1; d_{calc} 1.311 g/cm^3; μ(MoKα) 3.57 cm^{-1}; *F*(000) 632. The intensities of 5613 reflections (λ(MoKα) 0.71073 Å, ω scanning, 2θ < 58°) and 5327 independent reflections (R_{int} 0.0424) were determined on a Bruker SMART 1000 CCD diffractometer and used in the subsequent refinement. The structure was solved by the direct method and refined by least squares in an anisotropic-isotropic full-matrix approximation on F^2. The positions of hydrogen atoms were calculated geometrically and refined in an isotropic approximation according to the "rider" model. Final values of the probability factors for compound **8** were wR_2 0.1030 and *GOOF* 1.012 for all independent reflections (R_1 0.1405 calculated on *F* for 2620 fixed reflections with $I > 2\sigma(I)$. All calculations were carried out with the SHELXTL PLUS 5.0 set of programs [7].

The basic geometric parameters of a monocrystal of **8** are given in Tables 5, 6.

The data of the X-ray structural analysis of quinazoline **8** have been deposited in the Cambridge Crystallographic Data Center (CCDC 846361).

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