IMIDAZOQUINAZOLINODIONES - NEW RESULTS

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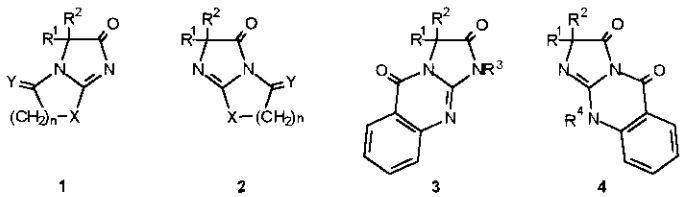
Abstract- X-Ray crystal structure determinations and spectral analyses (NMR, MS) shed new light on the reaction of 5-(*Z*)-arylidene-2-methylthioimidazolin-4-one (**5b**) with anthranilic acid, in which apart from the expected 2-(*Z*)-1-arylidene-2,3,5,10-tetrahydroimidazo[2,1-*b*]quinazoline-3,5-dione (**6b**) a new condensed heterocyclic system was identified, i.e. 2-(*Z*)-arylidene-1,2,4,5-tetrahydroimidazo [1,2-*a*]quinazoline-1,5-dione (**8b**). Reaction of the sodium salt of the 4-chloro-substituted arylidene derivative (**6a**) with methyl iodide surprisingly afforded 2- [(*Z*)-1-(4-chlorophenyl)methylene] - 3-methyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]-quinazoline-1,5-dione (**15**).

As a part of our studies on searching for compounds with anticonvulsant properties the known antiepileptic drug phenytoin [1] (5,5-diphenylhydantoin) was modified. Thus, bicyclic and tricyclic derivatives of 5,5-diphenyl-[2-4] and 5-arylidene-2-thiohydantoins[5-7] with general structures (**1** – **4**) were obtained (Scheme 1). Recently,[8] the possible mechanism of interaction of these hydantoins with the benzodiazepine binding site of the $GABA_A$ receptor has attracted our attention. In this context the annelated structures (**4**), derivatives of 5-arylidene-2-thiohydantoin, seemed the most interesting.

The synthesis of such compounds was already described by one of us.[7] Thus (Scheme 2), *S*-methylated derivatives of 5-arylidene-2-thiohydantoins (**5a**, **5b**) reacted with anthranilic acid (ANTA) to give the tricyclic structures of type (**4**). However, differences in the reaction behavior of **5a** and **5b** were observed. In the reaction of **5a** only one product (**6a**) was separated while in the case of **5b** two products were

obtained. Based on elemental analysis and ^{1}H-NMR and MS spectroscopy these products were assigned as the *Z* and *E* diastereomers (**6b** and **7b**).[7]

Scheme 1

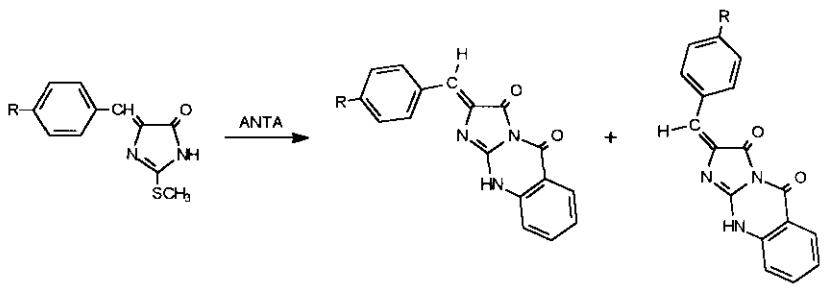


1 2 3 4

X = S, NH ; Y = H_2, O ; n = 1-3

R^1, R^2 = Ph, ArCH=

Scheme 2



5a: R = Cl
5b: R = H

6a: R = Cl
6b: R = H

7b: R = H

At that time despite repeated efforts an X-Ray crystal structure analysis was not feasible. With the recent availability of advanced X-Ray diffraction equipment, the successful crystal structure determination of the reaction products of **5b** with ANTA permitted a revision of the results towards structures (**6b**), and, instead of **7b**, towards **8b** (Scheme 4).

RESULTS AND DISCUSSION

Crystal Structures of 2-[(*Z*)-1-phenylmethylene]-2,3,5,10-tetrahydroimidazo[2,1-*b*]quinazoline-3,5-dione (6b) and 2-[(*Z*)-1-phenylmethylene]-1,2,4,5-tetrahydroimidazo[1,2-*a*]quinazoline-1,5-dione (8b)

The crystal structures of the two compounds were clarified by X-Ray single crystal methods in order to obtain a safe base for their constitution and stereochemistry. Both compounds were recrystallized from dimethyl sulfoxide (DMSO) yielding the corresponding crystalline solvates. While crystals of **6b·dmso** were suitable for X-Ray work, those of **8b·dmso** were soft and rather labile.[9] Therefore **8b** was recrystallized from dimethylformamide (DME) and yielded stable yellow prisms of **8b·dmf** which were subsequently studied by X-Ray diffraction. X-Ray structure analysis allowed to confirm the expected structure of **6b** and allowed to ascribe the proper structure of the second compound as **8b**. Technical details on the crystal structure determinations are described in the experimental section. Views of the molecules including the solvents as encounterd in the

crystalline state are shown in Figures 1 and 2. Salient atomic parameters are given in Tables 1 and 2, selected bond lengths and bond angles are compiled in Table 3.

Figure 1. Thermal ellipsoid plot (20% ellipsoids) of $C_{17}H_{11}N_3O_2 \cdot (CH_3)_2SO$ (**6b·dmso**).

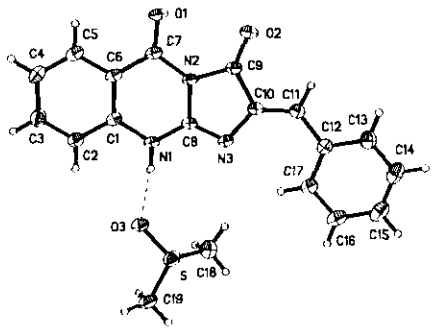
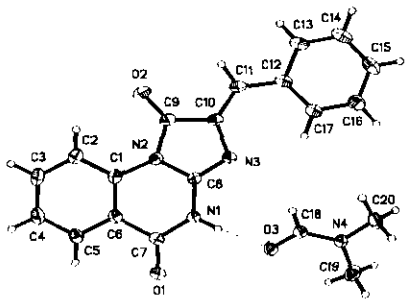


Figure 2. Thermal ellipsoid plots (20% ellipsoids) of $C_{17}H_{11}N_3O_2 \cdot HCON(CH_3)_2$ (**8b·dmf**).



The benzylideneimidazoquinazolinedione moieties of the two compounds are flat and show only r.m.s. deviations from common planes of 0.094 Å for **6b** (0.036 Å without benzylidene moiety), and 0.045 Å for **8b**. Thus, the nitrogen atoms are in sp^2-hybridized. The bond lengths in both compounds are consistent with the chemical structure diagrams (Figure 3, Scheme 4). The heterocyclic rings show some resonance effects in their C-C and C-N bond lengths, but the C(8)-N(3) bonds are in both compounds consistently the shortest ring bonds. This situation differs distinctly from the related *Z*-1-ethyl-3-(4-chloro-benzylidene)-1,2,3,5-tetrahydroimidazo[2,1-*b*]quinazoline-2,5-dione compound of type (**3**) [10] (Scheme 1) which contains a formal C-N double bond corresponding to C(8)-N(1) of **6b**.

Both **6b·dmso** and **8b·dmf** show clearcut and straight N-H...O hydrogen bonds from the imidazoquinazoline nitrogen N(1) to the solvent oxygen atoms. Both hydrogen bonds are astonishingly similar in size (Table 3) and can be regarded to contribute much to the good stability of the two solvate structures. However, the spatial arrangement of the constituents of the two compounds differs distinctly from one another: **6b·dmso** exhibits parallel to (100) a pronounced sheet-like arrangement of its constituents, whereas **8b·dmf** may be visualized as showing a herringbone-like spatial arrangement of the constituents.

Table 1. Atomic coordinates and equivalent isotropic displacement parameters of non-hydrogen atoms for $C_{17}H_{11}N_3O_2 \cdot (CH_3)_2SO$ (**6b**·**dmso**).

	x/a	y/b	z/c	U_{eq} [x 10^3 Å^2]
O(1)	0.3263(3)	0.7497(2)	0.4517(1)	68(1)
O(2)	0.2486(3)	0.9642(2)	0.3921(1)	69(1)
N(1)	0.2944(3)	0.6393(2)	0.2752(1)	44(1)
N(2)	0.2861(3)	0.7847(2)	0.3489(1)	43(1)
N(3)	0.2418(3)	0.8295(2)	0.2473(1)	45(1)
C(1)	0.3181(3)	0.5594(2)	0.3216(1)	42(1)
C(2)	0.3332(4)	0.4453(2)	0.3069(1)	53(1)
C(3)	0.3570(4)	0.3668(2)	0.3528(1)	64(1)
C(4)	0.3651(3)	0.3989(2)	0.4140(1)	65(1)
C(5)	0.3497(3)	0.5111(2)	0.4287(1)	55(1)
C(6)	0.3277(3)	0.5929(2)	0.3831(1)	44(1)
C(7)	0.3140(3)	0.7126(2)	0.3999(1)	47(1)
C(8)	0.2734(3)	0.7497(2)	0.2873(1)	40(1)
C(9)	0.2543(4)	0.9034(2)	0.3478(1)	49(1)
C(10)	0.2300(3)	0.9295(2)	0.2813(1)	46(1)
C(11)	0.2069(4)	1.0369(2)	0.2623(1)	51(1)
C(12)	0.1918(3)	1.0830(2)	0.2006(1)	49(1)
C(13)	0.2000(4)	1.2005(2)	0.1937(1)	63(1)
C(14)	0.1932(4)	1.2504(3)	0.1375(2)	77(1)
C(15)	0.1729(4)	1.1843(3)	0.0857(2)	76(1)
C(16)	0.1615(4)	1.0675(3)	0.0908(1)	68(1)
C(17)	0.1719(4)	1.0170(2)	0.1481(1)	55(1)
S	0.31434(12)	0.61025(6)	0.10103(3)	66(1)
O(3)	0.2855(4)	0.5481(2)	0.1600(1)	83(1)
C(18)	0.1003(6)	0.6934(3)	0.0873(2)	94(1)
C(19)	0.2663(5)	0.5092(3)	0.0426(1)	72(1)

Table 2. Atomic coordinates and equivalent isotropic displacement parameters of non-hydrogen atoms for $C_{17}H_{11}N_3O_2 \cdot HCON(CH_3)_2$ (**8b**·**dmf**).

	x/a	y/b	z/c	U_{eq} [x 10^3 Å^2]
O(1)	0.2396(2)	0.44935(7)	0.46245(9)	68(1)
O(2)	0.1266(2)	0.61531(7)	0.15868(10)	83(1)
N(1)	0.0133(2)	0.45177(7)	0.37416(9)	49(1)
N(2)	0.0344(2)	0.54791(7)	0.27544(9)	51(1)
N(3)	0.2700(2)	0.45495(7)	0.27800(9)	50(1)
C(1)	-0.1395(3)	0.58435(9)	0.30295(12)	52(1)
C(2)	-0.2132(3)	0.65047(10)	0.26767(14)	67(1)
C(3)	-0.3875(4)	0.68139(11)	0.29636(15)	77(1)
C(4)	-0.4891(3)	0.64837(11)	0.35863(15)	74(1)
C(5)	-0.4140(3)	0.58369(10)	0.39500(12)	63(1)
C(6)	-0.2380(3)	0.55110(9)	0.36764(11)	51(1)
C(7)	-0.1591(3)	0.48101(9)	0.40623(12)	51(1)
C(8)	0.1104(3)	0.48232(8)	0.31084(11)	45(1)
C(9)	0.1527(3)	0.56369(10)	0.20806(12)	58(1)
C(10)	0.3077(3)	0.50327(9)	0.21240(11)	52(1)
C(11)	0.4547(3)	0.49992(10)	0.15805(12)	57(1)
C(12)	0.6200(3)	0.44615(10)	0.15214(12)	57(1)
C(13)	0.7558(3)	0.45551(12)	0.08894(13)	70(1)
C(14)	0.9153(4)	0.40682(14)	0.08036(15)	83(1)
C(15)	0.9455(3)	0.34816(14)	0.13585(16)	81(1)
C(16)	0.8148(3)	0.33778(12)	0.19827(14)	72(1)
C(17)	0.6533(3)	0.38594(10)	0.20613(13)	64(1)
O(3)	0.1598(2)	0.31604(7)	0.41876(10)	74(1)
N(4)	0.4752(2)	0.25804(7)	0.44157(10)	55(1)
C(18)	0.3528(3)	0.31356(9)	0.41802(12)	56(1)
C(19)	0.3865(3)	0.19310(11)	0.47469(15)	82(1)
C(20)	0.7035(3)	0.26169(11)	0.44041(16)	77(1)

Reaction of 5 with ANTA

In order to explain the formation of quinazolinodione (**8b**) the reaction of **5a** and **5b** with a stoichiometric amount of ANTA was repeated. Additionally, similar reactions were carried out with substrates (**5**) containing *para*- dimethylamino-, methoxy- and nitro-substituents (**5c**, **5d** and **5e**, respectively). After refluxing the adducts in acetic acid for 4-5 h the separated solids were once recrystallized from DMF (**5a** - **5c**, **5e**) or acetic acid (**5d**). Based on ^{1}H-NMR spectra it was concluded that the course of the reactions

was different. Linear products (**6**) were obtained in predominance starting with **5a** and **5e**. In case of **5e** a shorter reaction time (5 h instead of 10 h) probably led to an intermediate and not to the cyclic acid structure. The prolonged time of the reaction (10 h) only, allowed to obtain the cyclic products (**6e** and **8e**) (3:1). In the case of unsubstituted **5b** - or its equivalents substituted with electron-donating groups (**5c** and **5d**) - both types of products were obtained in almost equal proportions. Table 4 presents a summary of the reaction times and product ratios obtained.

Table 3. Selected bond lengths [Å] and angles [°] for $C_{17}H_{11}N_3O_2{\cdot}(CH_3)_2SO$ **(6b·dmso)** and $C_{17}H_{11}N_3O_2{\cdot}HCON(CH_3)_2$ **(8b·dmf)**

	(6b.dmso)	**(8b.dmf)**
O(1)-C(7)	1.213(3)	1.218(2)
O(2)-C(9)	1.208(3)	1.218(2)
N(1)-C(1)	1.389(3)	
N(1)-C(7)		1.375(2)
N(1)-C(8)	1.342(3)	1.351(2)
N(2)-C(7)	1.408(3)	
N(2)-C(1)		1.410(2)
N(2)-C(8)	1.408(3)	1.389(2)
N(2)-C(9)	1.421(3)	1.397(2)
N(3)-C(8)	1.298(3)	1.299(2)
N(3)-C(10)	1.403(3)	1.396(2)
C(1)-C(6)	1.400(3)	1.394(2)
C(6)-C(7)	1.467(3)	1.484(2)
C(9)-C(10)	1.487(3)	1.484(2)
C(10)-C(11)	1.344(3)	1.342(2)
C(11)-C(12)	1.452(3)	1.459(3)
C-C phenyl	1.385(3)	1.383(2)
C(1)-N(1)-C(8)	121.8(2)	
C(7)-N(1)-C(8)		124.3(2)
C(7)-N(2)-C(8)	125.2(2)	
C(1)-N(2)-C(8)		122.9(2)
C(7)-N(2)-C(9)	128.8(2)	
C(1)-N(2)-C(8)		130.6(2)
C(8)-N(2)-C(9)	105.9(2)	106.4(2)
C(8)-N(3)-C(10)	105.6(2)	104.9(2)
N(2)-C(7)-C(6)	113.3(2)	116.1(2)
N(1)-C(8)-N(2)	118.3(2)	118.8(2)
N(1)-C(8)-N(3)	126.2(2)	125.5(2)
N(2)-C(8)-N(3)	115.5(2)	115.7(2)
N(2)-C(9)-C(10)	103.3(2)	103.4(2)
N(3)-C(10)-C(9)	109.7(2)	109.5(2)
N(3)-C(10)-C(11)	129.9(2)	129.0(2)
C(9)-C(10)-C(11)	120.3(2)	121.5(2)
C(10)-C(11)-C(12)	130.1(2)	129.9(2)

Hydrogen bonds					
	D - H ... A	d(D-H)	d(H..A)	<DHA	d(D...A)
(6b·dmso)	N(1)-H(1)...O(3)	0.86(2)	1.89(2)	172(1)	2.738(2)
(8b·dmf)	N(1)-H(1)...O(3)	0.86(3)	1.89(3)	168(1)	2.732(2)

In order to explain the formation of **6** and **8** two possible reaction mechanisms were considered. They are based on the observation described in the literature[11-13] that the generation of unexpected products in the reaction of hydantoins with compounds containing amino groups could result from the amino group attack on the CO group of the hydantoin ring, its opening and recyclization, as shown below (Scheme 3).

Scheme 3

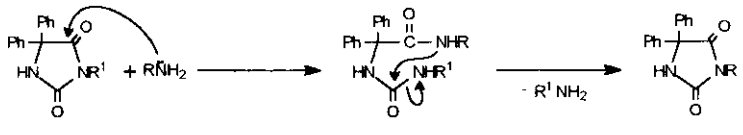
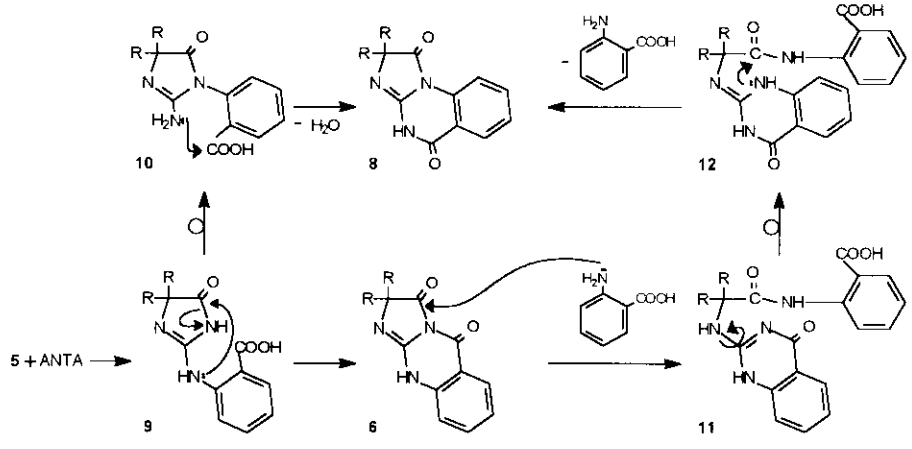


Table 4

		1 x ANTA		2 x ANTA	
Substrate No	R	Time [h]	Products **6 : 8**	Time [h]	Products **6 : 8**
5a	Cl	4	1 : 0	7	98 : 6
5b	H	5	1 : 1		
5c	$N(CH_3)_2$	4	1.2 :1		
5d	OCH_3	4	1 : 1	7	19 : 100
5e	NO_2	10	3 : 1	12	0 : 1

Thus (Scheme 4), formation of **6** is clear through intermediate (**9**). Formation of **8** could proceed *via* **9** and the nucleophilic attack of the amino group of ANTA on the carbonyl group, which proceeds intramolecular, leading to the rearrangement product (**10**) and subsequent cyclization giving product (**8**). The alternative route of the reaction begins with nucleophilic attack of the second ANTA molecule on **6**, followed by ring opening [**11**], rearrangement to intermediate (**12**) and elimination of ANTA with formation of **8**. For the second reaction pathway speaks the fact that products (**8d**) and (**8e**) are obtained in the reaction of **5d** and **5e** with excess of ANTA. A further support in favor of that pathway is that product (**6d**) reacted with excess of ANTA yielded **8d**. However, methylated **5a** as well as quinazolinedione (**6a**) with excess of ANTA didn't form significant amounts of **8a**.

Scheme 4



The proposed reaction mechanism may also explain the formation of the methylated derivatives of *para* substituted quinazolinodiones (**15**) and (**16**) (Scheme 5) (especially that of **15**, which seems to be an unexpected methylation product (**6a**)).

Thus, **6a** was refluxed in ethanol with a stoichiometric amount of sodium ethoxide in order to obtain its sodium salt.[7] The obtained salt was filtered, dissolved in DMF and alkylated with methyl iodide. In this way product (**15**) was obtained. Product (**15**) turned out to be different from **16**, the latter obtained as a result of the reaction of **5a** with *N*-methylanthranilic acid. The structures of **15** and **16** were assigned on basis of ^{1}H-NMR chemical shift considerations together with the results of NOE-difference experiments.

NMR Spectroscopic Investigations

The structures of compounds (**6a-e**, **8a-e**, **15**, and **16**) were confirmed by ^{1}H-NMR spectroscopic investigations. Full and unambiguous assignments were achieved on basis of chemical shift and coupling considerations, on NOE-difference experiments[14] and on 1D TOCSY spectra.[15] The latter helped to discriminate between spin systems of benzylidene group and the condensed benzene ring of the imidazoquinoline system on the one hand, and - on the other hand - between signals of compounds (**6**) from those of corresponding compounds (**8**) in mixtures of both of these species. The signals due to Ph H-2,6 of the (4-substituted) benzylidene system could be easily identified *via* a strong NOE upon irradiation of the spatially close =CH singlet (Figure 3).

Scheme 5

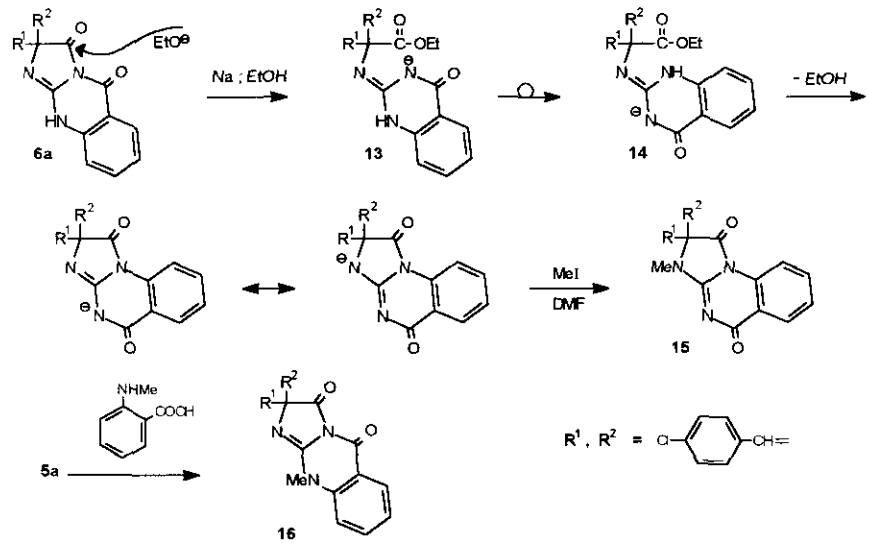
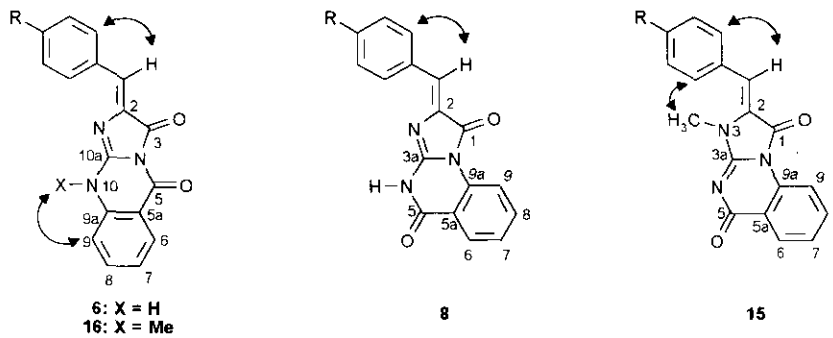


Figure 3. Important NOEs found with compounds (**6**, **8**, **15**, and **16**).



Linear compounds (**6**) are characterized by an NOE on the signal of H-9 upon perturbation of the NH-resonance, whereas with angular compounds (**8**) such a through-space connectivity was not observed

(Figure 3). With compounds (**6**) and (**8**) signals of protons H-6 and H-9 are double doublets (^3J 7-8 Hz, ^4J 1-1.5 Hz), whereas H-7 and H-8 have a triplet pattern (^3J 7-8 Hz) split by a smaller meta coupling (< 1.5 Hz). Both type of compounds show a dynamic behavior in DMSO-d_6 solution what is reflected in line broadening for nearly all signals. This phenomenon was also - more pronounced - observed in the ^{13}C-NMR spectra of **6b** and **8b**, which made it impossible to give a full and unambiguous assignment of carbon resonances. In comparison with linear compounds (**6**), angular systems of type (**8**) show larger chemical shifts for the ylidene-H (**6**: 6.71 - 6.78 ppm; **8**: 6.93 - 7.03 ppm) as well as for the signals of H-6 - H-9. The marked downfield shift of the signal due to H-9 (δ 8.53 - 8.62 ppm) in angular compounds (**8**) can be explained by the anisotropy of bond magnetic susceptibilty of C^1=O, coming spatially close to H-9. The chemical shifts of H-6 - H-9 in *N*-methyl compound (**15**) assign an angular structure similar to **8**, however, a marked NOE on Ph H-2,6 upon irradiation of the NMe resonance hints that the methyl group is attached to N-3 and not to N-4. Attachment of the methyl group at N-10 in the linear compound (**16**) is confirmed by a strong NOE on H-9 upon perturbation of the NMe signal. The most important NOEs found with **6**, **8**, **15**, and **16** are depicted in Figure 3, also showing the numbering of atoms used in the description of NMR spectra.

EXPERIMENTAL

Melting points are uncorrected. TLC was performed using Al. sheets 0.2 mm layer silica gel ($60F_{254}$ Merck); solvent system $CHCl_3$: AcOEt 1:1. IR were obtained (KBr disc) on Jasco FT IR instrument. UV spectra were measured on V-530 UV/VIS spectrometer. All NMR spectra were recorded on a Varian Unity*plus* spectrometer (299.95 MHz for ^{1}H) from DMSO-d_6 solutions at 28°C.

General procedure of the reaction of 5 with ANTA

A mixture of **5** (10 mmol) and ANTA (1.4 g, 10 mmol) in acetic acid (20 mL) was refluxed for 4-10 h (Table 4). On the next day the solid was filtered off and recrystallized from an appropriate solvent.

Reaction of 5a with ANTA

Raw solid contained **6a** and **8a** (4:1). The raw solid once crystallized from DMF contained **6a** , 1.6 g (yield 50%), mp 322-324 °C (lit.,[7] 322-324 °C).

6a: ^{1}H-NMR: δ (ppm) 6.73 (s, 1H, ylidene H), 7.22 (m, 1H, H-7), 7.23 (m, 1H, H-9), 7.48 (m, 2H, Ph H-3,5), 7.69 (m, 1H, H-8), 7.97 (m, 1H, H-6), 8.10 (m, 2H, Ph H-2,6), 12.40 (br s, 1H, NH).

8a: ^{1}H-NMR: δ (ppm) 6.98 (s, 1H, ylidene H), 7.43 (m, 1H, H-7), 7.51 (m, 2H, Ph H-3,5), 7.82 (m, 1H, H-8), 8.05 (m, 1H, H-6), 8.19 (m, 2H, Ph H-2,6), 8.56 (m, 1H, H-9), 12.40 (br s, 1H, NH).

Reaction of 5b with ANTA

Raw solid contained **6b** and **8b** (1:1). Upon one crystallization of the raw solid from DMF, the ratio of

6b : **8b** (1:1), was not changed. The raw solid 2.3 g (yield 79%) was fractionally recrystallized from acetic acid and then DMF giving:

2-[(*Z*)-1-Phenylmethylene]-2,3,5,10-tetrahydroimidazo[2,1-*b*]quinazoline-3,5-dione (6b):

0.87 g (yield 30%)mp 305-307 °C (lit.,[7] 305-307 °C). R_f = 0.73. ^{1}H-NMR: δ (ppm) 6.73 (s, 1H, ylidene H), 7.22 (m, 1H, H-7), 7.23 (m, 1H, H-9), 7.32 (m, 1H, Ph H-4), 7.42 (m, 2H, Ph H-3,5), 7.68 (m, 1H, H-8), 7.97 (m, 1H, H-6), 8.05 (m, 2H, Ph H-2,6), 12.23 (br s, 1H, NH).

2-[(*Z*)-1-Phenylmethylene]-1,2,4,5-tetrahydroimidazo[1,2-*a*]quinazoline-1,5-dione (8b):

1.04 g (yield 36%), mp 287-289 °C (lit.,[7] 287-289 °C). R_f = 0.78. ^{1}H-NMR : δ (ppm) 6.95 (s, 1H, ylidene H), 7.35 (m, 1H, Ph H-4), 7.41 (m, 1H, H-7), 7.42 (m, 2H, Ph H-3,5), 7.78 (m, 1H, H-8), 8.03 (m, 1H, H-6), 8.13 (m, 2H, Ph H-2,6), 8.53 (m, 1H, H-9), 12.60 (br s, 1H, NH).

Reaction of 5c with ANTA

The raw solid was once crystallized from DMF. Yield 54%. The resulting solid contained **6c** : **8c** (1.2 : 1).

6c: column chromatography, eluent CH_2Cl_2, red crystals. 1.16 g (yield 35%), mp 285-287 °C, R_f = 0.63. ^{1}H-NMR: δ (ppm) 2.98 (s, 6H, NMe_2), 6.71 (s, 1H, ylidene H), 6.72 (m, 2H, Ph H-3,5), 7.18 (m, 1H, H-7), 7.22 (m, 1H, H-9), 7.65 (m, 1H, H-8), 7.91 (m, 2H, Ph H-2,6), 7.96 (m, 1H, H-6), 12.15 (br s, 1H, NH). *Anal.* Calcd for $C_{19}H_{16}N_4O_2$: C, 68.66; H, 4.85; N, 16.86. Found: C, 68.65; H, 4.71; N, 16.53.

8c: 0.99 g (yield 30%), R_f = 0.72. ^{1}H-NMR: δ (ppm) 2.99 (s, 6H, NMe_2), 6.73 (m, 2H, Ph H-3,5), 6.93 (s, 1H, ylidene H), 7.40 (m, 1H, H-7), 7.79 (m, 1H, H-8), 8.01 (m, 2H, Ph H-2,6), 8.04 (m, 1H, H-6), 8.62 (m, 1H, H-9), 12.15 (br s, 1H, NH).

Reaction of 5d with ANTA

The obtained raw solid once crystallized from acetic acid contained **6d** : **8d** (1:1).

6d: Yield 35 %, mp 285-286 °C (acetic acid), R_f = 0.69. ^{1}H-NMR: δ (ppm) 3.80 (s, 3H, OMe), 6.74 (s, 1H, ylidene H), 6.99 (m, 2H, Ph H-3,5), 7.20 (m, 1H, H-7), 7.22 (m, 1H, H-9), 7.67 (m, 1H, H-8), 7.97 (m, 1H, H-6), 8.03 (m, 2H, Ph H-2,6), 12.30 (br s, 1H, NH). *Anal.* Calcd for $C_{18}H_{13}N_3O_3$: C, 67.70; H, 4.10; N, 13.16. Found: C, 67.69; H, 3.90; N, 13.04.

8d: Method a: The mixture of **5d** (1.24 g, 5 mmol) and ANTA (1.40 g, 10 mmol) in acetic acid (10 mL) was refluxed for 7 h. The solid obtained was recrystallized from acetic acid. It contained **6d** : **8d** (19:100). 1.29 g (yield 81 %). Method b: The mixture of **6d**: (1.60 g, 5 mmol) and ANTA (0.70 g, 5 mmol) in acetic acid (10 mL) was refluxed for 5 h then 0.70 g (5 mmol) of ANTA was added and the mixture was refluxed additionally 5 h. The solid obtained was recrystallized from acetic acid. 1.27 g (yield 80 %).

mp 288-291 °C, R_f = 0.74. ^{1}H-NMR: δ (ppm) 3.81 (s, 3H, OMe), 6.97 (s, 1H, ylidene H), 7.01 (m, 2H, Ph H-3,5), 7.41 (m, 1H, H-7), 7.80 (m, 1H, H-8), 8.04 (m, 1H, H-6), 8.14 (m, 2H, Ph H-2,6), 8.58 (m, 1H, H-9), 12.30 (br s, 1H, NH). *Anal.* Calcd for $C_{18}H_{13}N_3O_3$: C, 67.70; H, 4.10; N, 13.16. Found: C,

67.50; H, 3.96; N, 12.92.

Reaction of 5e with ANTA

The reaction mixture was refluxed for 5 h. The solid which appeared was checked by means of TLC (R_f = 0.00). The heating was continued for 10 h. The resulting solid was once crystallized from DMF. It contained **6e** : **8e** (3:1).

6e: R_f = 0.70 (in ammonia atmosphere the orange spot becomes quickly almost black, the colour disappears after few seconds). mp 329-332 °C (DMF). ^{1}H-NMR: δ (ppm) 6.78 (s, 1H, ylidene H), 7.24 (m, 1H, H-7), 7.25 (m, 1H, H-9), 7.70 (m, 1H, H-8), 7.98 (m, 1H, H-6), 8.24 (m, 2H, Ph H-3,5), 8.32 (m, 2H, Ph H-2,6), 12.65 (br s, 1H, NH). UV-VIS (DMF): 349 nm (log ε = 3.33), 435 nm (log ε = 2.92), 599 nm (log ε = 3.54). IR: 3434, 3247, 1761,1694, 1669, (C=O), 1616, 1581, 1511, 1335, 763. *Anal.* Calcd for $C_{17}H_{10}N_4O_4$: C, 61.08; H, 3.01; N, 16.76. Found: C, 61.05; H, 2.78; N, 16.43.

8e: obtained as **8d** - Method a: Reaction time 12 h(in ammonia atmosphere the yellow spot remains yellow). Yield 78 %, mp 343-345 °C (DMF). ^{1}H-NMR: δ (ppm) 7.03 (s, 1H, ylidene H), 7.43 (m, 1H, H-7), 7.82 (m, 1H, H-8), 8.05 (m, 1H, H-6), 8.26 (m, 2H, Ph H-3,5), 8.38 (m, 2H, Ph H-2,6), 8.53 (m, 1H, H-9), 12.65 (br s, 1H, NH). UV-VIS (DMF): 332 nm (log ε = 4.01), 418 nm (log ε = 3.94), 511 nm (log ε = 3.73). IR: 3432, 1733, 1697 (C=O), 1661, 1646, 1622, 1608, 1574, 1504, 1339, 760. *Anal.* Calcd for $C_{17}H_{10}N_4O_4$: C, 61.08; H, 3.01; N, 16.76. Found: C, 61.17; H, 2.96; N, 16.54.

2-[(*Z*)-1-(4-Chlorophenyl)methylene]-3-methyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]quinazoline-1,5-dione (15)

Described in literature [7] as 1-methyl-*Z*-2-(4-chlorobenzylidene)-2,3,4,5-tetrahydro[2,1-b]quinazoline-3,5-dione, mp 297-298 °C (lit., [7] 296-298 °C). ^{1}H-NMR: δ (ppm) 3.54 (s, 3H, 3-Me), 7.09 (s, 1H, ylidene H), 7.47 (m, 1H, H-7), 7.54 (m, 2H, Ph H-3,5), 7.86 (m, 1H, H-8), 8.12 (m, 1H, H-6), 8.27 (m, 2H, Ph H-2,6), 8.61 (m, 1H, H-9). IR: 1716, 1686 (C=O), 1648, 1564, 1483, 1168, 960, 760.

2-[(*Z*)-1-(4-Chlorophenyl)methylene]-10-methyl-2,3,5,10-tetrahydroimidazo[2,1-*b*]quinazoline-3,5-dione (16)

Described in literature[7], mp 316-317 °C (lit., [7] 315-317 °C) ^{1}H-NMR: δ (ppm) 3.74 (s, 1H, 10-Me), 6.82 (s, 1H, ylidene H), 7.33 (m, 1H, H-7), 7.50 (m, 2H, Ph H-3,5), 7.51 (m, 1H, H-9), 7.82 (m, 1H, H-8), 8.08 (m, 1H, H-6), 8.22 (m, 2H, Ph H-2,6). IR: 1780, 1756 (C=O), 1694, 1648, 1568, 1548, 760, 748.

X-Ray Structure Determination of 2-[(*Z*)-1-Phenylmethylene]-2,3,5,10-tetrahydroimidazo[2,1-*b*]-quinazoline-3,5-dione dimethyl sulfoxide solvate (6b.dmso)

Crystal data: $C_{19}H_{17}N_3O_3S$ = $C_{17}H_{11}N_3O_2 \cdot (CH_3)_2SO$, M_r = 367.42, monoclinic, space group $P2_1/c$ (No. 14), a = 6.849(3) Å, b = 11.834(4) Å, c = 21.868(8) Å, β = 93.15(1)°, V = 1769.7(12) Å^3, Z = 4, Dx = 1.379 g cm^{-3}, λ = 0.71073 Å, μ = 0.207 mm^{-1}, T = 301K. A yellow plate, 0.50 x 0.32 x 0.05 mm, crystallized from hot dimethyl sulfoxide was used for data collection with a Siemens Smart CCD

diffractometer (area detector, platform type 3-circle goniometer) and Mo Kα radiation (sealed X-Ray tube, graphite monochromator). Intensity data with $\theta \leq 25°$ were harvested over more than one hemisphere of the reciprocal space using 0.3° ω-scan frames. Data were corrected for Lp, decay, absorption and related effects with the multi-scan method using program SADABS[16] (correction factors 0.74 - 0.93); 9873 reflections collected, 3111 independent, $R_{int} = 0.032$. The structure was solved with direct methods and was refined with program SHELXL93.[16] Hydrogen atoms were located from a difference Fourier map and were refined riding with the atoms to which they were bonded. The final refinement varied 234 parameters and used all 3111 independent reflections weighted by $w=1/[\sigma^2(F_o^2)+(0.052P)^2+0.60P]$, where $P=(F_o^2+2F_c^2)/3$. Final $R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o| = 0.076$, wR2 = $[\Sigma(w(F_o^2-F_c^2)^2)/\Sigma(w(F_o^2)^2)]^{\cdot\cdot} = 0.119$ and $S = 1.04$ for all data; $R1 = 0.045$ for the 2192 reflections with $F_o^2 > 2\sigma(F_o^2)$. Excursions in final difference Fourier map between -0.205 and 0.176 e Å^{-3}. Atomic coordinates are presented in Table 1, selected bond lengths and angles in Table 3.[17]

X-Ray Structure Determination of 2-[(*Z*)-1-Phenylmethylene]-1,2,4,5-tetrahydroimidazo[1,2-*a*]quinazoline-1,5-dione dimethylformamide solvate (8b.dmf)

Crystal data: $C_{17}H_{11}N_3O_2 \cdot HCON(CH_3)_2 = C_{20}H_{18}N_4O_3$, $M_r = 362.38$, monoclinic, space group $P2_1/c$ (No. 14), $a = 6.353(2)$ Å, $b = 18.495(5)$ Å, $c = 15.437(5)$ Å, $\beta = 98.10(2)°$, $V = 1795.7(9)$ Å^3, $Z = 4$, Dx = 1.340 g cm^{-3}, $\lambda = 0.71073$ Å, $\mu = 0.093$ mm^{-1}, T = 301K. A yellow prism, 0.6 x 0.2 x 0.2 mm, crystallized from dimethylformamide at rt was used for data collection with a Siemens Smart CCD diffractometer. Intensity data with $\theta \leq 25°$ were collected over more than one hemisphere of the reciprocal space using 0.3° ω-scan frames. They were corrected for Lp, decay, absorption and related effects (correction factors 0.57 - 0.96); 11718 reflections collected, 3163 independent, $R_{int} = 0.040$. Structure solution with direct methods, structure refinement with SHELXL93. Hydrogen atoms were located from a difference Fourier map and were refined riding with the atoms to which they were bonded. The final refinement varied 248 parameters and used all 3163 independent reflections weighted by $w=1/[\sigma^2(F_o^2)+(0.051P)^2+0.08P]$. Final $R1 = 0.071$, wR2 = 0.107 and $S = 1.01$ for all data; $R1 = 0.039$ for the 2090 reflections with $F_o^2 > 2\sigma(F_o^2)$. Excursions in final difference Fourier map between -0.129 and 0.155 e Å^{-3}. Atomic coordinates are presented in Table 2.[17]

ACKNOWLEDGEMENT:

The authors are grateful to Mrs Maria Kaleta for excellent technical assistance.

The financial support of the synthetic part of research carried out under the Polish State Committee for Scientific Research, grant no 4 P05F 007 13 is gratefuly acknowledged.

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Received, 15th March, 1999