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TAUTOMERISM AND X-RAY STRUCTURE OF DIHYDRO-5*H*-1,3,4-BENZOTRIAZEPIN-5-ONES

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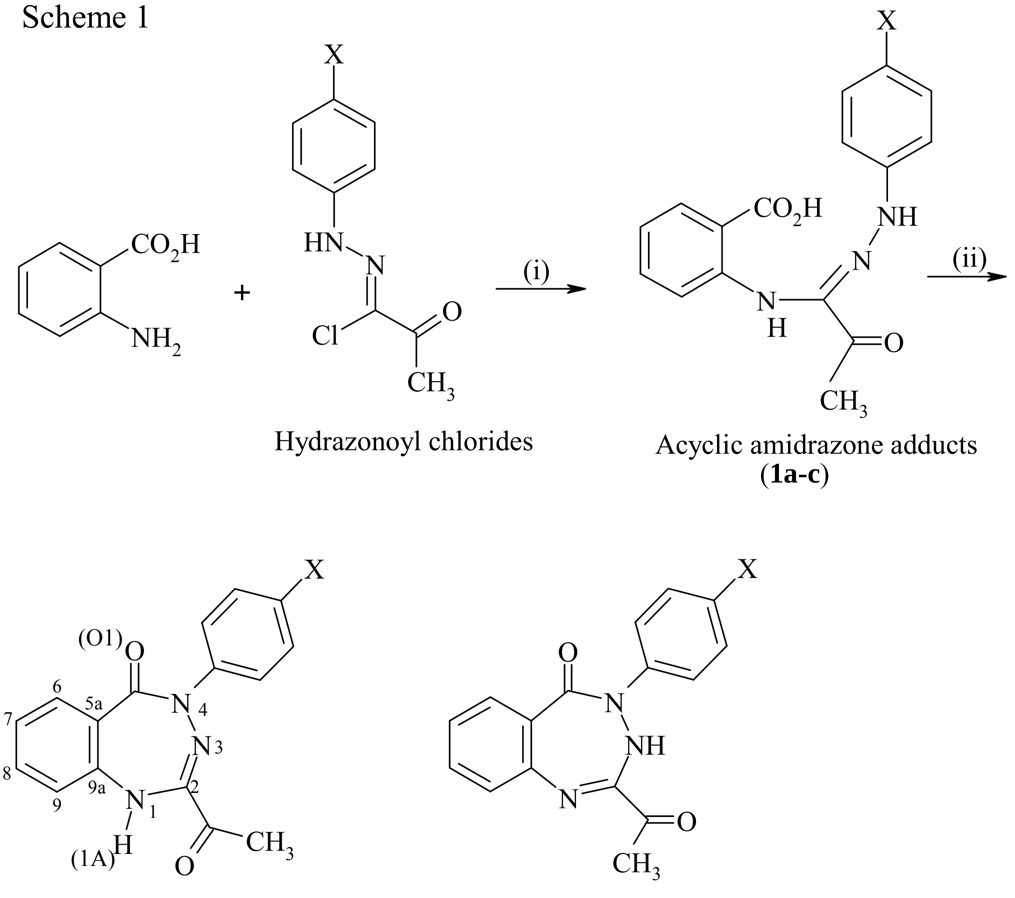
Abstract– Single X-Ray crystal structure determination of dihydro-5*H*-1,3,4-benzotriazepin-5-one (**2b**) revealed that the mobile hydrogen is σ–bonded to N1, while the double bond is situated between C2-N3. In this prevailing 1,4-dihydro tautomer (**2A**) (preferred over the alternate 3,4-dihydro form **2B**), both azomethine C2-N3 atoms are folded away, out of the plane comprising the rest bicyclic skeletal atoms, in a "*boat*"-like manner. Cyclocondensation of the *C*-acetylcarbohydrazonamides (**1a**, **b**) with acetic anhydride is reinvestigated and found to deliver the respective **2a**, **b**, but not the isomeric 4-(3*H*)quinazolinones (**3a**, **b**) as was previously reported.

INTRODUCTION

Quite recently, we have reported on a new, convenient and unequivocal synthetic route towards dihydro-1,3,4-benzotriazepin-5-ones,[1] exemplified by **2** shown in Scheme 1. Dihydrobenzotriazepinones (**2**) are likely to exist in the tautomeric form **(A)**, or as the alternate tautomer **(B)**.[2] This dimly situation can best be resolved by single X-Ray crystal structure determination. In the event, an X-Ray structure of representative **2b** has been done, and the crystallographic data revealed that **2b** exists, at least in the solid state, as tautomer (**A**) (*vide infra*). Accordingly, the factual ring system of compounds (**2**) is named (IUPAC) as 1,4-dihydro-5*H*-1,3,4-benzotriazepin-5-one.

Scheme 1



1,4-Dihydro-(**2a**-**c**)

(A)

3,4-Dihydro-(**2a**-**c**)

(B)

(i) aq. MeOH, THF, NEt$_3$ / 0 ^{0}C $\longrightarrow$ 20 ^{0}C, 2 - 3 h
(ii) 1,1'-Carbonyldiimidazole, THF / 20 ^{0}C, 1 - 2 h

Compounds (**1**) and (**2**)

Entry	**a**	**b**	**c**
X	H	Me	Cl

RESULTS AND DISCUSSION

The present work deals with the results of X-Ray crystal structure determination of **2b**, and for which relevant crystallographic data are summarized in Tables 1 and 2. The molecular structure of **2b**, based on crystallographic data, is displayed in Figure 1. These data revealed that the mobile hydrogen (H_{1A}) is σ–bonded to N1, while the double bond is localized at the C2-N3 locus (Figure 1 and Table 2). As can be seen from Table 2, the N1-C2 bond length is 1.364(3) Å (an acceptable value for C-N / sp^2- sp^3 σ-bond), whereas that of C2-N3 is truly shorter, being 1.277(3) Å in accordance with an azomethine π-bond character. Thus, the amidrazone constitution of the four atom array N1-C2-N3-N4 which prevails in the acyclic precursor (**1b,** Scheme 1), is also retained in the cyclized product (**2b**). Collectively, the data noted above are in conformity with tautomer **(A)** as the more stable predominant form in the crystal. Calculation relating to the plane of the 1,4-dihydro-1,3,4-triazepine ring shows that the five consecutive atoms N1-C9A-C5A-C5-N4 are lying quite well in the same plane and are planar with the benzo-fused ring, whereas the other two complementary azomethine atoms C2-N3 are folded away, out of the plane, in a "*boat*"-like manner (Figure 1). The solid state structure **(A)** is stabilized by an intermolecular hydrogen bond between N-H1A · · · O1$^{\#}$.[3]

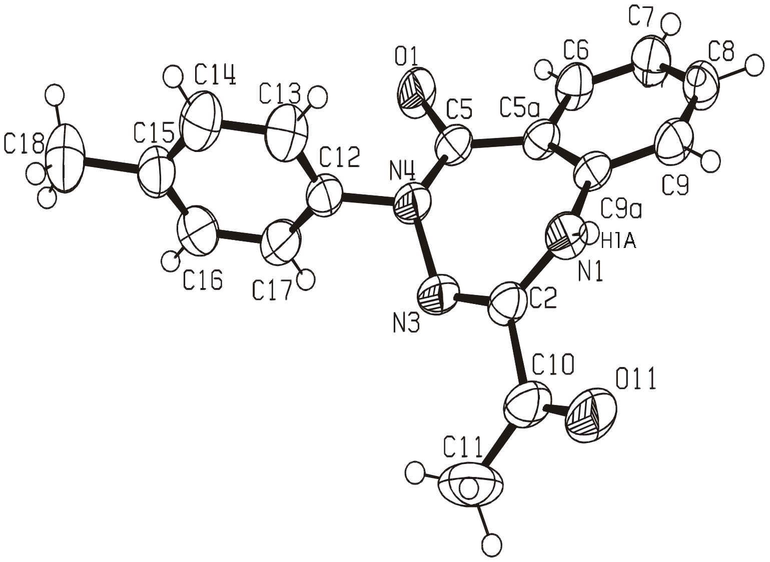


Figure 1. ORTEP plot of the molecular structure of **2b(A)**

Table 1. Summary of the Crystal Data and Structure Refinement Parameters for **2b(A)**

Molecular formula	$C_{17}H_{15}N_3O_2$
Formula weight	293.32
Temperature (K)	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
Unit cell dimensions	
a (Å)	11.157(1)
b (Å)	9.772(1)
c (Å)	13.985(2)
α (^{0})	90
β (^{0})	98.25(1)
γ (^{0})	90
Volume (Å^3)	1509.0(3)

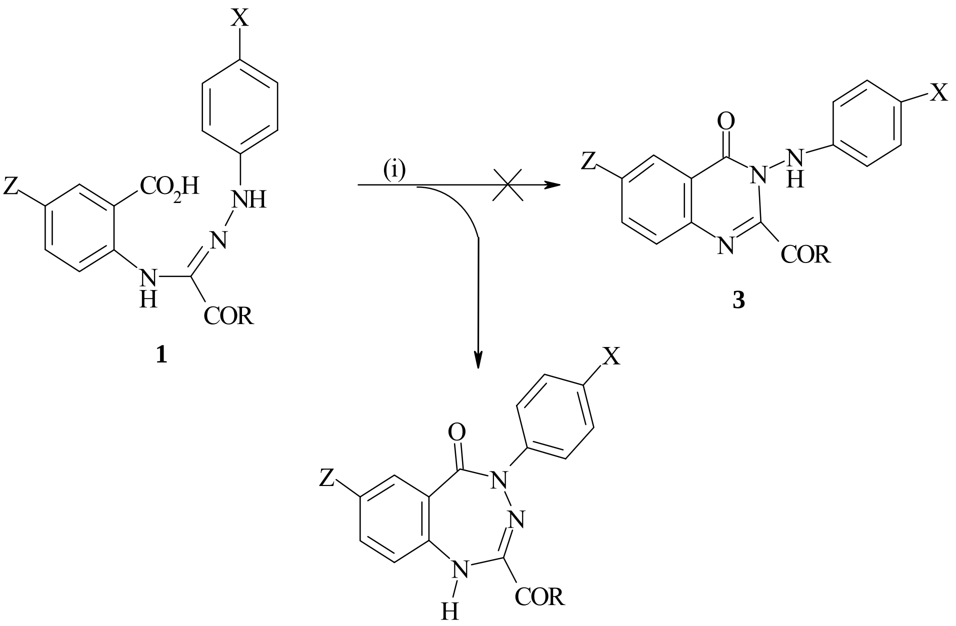
Z	4
Calculated density (mg / m^3)	1.291
Absorption coefficient (mm^{-1})	0.706
F (000)	616
Crystal size (mm)	0.22 x 0.12 x 0.06
Index range	$-13 \le h \le 0; 0 \le k \le 11; -16 \le l \le 16$
Reflections collected	2880
Independent reflections	2734 [$R\ int = 0.0392$]
Reflections observed	1817
Weight scheme	Calc $w = 1 / [\sigma^2 (F_0)^2 + (0.0982P)^2 + 0.0000P]$
	where $P = [(F_0)^2 + 2(F_c)^2] / 3$
Data / restraints / parameters	2734 / 0 / 199
Goodness-of-fit on F^2	1.009
Final R indices [$I > 2\sigma (I)$]	$R_1 = 0.0553$, $wR_2 = 0.1459$
R indices (all data)	$R_1 = 0.0852$, $wR_2 = 0.1564$
Largest difference peak (e. Å^{-3})	0.364
Largest difference hole (e. Å^{-3})	-0.249

Table 2. Selected Bond Lengths (Å) and Angles (°) for **2b(A)**

N1- C9a	1.400(3)	C2- N1- C9a	123.95(19)
N1- C2	1.364(3)	N3- C2- N1	129.1(2)
N3- C2	1.277(3)	C2- N3- N4	117.7(2)
N3- N4	1.419(2)	N3- N4- C5	124.76(19)
N4- C5	1.370(3)	N4- C5- C5a	120.96(17)
C5- C5a	1.472(3)	C5- C5a- C9a	125.17(19)
C5a- C9a	1.399(3)	C5a- C9a- N1	122.5(2)
N1- H1A	0.8600	C2- N1- H1A	118.0
C2- C10	1.523(3)	N1- C2- C10	115.1(2)
N4- C12	1.448(3)	N3- N4- C12	111.81(17)
C5- O1	1.233(2)	N4- C5- O1	118.7(2)

In this context, it is worth mentioning that the acyclic amidrazone adduct (**1a**) was reported [4] to undergo ring closure into 2-acetyl-3-phenylamino-4-(3*H*)quinazolinone (**3a**) upon refluxing in acetic anhydride for 20 min. (Scheme 2). Under similar reaction conditions, the amidrazone analogs (**1d-f**) were likewise reported [4] to yield the respective 4-(3*H*)quinazolinones (**3d-f**, Scheme 2). Having **1a** at hand, we have reinvestigated its reaction with acetic anhydride at reflux. Herein, the main isolable reaction product has been found to be identical with an authentic sample of 2-acetyl-4-phenyl-1,4-dihydro-1*H*-1,3,4-benzotriazepin-5-one (**2a**) which was previously prepared and characterized[1] *via* the reaction of **1a** with 1,1'-carbonyldiimidazole (Scheme 1). Similarly, the dihydrobenzotriazepinone (**2b**), for which an X-Ray crystal structure is presented here (*vide supra*), has also been obtained by cyclization of **1b** with acetic anhydride.

Scheme 2



2

Compounds (**1** - **3**)

No.	R	X	Z
a	Me	H	H
d	Me	H	NO_2
e	OEt	H	H
f	OEt	OMe	H

$$(\mathbf{1a, b}) \xrightarrow{(i)} (\mathbf{2a, b})$$

(i) $(CH_3CO)_2O$ / reflux, 20-30 min.

Accordingly, and based on the available data as presented herein and in previous publication,[1] we conclude that the reported synthesis of presumed 4-(3*H*) quinazolinones (**3a,d-f**) [4] is at fault, and the structures of the cyclized products of **1a,d-f** with acetic anhydride should be correctly reassigned as the respective 1,4-dihydro-1,3,4-benzotriazepin-5-ones (**2a,d-f**) (Scheme 2).

EXPERIMENTAL

2-Acetyl-4-phenyl-1,4-dihydro-1H-1,3,4-benzotriazepin-5-one(2a)

Acetic anhydride method

The acyclic amidrazone adduct (**1a**)[1] (0.89 g , 3 mmol ; mp 210-211 °C [1] ; 199-200 °C [4]) was dissolved in acetic anhydride (12 mL) and refluxed for 30 min. The reaction mixture was then cooled, carefully diluted with cold water (60 mL) and extracted with isopropyl ether (2 x 30 mL). Evaporation of the organic solvent gave a solid product which was recrystallized from chloroform /cyclohexane . Yield of **2a** = 0.52 g (62 %), mp 152-153 °C, undepressed upon admixture with an authentic sample [1] of **2a** (lit., [1] mp 152-153 °C; lit., [4] mp 151-152 °C - erroneously presumed to have the quinazolinone structure (**3a**) [4]).

3-Acetyl-4-(4-methylphenyl)-1,4-dihydro-1H-1,3,4-benzotriazepin-5-one (2b)

A solution of **1b** [1] (0.93 g, 3 mmol) in acetic anhydride (12 mL) was refluxed for 30 min. Work-up of the reaction mixture as describrd for **2a** above, furnished a yellow solid product which was recrystallized from dichloromethane / *n*-hexane. Yield of **2b** = 0.58 g (66 %), mp 155-156 °C, undepressed upon admixture with an authentic sample of of **2b** (lit.,[1] mp 155-156 °C).

COLLECTION OF X-RAY DIFFRACTION DATA AND STRUCTURE ANALYSIS

Yellow needle crystals were grown by allowing a clear solution of **2b** in CH_2Cl_2 / n-hexane (2 : 1, v / v) to evaporate slowly at rt such that its volume was reduced by about 25% over 4-6 days. Data collection was made at 20 °C, using an ENRAF-NONIUS CAD4 diffractometer operating in the omega/theta scan mode. Reflections were collected within the range $\theta = 4.00\text{-}67.88^0$ using CuK_α radiation ($\lambda = 1.54179$ Å). Lp-corrections were applied using XCAD4 program (Harms, 1996).[5] The structure was solved by direct methods. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares procedure based on F^2 using all unique data. The hydrogen atoms were refined isotropically using riding model. SHELX-97 program package was used for calculations.[6] ORTEP3 program was used for molecular graphics calculations.[7]

Further information of the crystal structure determination and X-Ray data can be ordered from the Cambridge Crystallographic Data Center under the depository number CCDC 176869.

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REFERENCES AND NOTES

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2. IUPAC name for tautomer **2b(B)**: 2-Acetyl-4-(4-methylphenyl)-3,4-dihydro-*5H*-1,3,4-benzotriazepin-5-one.
3. The symbol $^{\#}$ denotes symmetry equivalent atom at $x, -y+1/2, z+1/2$.
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