Crystal Structural Determination of Ring-Chain Tautomers of 1,2,3,4-Tetrahydro-*s*-tetrazines

R. Boese*

Institut für Anorganische Chemie der Universität-GH Essen,
45117 Essen, Germany

M. M. El-Abadelah* and A. Q. Hussein

Chemistry Department, Jordan University,
Amman, Jordan

A. S. Abushamleh

Natural Science Department, Mu'tah University,
Karak, Jordan

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1,2,3,4-Tetrahydro-1-methyl-3-(*p*-bromophenyl)-4,6-diphenyl-*s*-tetrazine (**3a**), exhibiting "ring ⇋ chain" tautomerism in solutions, exists as the ring tautomer in the solid phase, as proved by X-ray crystal structure determination. However, the 6-acetyl analogue **3b** acquires the chain form in the crystalline state.

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The reaction of hydrazonoyl chlorides **1** with methylhydrazones of aliphatic aldehydes and ketones has been found to provide a convenient route to 1,2,3,4-tetrahydro-*s*-tetrazines [1]. Those tetrahydro-*s*-tetrazines **3**, derived from methylhydrazones of aromatic aldehydes **2** (Scheme 1) exhibit "ring-chain" tautomerism in solution, as evidenced by ^{1}H-nmr and ^{13}C-nmr spectroscopic data [2]. The extent of the ring-chain equilibrium in these compounds varies widely depending both on steric and electronic effects exerted by the substituents at the heteroring [3,4]. Thus, the ratio of the ring tautomer in the case of the 6-phenyl derivative **3a** is 86% (in deuteriochloroform), whereas it amounts only 53% for the 6-acetyl analogue **3b** [3].

Compounds **3a,b** gave sharp melting points which remain unchanged upon repeated crystallizations from various solvents, and no change was observed in their nmr spectra. Examination (tlc) of these compounds using different adsorbents and eluents gave single spots. These findings suggest that compounds **3** exist in the solid phase as one tautomeric form, the identity of which is best resolved by single crystal X-ray structure determination.

Crystal structure determinations for *s*-tetrazines [5], 1,6-dihydro-*s*-tetrazines [6] and hexahydro-*s*-tetrazines [7] were reported. However, crystal structure of 1,2,3,4-tetrahydro-*s*-tetrazines is hitherto unreported in the literature. The title investigation is therefore undertaken to ascertain the structure of the tautomeric form in the crystals of compounds **3a,b** as model compounds of 1,2,3,4-tetrahydro-*s*-tetrazines showing appreciable differences of their "ring-chain" tautomeric equilibria in solution.

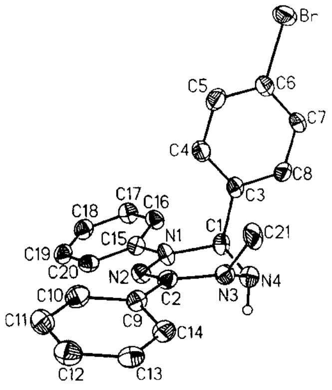
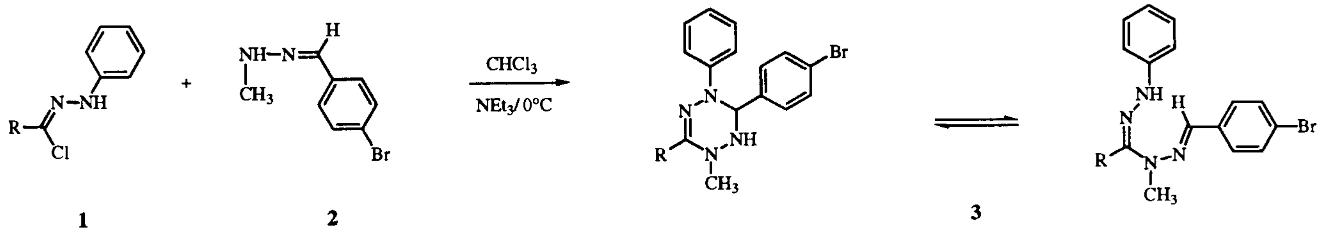


Figure 1. ORTEP-plot of the molecular structure of **3a** with the envelope conformation of the ring. The ellipsoids are drawn at the 50% level, hydrogen atoms except for H-(N) are omitted for clarity.

Scheme 1



1 **2** **3**

No.	R
3a	C_6H_5
3b	$COCH_3$

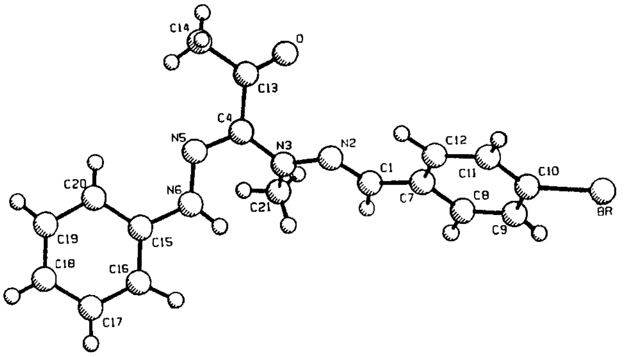


Figure 2. Pluto-plot of the molecular structure of **3b**.

Table 1

Atomic Coordinates (x10^4) and Equivalent Isotropic Displacement Factors (Å^2 x 10^3) for **3a**

atom	x	y	z	U_{eq}
Br	2332(1)	1363(1)	6715(1)	47(1)
N(1)	507(3)	-873(4)	1574(3)	26(2)
N(2)	1196(3)	-622(4)	1071(3)	23(2)
N(3)	979(3)	1535(4)	1270(3)	24(2)
N(4)	-39(4)	1258(4)	1355(4)	25(2)
C(1)	23(4)	130(5)	1960(4)	24(2)
C(2)	1467(4)	507(5)	1005(4)	24(2)
C(3)	605(4)	395(4)	3138(4)	24(2)
C(4)	1670(4)	23(5)	3706(4)	29(2)
C(5)	2201(4)	321(5)	4769(4)	31(2)
C(6)	1644(4)	986(5)	5249(4)	29(2)
C(7)	569(4)	1358(5)	4698(4)	31(2)
C(8)	66(4)	1066(5)	3643(4)	28(2)
C(9)	2229(4)	734(5)	494(4)	23(2)
C(10)	2880(4)	-236(5)	389(4)	30(2)
C(11)	3542(4)	-72(5)	-162(4)	31(2)
C(12)	3585(4)	1068(5)	-608(4)	33(2)
C(13)	2960(4)	2036(6)	-503(4)	30(2)
C(14)	2279(4)	1873(5)	24(4)	28(2)
C(15)	316(4)	-2133(5)	1701(4)	24(2)
C(16)	-181(4)	-2473(5)	2380(4)	27(2)
C(17)	-388(5)	-3708(5)	2505(5)	31(2)
C(18)	-76(4)	-4624(5)	1981(4)	32(2)
C(19)	437(4)	-4287(5)	1318(4)	30(2)
C(20)	632(4)	-3050(5)	1171(4)	25(2)
C(21)	1634(4)	2475(5)	2014(4)	32(2)

Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

The results of the X-ray crystal structure determination for compound **3a** clearly show that this compound is cyclic and adopts an envelope conformation. The molecular structure of **3a** is displayed in Figure 1; the atomic coordinate and relevant bond distances and angles are given in Tables 1 and 2. In the case of compound **3b**, X-ray data show that this compound has a non-cyclic structure (chain tautomer). The molecular structure of this compound is displayed in Figure 2, the atomic coordinates and relevant bond distances and angles are given in Tables 3 and 4. For both structures all bond lengths and angles are in normal ranges.

In conclusion, this study indicates that the title 1,2,3,4-tetrahydro-*s*-tetrazines, having relatively high ratio (>80%) of the ring tautomer in solution (deuteriochloroform), are cyclic in the solid state as demonstrated by **3a**. However, when the ratio of the chain tautomer in solution

Table 2

Relevant Lengths (Å), Angles and Torsion Angles (°) for **3a**

Br-C(6)	1.896(5)
N(1)-C(1)	1.461(7)
N(2)-C(2)	1.282(7)
N(3)-C(2)	1.403(7)
N(4)-C(1)	1.455(7)
C(2)-C(9)	1.462(9)
N(1)-N(2)	1.374(7)
N(1)-C(15)	1.404(7)
N(3)-N(4)	1.440(7)
N(3)-C(21)	1.461(6)
C(1)-C(3)	1.519(7)
N(2)-N(1)-C(1)	120.8(4)
C(1)-N(1)-C(15)	122.9(5)
N(4)-N(3)-C(2)	113.9(4)
N(1)-C(1)-N(4)	110.3(5)
N(4)-C(1)-C(3)	109.9(4)
N(2)-C(2)-C(9)	117.5(5)
N(2)-N(1)-C(15)	116.2(5)
N(1)-N(2)-C(2)	119.0(5)
N(4)-N(3)-C(21)	114.5(5)
N(3)-N(4)-C(1)	111.9(4)
N(1)-C(1)-C(3)	114.1(4)
N(2)-C(2)-N(3)	123.9(5)
C(1)-N(1)-N(2)-C(2)	4.5
C(2)-N(3)-N(4)-C(1)	45.7
C(21)-N(3)-N(4)-C(1)	-99.7
N(2)-N(1)-C(1)-N(4)	25.4
N(2)-N(1)-C(1)-C(3)	-98.8
C(15)-N(1)-C(1)-C(3)	80.3
N(3)-N(4)-C(1)-N(1)	-49.1
N(3)-N(4)-C(1)-C(3)	77.5
N(1)-N(2)-C(2)-N(3)	-10.1
N(4)-N(3)-C(2)-N(2)	-15.8
C(21)-N(3)-C(2)-N(2)	127.2
C(21)-N(3)-C(2)-C(9)	-61.0
N(3)-C(2)-C(9)-C(14)	-16.7
N(2)-N(1)-C(15)-C(16)	166.9

Table 3

Atomic Coordinates and Equivalent Isotropic Displacement Factors for **3b**

atom	x	y	z	B(eq)
Br	0.57068(4)	0.16398(6)	0.56109(3)	5.31(3)
O	1.2534(2)	0.6913(3)	0.6330(2)	4.1(1)
N2	1.1370(2)	0.4594(4)	0.7190(2)	3.1(1)
N3	1.2376(2)	0.5205(4)	0.7681(2)	3.4(1)
N5	1.4406(2)	0.4646(4)	0.7780(2)	3.2(1)
N6	1.4428(3)	0.3829(4)	0.8425(2)	3.7(2)
C1	1.0400(3)	0.4700(5)	0.7397(2)	3.2(2)
C4	1.3399(3)	0.5272(5)	0.7396(2)	3.0(2)
C7	0.9294(3)	0.3966(5)	0.6936(2)	3.0(2)
C8	0.8289(3)	0.4110(6)	0.7206(3)	4.1(2)
C9	0.7230(4)	0.3405(6)	0.6817(3)	4.2(2)
C10	0.7175(3)	0.2600(5)	0.6148(2)	3.5(2)
C11	0.8157(4)	0.2432(6)	0.5858(3)	4.2(2)
C12	0.9213(4)	0.3114(5)	0.6259(2)	3.7(2)
C13	1.3396(3)	0.6168(5)	0.6684(2)	3.2(2)
C14	1.4503(4)	0.6129(8)	0.6401(3)	4.2(2)
C15	1.5482(3)	0.3125(4)	0.8866(2)	3.0(2)
C16	1.5426(4)	0.2129(5)	0.9478(2)	3.7(2)
C17	1.6436(4)	0.1434(6)	0.9922(3)	4.3(2)
C18	1.7509(4)	0.1715(6)	0.9771(3)	4.6(2)
C19	1.7573(4)	0.2708(6)	0.9173(3)	4.7(2)
C20	1.6564(3)	0.3432(6)	0.8718(3)	3.8(2)
C21	1.2354(4)	0.6080(6)	0.8379(3)	3.8(2)

Table 4

Relevant Bond Lengths (Å), Angles and Torsion Angles (°) for **3b**

Br-C(10)	1.907(4)
O-C(13)	1.211(4)
N(2)-C(1)	1.281(4)
N(2)-N(3)	1.367(4)
N(3)-C(4)	1.414(4)
N(3)-C(21)	1.445(5)
N(5)-C(4)	1.304(4)
N(5)-N(6)	1.328(4)
N(6)-C(15)	1.404(5)
C(1)-C(7)	1.471(5)
C(4)-C(13)	1.468(5)
C(1)-N(2)-N(3)	117.9(3)
C(4)-N(3)-C(21)	119.5(3)
C(4)-N(5)-N(6)	118.0(3)
N(5)-N(6)-C(15)	121.0(3)
N(2)-C(1)-C(7)	121.6(4)
N(5)-C(4)-N(3)	121.8(3)
N(5)-C(4)-C(13)	117.1(3)
N(3)-C(4)-C(13)	121.0(3)
O-C(13)-C(4)-N(5)	-173.0(4)
O-C(13)-C(4)-N(3)	2.1(6)
N(2)-N(3)-C(4)-C(13)	58.5(5)
N(3)-N(2)-C(1)-C(7)	-175.1(3)
N(6)-N(5)-C(4)-C(13)	-179.9(6)
C(1)-N(2)-N(3)-C(4)	-171.7(3)
C(1)-N(2)-N(3)-C(21)	-5.7(6)
C(4)-N(5)-N(6)-C(15)	-180.0(5)

is about 50% or higher, the title compounds acquire the non-cyclic structure in the solid as represented by **3b**. The results presented here, explain the controversy in the literature [1-4,8] concerning the actual structure of 1,2,3,4-tetrahydro-*s*-tetrazines and their non-cyclic equivalents.

EXPERIMENTAL

The ^{1}H- and ^{13}C-nmr spectra (in deuteriochloroform): were recorded on a Varian XL 200 instrument at 21°. The EI mass spectrum was run on a Finnigan MAT 731 spectrometer at 70 eV. Elemental microanalyses was performed at MHW Laboratories, Phoenix, Arizona, USA.

X-ray Structure Determination of **3a**.

Approximate crystal dimensions 0.32•0.27•0.14 mm^3, measured on a Nicolet R3m/V diffractometer with Mo-K$_\alpha$-radiation at 103 K. Cell dimensions, refined from the angle settings of 30 reflections: a = 13.350(4), b = 10.777(4), c = 13.684(4) Å, β = 112.96(2)°, V = 1812(1) Å^3; Z = 4, d$_{cal.}$ = 1.492 gcm^{-3}, μ = 0.225 mm^{-1}, monoclinic, space group $P\,2_1/n$, data collection of 2858 unique intensities ($2\theta_{max}$ = 45°), 2151 observed ($F_o \geq 4\sigma(F)$), structure solution by Direct Methods and refinements on F (full matrix) with SHELXTL-Plus, 256 parameters, rigid groups for hydrogen atoms with individual isotropical displacement parameters, and ADPs for all other atoms. R = 0.054, R$_w$ = 0.059, w^{-1} = ($\sigma^2(F_o) + 0.004 \cdot F_o^2$). Maximum residual electron density 0.89 e/Å^3.

X-ray Structure Determination of **3b**.

Approximate crystal dimensions 0.50•0.30•0.30 mm^3, measured on a Rigaku AFC5R diffractometer with Mo-K$_\alpha$-radiation from a 12kW rotating anode at room temperature. Cell dimensions, refined from the angle settings of 25 reflections: a = 11.672(1), b = 8.364(2), c = 17.744(2) Å, β = 105.090(7)°, V = 1672.5(4) Å^3; Z = 4, d$_{cal.}$ = 1.482 gcm^{-3}, μ = 2.44 mm^{-1}, empirical absorption correction (min/max transmission 0.90/1.00) monoclinic, space group $P2_1/n$, data collection of 2363 unique intensities ($2\theta_{max}$ = 45°), 1594 observed ($I \geq 3\sigma(I)$), structure solution by Direct Methods (MITHRIL and DIRFIF) and refinements on F (full matrix) with TEXSAN, 276 parameters, all atoms refined with ADPs except hydrogen atoms which were refined with isotropical displacement parameters; R = 0.032, R$_w$ = 0.039, w^{-1} = $\sigma^2(F_o)$; maximum residual electron density 0.38 e/Å^3.

Preparation of Compounds **3a,b**.

Compound **3a** was prepared from *p*-bromobenzaldehyde methylhydrazone [9] and *N*-phenylbenzohydrazonoyl chloride [10] following reported procedures [2], yield = 82%, mp 126-127° (faint yellow prismatic needles); ms: M$^+$ 404/406; ^{1}H-nmr (ring tautomer): δ 2.37 (s, 3H, N-CH$_3$), 4.49 (d, J = 2 Hz, 1H, NH), 5.81 (brs, 1H, C$_6$-H); (chain tautomer): δ 3.22 (s, 3H, N-CH$_3$), 8.94 (s, 1H, NH); ^{13}C-nmr (ring tautomer): δ 43.28 (N-CH$_3$), 68.3 (C-6); (chain tautomer): δ 38.4 (N-CH$_3$).

Anal. Calcd. for $C_{21}H_{18}BrN_4$: C, 62.08; H, 4.46; N, 13.79. Found: C, 62.14; H, 4.41; N, 13.68.

The preparation of compound **3b**, as well as its physical and spectral properties, have been reported previously [2].

For crystal structure determination, compounds **3a,b** were allowed to crystallize slowly from 95% ethanol, and the crystals were dried *in vacuo* overnight at room temperature.

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REFERENCES AND NOTES

[1] M. M. El-Abadelah, A. Q. Hussein, M. R. Kamal and K. H. Al-Adhami, *Heterocycles*, **27**, 917 (1988).

[2] A. Q. Hussein, M. M. El-Abadelah, K. H. Al-Adhami and A. S. Abushamleh, *Heterocycles*, **29**, 1163 (1989).

[3] M. M. El-Abadelah, A. Q. Hussein and H. A. Saadeh, *Heterocycles*, **32**, 1063 (1991).

[4] M. M. El-Abadelah, A. Q. Hussein and A. S. Abushamleh, *J. Prakt. Chem.*, **333**, 61 (1991).

[5] F. Bertinotti, G. Giacomello and A. M. Liquori, *Acta Crystallogr.*, **8**, 513 (1955).

[6] C. H. Stam, A. D. Counotte-Potman and H. C. van der Plas, *J. Org. Chem.*, **47**, 2856 (1982).

[7] G. B. Ansell, J. L. Erickson and D. W. Moore, *Chem. Commun.*, 446 (1970).

[8] R. Grashey, M. Baumann and H. Bauer, *Chem. Z.*, **96**, 224 (1972); B. I. Buzykin, N. G. Gazetdinova, S. K. Yakupova, A. P. Stolyarova, Z. S. Titova and Yu. P. Kitaev, *Izv. Akad. Nauk. SSSR. Ser. Khim.*, 1588 (1983).

[9] W. Sucrow, C. Mentzel and M. Slopianka, *Chem. Ber.*, **106**, 450 (1973).

[10] H. v. Pechmann and L. Seeberger, *Chem. Ber.*, **27**, 2121 (1894); R. Huisgen, M. Seidel, G. Wallbillich and H. Knupfer, *Tetrahedron*, **17**, 3 (1962).