



CRYSTAL STRUCTURES AND STABILITY OF HYDRATES AND DEUTERIOHYDRATES OF QUINOLINE N-OXIDES

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The protiated (H_2O) and deuterated (D_2O) crystallohydrates of quinoline N-oxide, 2-methylquinoline N-oxide and 4-methylquinoline N-oxide demonstrate different behavior at ambient conditions, namely, the deuterated dihydrates undergo solid state transformation into crystalline anhydrous or hemihydrate forms, while protiated dihydrates loss 3D periodicity. In attempts to explain this phenomenon, the crystal structures of the six compounds – namely, quinoline N-oxide and quinoline N-oxide dihydrate, 2-methylquinoline N-oxide hemideuteriohydrate and 4-methylquinoline N-oxide dihydrate, 4-methylquinoline N-oxide and 4-methylquinoline N-oxide dihydrate – were analyzed.

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calculations of model crystalline samples, for example, such as hydrated and deuterated quinoline N-oxide and its derivatives.

Recently, we have published the results of spectral and thermochemical investigation of physicochemical properties of quinoline N-oxide crystallohydrates with H_2O and D_2O .¹² We established that at boiling quinoline N-oxide in D_2O proceeds chemical reaction affording isoindoline-1,3-dione (phthalimide), that was not a case at boiling quinoline N-oxide in H_2O . Also we have found, that quinoline N-oxide form a stable dihydrate with two independent and energetically different H_2O molecules, and complete dehydration of quinoline N-oxide occurs when temperature reaches 150 °C. Later we have discovered that deuterated quinoline N-oxide, which is isostructural with the dihydrated protiated form, transforms into anhydrous crystalline form at ambient conditions within an hour. The same difference in the dehydration processes has been observed for protiated (H_2O) and deuterated (D_2O) crystallohydrates of 2-methylquinoline N-oxide and 4-methylquinoline N-oxide. Trying to find the possible reasons of this difference in conditions of dehydration between the protiated and deuterated crystallohydrates of quinoline N-oxides, the crystal structures of the six compounds – namely, quinoline N-oxide (**1**) and quinoline N-oxide dihydrate (**1d**, **d** – dihydrate),¹³ 2-methylquinoline N-oxide hemideuteriohydrate ($0.5D_2O$) (**2h**, **h** – hemideuteriohydrate) and 2-methylquinoline N-oxide dihydrate (**2d**), 4-methylquinoline N-oxide (**3**) and its dihydrate (**3d**) – were analyzed. Compounds **1**, **2h** and **3** were obtained as microcrystalline powders from the corresponding dideuteriohydrates ($.2D_2O$) after one hour exposure at ambient conditions ($T = 25$ °C).

Introduction

The field of isotope effects has expanded exponentially in the last years.¹ A quick glance in recent publications shows that researchers examine isotope effects on hydrogen bond structure,^{2,3} conformational changes,⁴ the end product of organic reaction,^{5,6} volumetric properties of dilute solutions⁷ among many others phenomena. Moreover, the effect of the replacement of hydrogen (H) with deuterium (D) in biological systems is well documented,^{8,9} and the possible role of naturally occurring D in the living organism has been investigated. As brief examples of the latter, Somlyai with colleagues¹⁰ have shown that naturally occurring deuterium is essential for the normal growth rate of cells, and Olgun¹¹ concluded that deuteration may interfere with the conformations and functions of many macromolecules and contribute to some pathologies like heavy water toxicity and aging. The aforementioned examples demonstrate the need for more detailed studies on the nature of these effects with the use of quantum chemical calculations.

The reliability of the results obtained by these computational methods in the case of bulky three-dimensional object has to be supported by the preliminary

Experimental

All reagents were of commercial quality and were used as received. Solvents were dried and purified using standard techniques.

Compounds **1**, **2** and **3** were initially obtained as amorphous viscous mass from the corresponding quinolines by oxidation with the hydrogen peroxide in accordance with the known procedure.¹⁴ N-oxides dihydrates were obtained by recrystallization from H₂O. Deuteriohydrates were obtained by dehydration of hydrates in the presence of P₂O₅ to the constant mass and dissolution of the obtained N-oxides in the minimal amount of D₂O at room temperature. The solutions thus obtained were stored in the presence of P₂O₅ until formation of heterogenic mixture of the crystals and liquid phase. Selected crystals were quickly grinded into powder and measured on powder diffractometer within 5 min to be sure the samples are isostructural to corresponding dihydrates **1d**, **2d** and **3d**. Powder samples of the compounds **1**, **2h** and **3** were obtained from the corresponding deuteriohydrates **1d**, **2d** and **3d** after they were kept for 1 h in an open air at ambient conditions.

X-Ray Crystallography

The solid state crystal structures of compounds **2d** and **3d** (Table 1) were obtained from X-ray single-crystal diffraction data, collected using a CAD4 (CuK α radiation) diffractometer. Crystal structures of compounds **1**, **2h** and **3** (Table 2) were determined by powder diffraction methods.¹⁵ with the use of powder patterns measured with a G670 Guinier camera diffractometer (CuK α radiation) at ambient conditions ($T = 295(2)$ K).

Table 1. Crystal data for **2d** and **3d** (single-crystal samples).

	2d	3d
CCSD number	978214	978216
Empirical formula	C ₁₀ H ₉ NO.2H ₂ O	C ₁₀ H ₉ NO.2H ₂ O
FW	195.21	195.21
Crystal size, mm ³	0.50x0.15x0.10	0.20x0.20x0.10
Crystal form, colour	prism, colourless	prism, colourless
Crystal system	Monoclinic	Triclinic
Space group	<i>P2₁/c</i>	<i>P-1</i>
Unit cell dimensions		
<i>a</i> / Å	6.772(5)	6.815(4)
<i>b</i> / Å	15.829(5)	8.940(4)
<i>c</i> / Å	9.608(2)	9.100(4)
α / °	90	107.83(3)
β / °	106.39(4)	110.45(4)
γ / °	90	92.03(4)
<i>V</i> / Å ³	988.0(8)	488.2(5)
<i>Z</i>	4	2
Radiation	CuK α	CuK α
μ / mm ⁻¹	0.807	0.816
No. reflns	2474/1870	2014/1846
collected/independent	[<i>R</i> (int) = 0.117]	[<i>R</i> (int) = 0.036]
No. params/restraints	140/6	141/6
Final <i>R</i> indices	<i>R</i> (<i>F</i>) = 0.062 (876 reflns with <i>I</i> > 2 σ (<i>I</i>)), <i>wR</i> (<i>F</i> ²) = 0.212	<i>R</i> (<i>F</i>) = 0.068 (1059 reflns with <i>I</i> > σ (<i>I</i>)), <i>wR</i> (<i>F</i> ²) = 0.259
GOF	1.021	1.038

The crystal structures of **2d** and **3d** were solved with *SHELXS97* using direct methods, completed by subsequent Fourier syntheses, and refined with *SHELXL97*¹⁶ by full-matrix least-squares procedures on *F*². All non-hydrogen atoms were refined with anisotropic displacement

parameters. C-bound H atoms were placed in idealized positions and refined using a riding model. The crystalline water H atoms were located on a difference map and refined with O–H bond lengths restrained to 0.85(4) Å.

The monoclinic (**1** and **2h**) and triclinic (**3**) unit-cell dimensions were determined from powder patterns using three indexing programs: TREOR90,¹⁷ ITO¹⁸ and AUTOX.¹⁹ Based on systematic extinctions the space groups for **1** and **2h** were determined to be *Pn* and *C2/c*, respectively. For **3**, centrosymmetric space group *P-1* was assigned. The unit-cell parameters and space groups were further tested using a Pawley fit²⁰ and confirmed by crystal structure solution. The crystal structures have been solved with the use of simulated annealing technique.²¹ The molecular model for quinoline N-oxide has been taken from the Cambridge Structural Database (CSD, Version 5.33),²² and molecular models for 2- and 4-methylquinoline N-oxides were taken from the refined structures **2d** and **3d**, respectively. In the subsequent direct space search for each compound, the rigid molecular model without H atoms was used with the six varied degrees of freedom. In **2h**, the water O atom situated on a twofold rotational axis has been located on a difference Fourier map. The solution found was fitted with the program MRIA²³ in the bond-restrained Rietveld refinement using a split-type pseudo-Voigt peak profile function²⁴ and March-Dollase²⁵ formalism of preferred orientation correction.

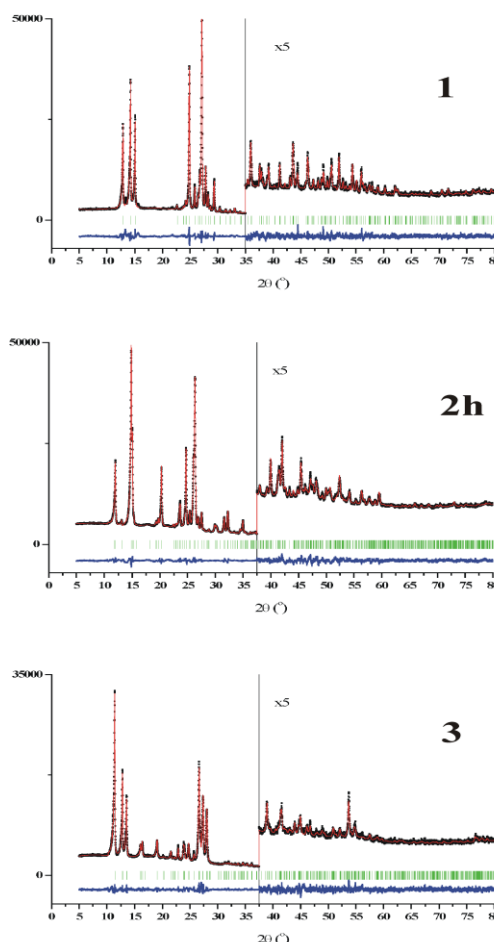


Figure 1. The final Rietveld plots for the patterns of **1** (top), **2h** (middle) and **3** (bottom) showing the experimental (black dots), calculated (red) and difference (blue) curves. The vertical bars denote calculated positions of the diffraction peaks.

Table 2. Crystal data for **1d**,¹³ **1**, **2h** and **3** (powder samples).

	1d ¹³	1	2h	3
CCSD number	193774	978212	978213	978215
Empirical formula	C ₉ H ₇ NO.2H ₂ O	C ₉ H ₇ NO	C ₁₀ H ₉ NO.0.5D ₂ O	C ₁₀ H ₉ NO
FW		145.16	169.19	159.18
Particle morphology, colour	prism, colourless	platelets, colourless	prism, colourless	prism, colourless
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	<i>P2₁/n</i>	<i>Pn</i>	<i>C2/c</i>	<i>P-1</i>
Unit cell dimensions				
<i>a</i> , Å	9.484(3)	12.6462(14)	12.7754(15)	7.7500(8)
<i>b</i> , Å	16.235(5)	3.7354(7)	9.7518(8)	8.6446(12)
<i>c</i> , Å	6.907(2)	7.4642(9)	14.6743(17)	6.8282(8)
α , °	90	90	90	103.93(2)
β , °	118.25(2)	100.297(17)	112.81(2)	105.26(2)
γ , °	90	90	90	65.31(2)
<i>V</i> /Å ³	936.8(8)	346.92(9)	1685.2(3)	396.50(8)
<i>Z</i>	4	2	8	2
Radiation	CuK α 1	CuK α 1	CuK α 1	CuK α 1
μ , mm ⁻¹		0.744	0.728	0.697
2 θ _{min} – 2 θ _{max} , increment		5.00 – 80.00, 0.01	5.00 – 80.00, 0.01	5.00 – 80.00, 0.01
No. params/restraints		73/45	79/53	77/51
<i>R_p</i> / <i>R_{wp}</i> / <i>R_{exp}</i> **		0.038/0.051/0.018	0.022/0.028/0.015	0.030/0.040/0.019
GOF		2.658	1.734	1.937

** *R_p*, *R_{wp}* and *R_{exp}* are defined according to Ref.²⁹

Restraints were applied to the intramolecular bond lengths and contacts (<2.8 Å), the strength of the restraints was a function of interatomic separation and, for intramolecular bond lengths, corresponded to r.m.s. deviation 0.02 Å. Additional restraints were applied to the planarity of the molecular skeleton, with the maximal allowed deviation from the mean plane 0.03 Å. All non-H atoms were refined isotropically. In all structures, H and D atoms were positioned geometrically (C-H 0.93-0.96 Å; O-D 0.88 Å) and not refined. The diffraction profiles for all compounds after the final bond-restrained Rietveld refinements are shown

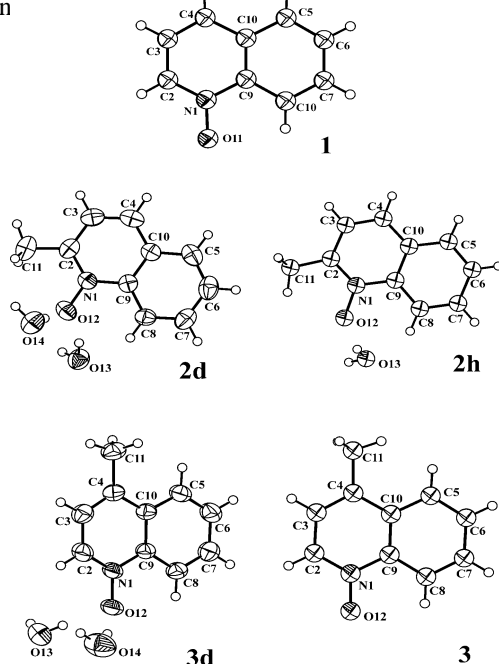


Figure 2. The content of asymmetric unit in the investigated compounds showing the atomic numbering and 50 % probability displacement ellipsoids for **2d** and **3d**, and spheres for **1**, **2h** and **3**.

Results and Discussion

The crystal structures **1**, **2h**, **2d**, **3** and **3d**²⁶ (Figure 2, drawn with *PLATON*²⁷) are new, and, therefore, they will be briefly discussed here.

In **1**, the short axis *b* [= 3.7354(7) Å] reveals an existence of $\pi \dots \pi$ interactions between the quinoline N-oxide molecules, which form stacks in [010]. Weak intermolecular C – H ... O interactions (Table 3) link further these stacks into layers parallel to (101) (Figure 3; Figures 3 – 7 drawn with *Mercury*²⁸).

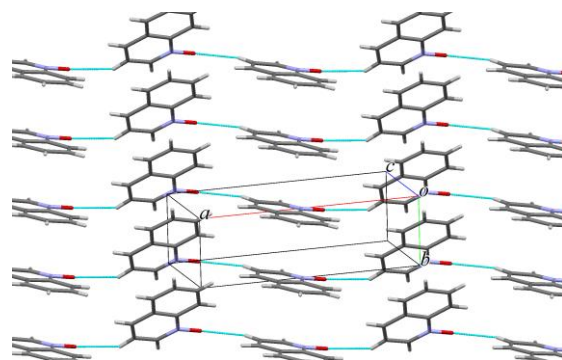


Figure 3. A portion of the crystal packing in **1**, showing the stacks of the molecules and weak C – H ... O interactions as green thin lines.

In **2h**, the lattice water molecule (D₂O) situated on two-fold rotational axis is hydrogen-bonded (Table 3) with two 2-methylquinoline N-oxide (*M*) molecules thus forming the 2*M*.D₂O structural unit. Further, these 2*M*.D₂O units interact through $\pi \dots \pi$ interactions proved by short distance of 3.643(8) Å between the centroids of aromatic rings, so 2*M*.D₂O units are arranged into chains extended in [10-1] (Figure 4). Finally, weak intermolecular C – H ... O hydrogen bonds (Table 3) consolidate the crystal packing.

Table 3. Hydrogen-bonding geometry (Å, °) in **1**, **2h**, **2d** and **3d**.

	D–H...A	D–H	H...A	D...A	D–H...A
1	C3–H3...O11 ⁱ	0.93	2.58	3.236(14)	128
2h	O13–D13...O12	0.88	2.00	2.866(12)	167
	C3–H3...O13 ⁱⁱ	0.93	2.45	3.320(10)	155
	C5–H5...O13 ⁱⁱⁱ	0.93	2.57	3.325(11)	139
2d	O13–H131...O14 ^{iv}	0.85(3)	1.97(4)	2.817(5)	174(4)
	O13–H132...O12	0.85(4)	1.98(3)	2.815(5)	165(4)
	O14–H141...O12	0.85(4)	1.99(3)	2.836(5)	173(4)
	O14–H142...O13 ^v	0.85(2)	2.02(2)	2.861(5)	171(3)
3d	O13–H131...O12	0.85(5)	1.94(5)	2.778(5)	167(5)
	O13–H132...O14 ^{iv}	0.84(6)	2.09(6)	2.819(7)	145(6)
	O14–H141...O12	0.85(6)	1.96(7)	2.797(6)	169(7)
	O14–H142...O13 ^{vi}	0.85(5)	1.94(5)	2.784(6)	170(8)

Symmetry codes: (i) $x+1/2, -y, 1/2+z$; (ii) $-1/2+x, 1/2+y, z$; (iii) $-1/x, -1/2+y, z$; (iv) $-1+x, y, z$; (v) $1+x, 1/2-y, 1/2+z$; (vi) $-x, -y, -z$.

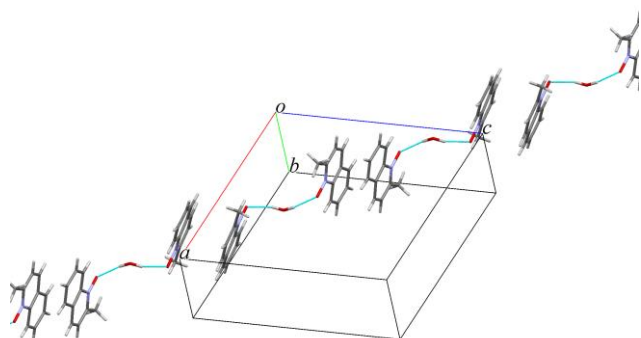


Figure 4. A portion of the crystal packing in **2h**, showing the $2M.D_2O$ structural units ($M = 2$ -methylquinoline N-oxide) linked through $\pi \dots \pi$ interactions into chains in $[10-1]$. Thin green lines denote $O-H \dots O$ hydrogen bonds.

In **2d**, the 2-methylquinoline N-oxide molecules form stacks in $[100]$ with the short distances of 3.614(8) and 3.755(9) Å between the centroids of aromatic rings within the stack. The lattice water molecules filling the space between the stacks are involved in $O-H \dots O$ hydrogen bonding (Table 3) thus consolidating the crystal packing (Figure 5).

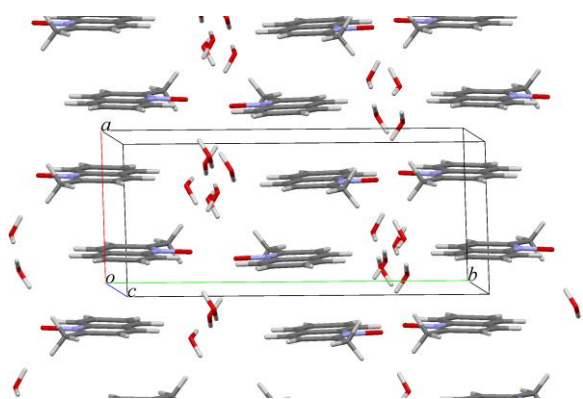


Figure 5. A portion of the crystal packing in **2d**, showing the stacks of the molecules and lattice water molecules filling the space between them.

In **3**, the 4-methylquinoline N-oxide molecules form stacks in $[001]$ with the shortest distances of 3.516(7) and 3.690(9) Å between the centroids of aromatic rings within the stack. The weak Van der Waals interactions consolidate further the crystal packing (Figure 6).

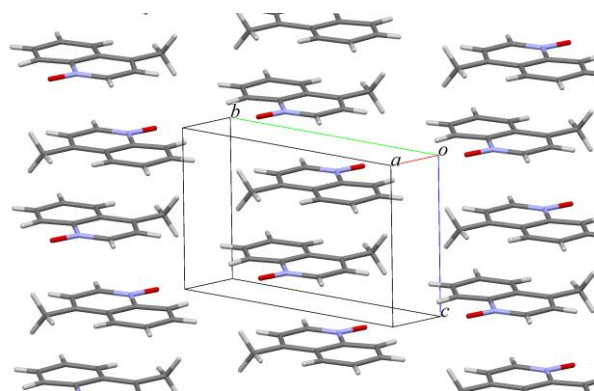


Figure 6. A portion of the crystal packing in **3**, showing the stacks of the molecules.

The crystal packing of **3d** is similar to that in **2d**. The 4-methylquinoline N-oxide molecules form stacks in $[100]$ with the short distances of 3.669(7) and 3.696(7) Å between the centroids of aromatic rings within the stack. The lattice water molecules fill the space between the stacks and participate in $O-H \dots O$ hydrogen bonding (Table 3) thus consolidating the crystal packing (Figure 7).

The crystal structures of the five compounds discussed in this paper (**1**, **1d**, **2d**, **3** and **3d**) contain stacks of the molecules, which aggregate further either through $O-H \dots O$ hydrogen bonds in the dihydrates **1d**, **2d** and **3d**, or *via* weak non-classical $C-H \dots O$ hydrogen bonds and Van der Waals interactions in the anhydrous forms **1** and **3**. Comparing the crystal structures of **1d** and **3d** with their anhydrous forms **1** and **3**, respectively, one can suggest a simple model of the dehydration process based on the destruction of $O-H(D) \dots O$ hydrogen bonds, elimination of the $H(D)_2O$ molecules from the channels between the stacks and subsequent convergence, or collapse, of the stacks.

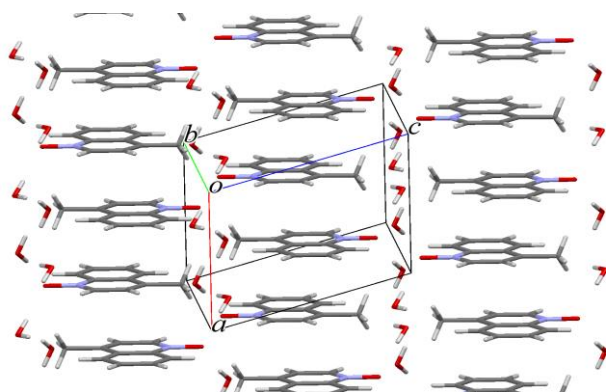


Figure 7. A portion of the crystal packing in **3d**, showing the stacks of the molecules and lattice water molecules filling the space between them.

This model assumes that $\pi \dots \pi$ interactions are most important in our compounds, because they pack the molecules into stacks which serve as rigid building blocks in further solid state transformations. However, the transformation **2d** \rightarrow **2h** can not be described in the framework of the aforementioned model of dehydration. Indeed, stacks of the 2-methylquinoline N-oxide molecules observed in **2d** are absent in **2h**. It means that stacks of the quinoline N-oxide molecules can not be considered as rigid building blocks in the hydration/dehydration process. A proper model for such process should take into account a competition between various intermolecular interactions.

Our attempts to obtain at ambient conditions anhydrous forms **1**, **2**, **3** and a hemihydrate form **2h**, starting from the corresponding dihydrates ($2\text{H}_2\text{O}$) resulted in their transformation into liquid state caused by an absorption of atmospheric water molecules. Attempts to reproduce these solid state transformations at room temperature *in vacuo* failed too – all crystallites were destroyed and transformed into amorphous state. Therefore, we conclude that protiated (H_2O) and deuteriated (D_2O) dihydrates of (2- and 4-methyl) quinoline N-oxides demonstrate different behavior at ambient conditions, namely, the deuteriated dihydrates undergo solid state transformation into crystalline anhydrous or hemihydrate forms, while protiated dihydrates loss 3D periodicity. A comparison of the crystal structures of crystallohydrates **1d**, **2h**, **2d**, **3d** and anhydrous forms **1** and **3** does not allow us to explain properly this phenomenon – further experimental studies are required.

References

- Kohen, A., Limbach, H.-H., (Eds), *Isotope Effects in Chemistry and Biology*. CRC Press/Taylor and Francis Group: Boca Raton, FL, **2006**.
- Rich, C. C., McHale, J. L., *Phys. Chem. Chem. Phys.*, **2012**, *14*, 2362.
- Arai, H., Horikawa, Y., Sadakane, K., Tokushima, T., Harada, Y., Senba, Y., Ohashi, H., Takata, Y., Shin, S., *Phys. Chem. Chem. Phys.*, **2012**, *14*, 1576.
- Hatano, N., Watanabe, M., Takekiyo, T., Abe, H., Yoshimura, Y., *J. Phys. Chem. A*, **2012**, *116*, 1208.
- Dougan, B.A., Xue, Z.L., *Science China – Chem.*, **2011**, *54*, 1903–1908.
- Segapelo, T. V., Guzei, I. A., Spencer, L. C. and Darkwa, J., *Inorg. Chem. Commun.*, **2011**, *14*, 1706.
- Ivanov, E.V., *J. Chem. Thermodyn.*, **2012**, *47*, 162.
- Rundel, P.W., Ehleringer, J.R., Nagy, K.A., *Stable isotopes in Ecological Research*, Springer, New York, **1988**.
- Katz, J.J., Crespi, H.L., in: *Isotope Effects in Chemical Reactions* (C.J. Collins and N.S. Bowman, Eds.), Van Nostrand Reinhold, New York, pp. 286–363, **1971**.
- Somlyai, G., Jancso, G., Jakli, G., Vass, K., Barna, B., Lakics, V., Gaal, T., *FEBS Lett.* **1993**, *317*, 1.
- Olgun, A., *Theor. Biol. Med. Model.*, **2007**, *4*.
- Gubarev, Yu. A., Lebedeva, N. Sh., Andreev, V. P., Girichev, G.V., *Russ. J. General Chem.*, **2008**, *79*, 1183.
- Ivashevskaja, S. N., Aleshina, L. A., Andreev, V. P., Nizhnik, Y. P., Chernyshev, V. V., *Acta Cryst.*, **2002**, *E58*, o920.
- Ochiai, E., *J. Org. Chem.*, **1953**, *18*, 534.
- (a) Harris, K. D. M.; Tremayne, M.; Lightfoot, P.; Bruce, P. G., *J. Am. Chem. Soc.*, **1994**, *116*, 3543; (b) Harris, K. D. M.; Tremayne, M.; Kariuki, B. M., *Angew. Chem., Int. Ed.*, **2001**, *40*, 1626; (c) Chernyshev, V. V., *Izv. Akad. Nauk, Ser. Khim.*, **2001**, 2171 (In Russian) [*Russ. Chem. Bull.*, **2001**, *50*, 2273]; (d) David, W. I. F., Shankland, K., McCusker, L. B., Baerlocher, C., (Eds.) *Structure Determination from Powder Diffraction Data*, OUP/IUCr, **2002**; (e) Cheung, E. Y., Kitchin, S. J., Harris, K. D. M., Imai, Y., Tajima, N., Kuroda, R., *J. Am. Chem. Soc.*, **2003**, *125*, 14658; (f) Tremayne, M. *Phil. Trans. Roy. Soc.*, **2004**, *362*, 2691; (g) Favre-Nicolin, V., Cerny, R., *Z. Kristallogr.*, **2004**, *219*, 847; (h) Tsue, H., Horiguchi, M., Tamura, R., Fujii, K., Uekusa, H., *J. Synth. Org. Chem. Japan*, **2007**, *65*, 1203; (i) David, W. I. F., Shankland, K., *Acta Cryst.*, **2008**, *64*, 52.
- Sheldrick, G. M., *Acta Cryst.*, **2008**, *A64*, 112.
- Werner, P.-E., Eriksson, L., Westdahl, M., *J. Appl. Cryst.*, **1985**, *18*, 367.
- Visser, J. W., *J. Appl. Cryst.*, **1969**, *2*, 89.
- (a) Zlokazov, V. B., *J. Appl. Cryst.*, **1992**, *25*, 69; (b) Zlokazov, V. B., *Comput. Phys. Commun.*, **1995**, *85*, 415.
- Pawley, G. S., *J. Appl. Cryst.*, **1981**, *14*, 357.
- Zhukov, S. G., Chernyshev, V. V., Babaev, E. V., Sonneveld, E. J., Schenk, H., *Z. Kristallogr.*, **2001**, *216*, 5.
- Allen, F. H., *Acta Cryst.*, **2002**, *B58*, 380.
- Zlokazov, V. B., Chernyshev, V.V., *J. Appl. Cryst.*, **1992**, *25*, 447.
- Toraya, H., *J. Appl. Cryst.*, **1986**, *19*, 440.
- Dollase, W. A., *J. Appl. Cryst.*, **1986**, *19*, 267.
- The crystal structures **1**, **2h**, **2d**, **3** and **3d** were deposited with CCDC (Nos. 978212–978216). These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033.
- Spek, A. L. *J. Appl. Cryst.* **2003**, *36*, 7.
- Macrae, C. F., Bruno, I. J., Chisholm, J. A., Edgington, P. R., McCabe, P., Pidcock, E., Rodriguez-Monge, L., Taylor, R., van de Streek, J., Wood, P. A., *J. Appl. Cryst.*, **2008**, *41*, 466.
- Young, R. A., Wiles, D. B., *J. Appl. Cryst.*, **1982**, *15*, 430.

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