Asian Journal of Chemistry Vol. 20, No. 6 (2008), 4706-4712

Synthesis and Conformational Analysis of 3,5,7-Triaryl-1,3,5,7-oxatriazocanes

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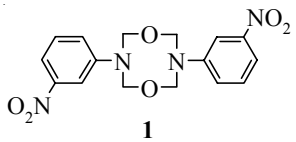
By condensation of arylamines and formaldehyde in equimolar ratio, using formic acid as catalyst and acetonitrile as a solvent at room temperature, 3,5,7-triaryl-1,3,5,7-oxatriazocanes (**2-5**) were formed. The composition and structural formula of all compounds were confirmed by elemental analysis, IR, MS and NMR spectroscopy methods. Theoretical calculation were used for conformational analysis of 3,5,7-tri(4-chlorophenyl)-1,3,5,7-oxatriazocane in the gas phase at HF/3-21+g(d,p) level of computational study. Results show that stability of various structures are in the order: crown > saddle > boat chair family.

Key Words: 3,5,7-Triaryl-1,3,5,7-oxatriazocane, *ab initio* Calculation, Conformational analysis.

INTRODUCTION

Cyclooctanes have been studied by numerous methods such as dipole moment and electron diffraction measurements, infrared, Raman, nuclear magnetic resonance (NMR) and X-ray diffraction[1-8]. Cyclooctane could exist in some conformations, in which boat-chair and crown are usually known as the most stable conformation. Compounds with special substitution patterns or with heteroatoms often exist partially or mainly in crown conformation[9,10]. Replacement of CH_2 group in cyclooctane by heteroatomes such as N, O and S leads to different conformational structures[11-14]. In our proceeding paper, we reported the synthesis, conformation analysis, X-ray structural determination and anomeric effect of 3,7-diaryl-1,5-dioxa-3,7-diazacyclooctane (**1**)[15,16]. In the present work, we report the synthesis of 3,5,7-triaryl-1,3,5,7-oxatriazocane along with theoretical calculation and conformational analysis of 3,5,7-tri(4-chlorophenyl)-1,3,5,7-oxatriazocane in the gas phase at HF/3-21+g(d,p) computational level.



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EXPERIMENTAL

All commercially available chemical reagents were used without further purification. Melting points were determined with an electrothermal 9200 apparatus and are uncorrected. Elemental analyses were carried out using a C, H, N Rapid-Heraeus apparatus. Mass data was obtained on a FISONS TRIO 1000 GC-Mass instrument. Infrared spectrum was recorded on a Shimadzu 4300 spectrometer. The NMR spectrum was recorded on a Brucker DRX-500 Avance spectrometer.

Synthesis of 3,5,7-tri(4-chlorophenyl)-1,3,5,7-oxatriazocane (2): To a stirred solution of 4-chloroaniline (1.91 g, 15 mmol) and formic acid (0.1 g, of 98 % aqueous solution, 2.2 mmol) in acetonitrile (75 mL) at 25 °C, formaldehyde (1.62 g, of 37 % aqueous solution, 20 mmol) was added slowly. The solution was stirred at room temperature for 24 h until a white precipitate was formed. The mixture was filtered, the precipitate washed with cold acetonitrile and recrystallized from THF. Yield: 0.90 g (84 %), m.p. 240 °C. IR (KBr, ν_{max}, cm^{-1}): 1595, 1490 (C=C), 1409, 1363 (CH_2), 1257, 1165 (C-N), 1022 (C-O), 962, 927 C-Cl). ^{1}H NMR (Acetone-d_6, 30 °C) ppm: 6.66, 6.68, 7.33, 7.35 (dd, 8H, J = 8.98 Hz), 7.06, 7.07, 7.29, 7.30 (dd, 4H, J = 8.61 Hz), 4.99 (s, 4H, CH_2), 4.95 (s, 4H, CH_2). ^{1}H NMR (Pyridine-d_5, 25 °C) ppm: 6.68, 6.69. 7.28, 7.29 (dd, 8H, J = 7.65 Hz), 6.70, 6.71, 7.23, 7.24 (dd, 4H, J = 7.34 Hz), 4.94 (s, 4H, CH_2), 4.83 (s, 4H, CH_2). ^{13}C NMR (Pyridine-d_5, 25 °C) ppm: 146.54, 146.37, 136.76, 136.67, 130.71, 130.29, 116.46, 116.29, 67.41, 62.73. The EI-MS, m/z: 454 (m^+), 368, 183, 155, 77. Elemental analysis calculated for $C_{22}H_{20}N_3OCl_3$: C, 58.66; H, 4.44; N, 9.33; Cl, 23.66. Found: C, 58.64; H, 4.41; N, 9.36; Cl, 23.68. Condensation of 4-bromo-, 4-cyano- and 3-nitroaniline with formaldehyde under similar condition leads to **3-5**.

3: Yield: 1.75 g (60 %), m.p. 242 °C. IR (KBr, ν_{max}, cm^{-1}): 1585, 1492 (C=C), 1253, 1163 (C-N), 1016 (C-O), 927 (C-Br). ^{1}H NMR (Acetone-d_6, 25 °C) ppm: 6.67, 6.68, 7.34, 7.35 (dd, 8H, J = 8.97 Hz), 7.04, 7.06, 7.30, 7.31 (dd, 4H, J = 8.64 Hz), 5.00 (s, 4H, CH_2), 4.95 (s, 4H, CH_2). ^{13}C NMR (Acetone-d_6, 25 °C) ppm: 145.93, 145.86, 136.64, 136.51, 130.58, 130.17, 116.33, 116.16, 68.79, 63.03. The EI-MS, m/z: 584 (m^+), 368, 183, 155, 77. Elemental analysis calculated for $C_{22}H_{20}N_3OBr_3$: C, 45.28; H, 3.43; N, 7.20; Br, 41.16. Found: C, 45.27; H, 3.41; N, 7.21; Br, 41.17.

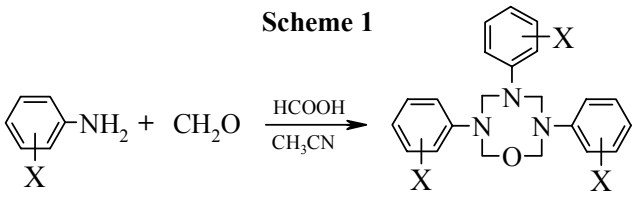
4: Yield: 0.75 g (38.4 %), m.p. 266 °C. IR (KBr, ν_{max}, cm^{-1}): 2224 (C=N), 1596, 1494 (C=C), 1313, 1217, 1161 (C-N), 995 (C-O). ^{1}H NMR (Acetone-d_6, 25 °C) ppm: 7.11, 7.12, 7.49, 7.48 (dd, 8H, J = 8.46 Hz), 7.27, 7.25, 7.46, 7.47 (dd, 4H, J = 7.45 Hz), 5.32 (s, 4H, CH_2), 5.20 (s, 4H, CH_2). The EI-MS, m/z: 423 (m^+), 146, 130, 104, 77. Elemental analysis calculated for $C_{25}H_{20}N_6O$: C, 71.43; H, 4.76; N, 20.00. Found: C, 71.38; H, 4.74; N, 20.03.

5: Yield: 0.26 g (28.8 %), m.p. 290 °C. IR (KBr, ν_{max}, cm^{-1}): 1618, 1537 (C=C), 1528, 1346 (NO2), 1450, 1408 (CH_2), 1274, 1205, 1164 (C-N), 1102 (C-O), 962, 927 (C-Cl). ^{1}H NMR (Acetone-d_6, 25 °C) ppm: 7.82-7.27 (m, 12H), 5.19 (s, 4H, CH_2), 5.16 (s, 4H, CH_2). The EI-MS, m/z: 484 (m^+), 166, 150, 138, 77. Elemental analysis calculated for $C_{22}H_{20}N_6O_7$: C, 55.00; H, 4.16; N, 17.50. Found: C, 55.97; H, 4.17; N, 17.39.

RESULTS AND DISCUSSION

Condensation was performed with formaldehyde and arylamines *via* a direct, one pot synthesis of 3,5,7-triphenyl-1,3,5,7-oxatriazocane derivatives (**2-5**). Substituents are including 4-chloro, 4-bromo, 4-cyano and 3-nitro phenyl (**Scheme-1**).

Scheme 1



2, X= 4-Cl
3, X= 4-Br
4, X= 4-CN
5, X= 4-NO_2

In the case of **2**, the EI mass spectrum, showed a molecular ion peak at m/z 454 and elemental analysis is consistent for $C_{22}H_{20}N_3OCl_3$. In the IR spectrum of **2** both amine and carbonyl absorptions did not observe. Characteristics of the proton spectrum are two singlet at δ 4.83 and 4.94 ppm for CH_2 and two doublet of doublet at 6.70, 6.71 and 7.23, 7.24 for CH aromatic rings protons. In ^{13}C NMR spectrum of **2** the carbon resonance of CH_2 groups is found to be at the 67.41 and 62.73 ppm. The aromatic carbons appeared at 116.29-146.54 ppm. The IR, ^{1}H and ^{13}C NMR data for compounds **3-5** are similar to those found for **2**. These previously unreported compounds were obtained from reaction mixture in a highly pure crystalline form in 30-60 % yield. Reactions are fast and complete in a few hours. Best yields are obtained at pH = 8-9 but drastically reduced under highly basic or acidic conditions. The composition and structural formula of **2-5** were confirmed by a combination of elemental analysis, IR, MS and NMR methods.

ab initio Calculations were applied for conformational analysis of 3,5,7-tri(4-chlorophenyl)-1,3,5,7-oxatriazocane in the gas phase at HF/3-21+g(d,p) computational levels. For these calculations crown, saddle and boat-chair were considered as possible conformers of 3,5,7-tri(4-chlorophenyl)-1,3,5,7-oxatriazocanes (Fig. 1).

Theoretical calculations show global minimums for crown, saddle and boat-chair conformers with differences in total energy -7.21, -5.82 and 0 relative to boat-chair as the less stable conformer, respectively. The calculated energy for different conformations is given in Table 1.

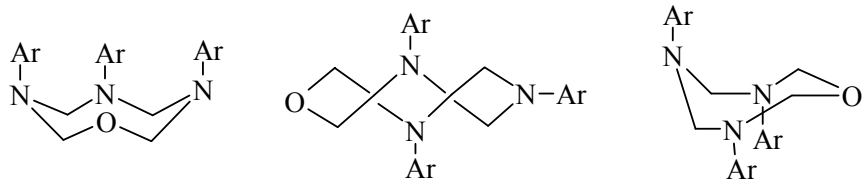


Fig. 1. Possible conformers of **2**

TABLE-1
CALCULATED TOTAL ENERGY, DIFFERENCE IN TOTAL ENERGY (ΔE) AND ZPVE for **2**

Conformer	Total energy (au)	ΔE (kcal mol^{-1})	ZPVE (au)
Crown	-2449.36787	-7.21	0.445726
Saddle	-2449.36565	-5.82	0.445029
Boat chair	-2449.356382	0	0.445580

The calculated energies correctly predict that the crown conformation is preferred over the saddle and boat-chair conformations (Fig. 2). Harmonic vibrational frequency calculations at HF/3-21+g(d,p) level confirmed the structures as minima and enabled the evaluation of zero-point vibrational energies (ZPVE). The torsional angles (ω) as well as other structural properties, bond length and bond angles were measured for previously optimized conformers crown, saddle and boat-chair (Tables 2-4).

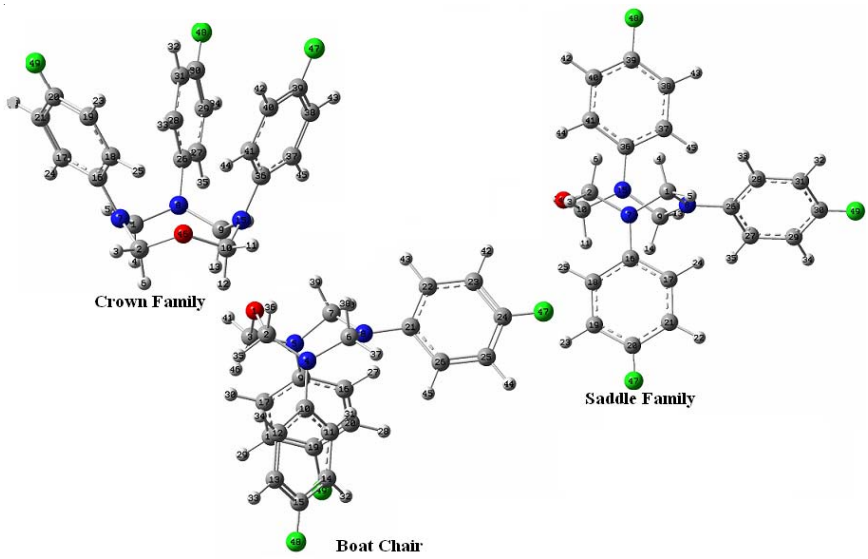


Fig. 2. Optimized Crown conformers of **2**

TABLE-2
CALCULATED GEOMETRICAL PROPERTIES FOR
CROWN CONFORMER OF **2** AT HF/3-21+G(d,p)

Bond length (Å)		Bond angles (º)		Torsion angles (º)	
O(1)-C(2)	1.45765	O(1)-C(2)-N(4)	113.4	O(1)-C(2)-N(4)-C(6)	65.3
O(1)-C(3)	1.43185	C(2)-N(4)-C(6)	117.7	O(1)-C(3)-N(5)-C(7)	-20.5
C(2)-N(4)	1.44040	O(46)-C(2)-N(7)	115.1	O(46)-C(2)-N(7)-C(1)	87.9
O(46)-C(10)	1.45600	C(2)-N(7)-C(1)	118.8	O(46)-C(10)-N(15)-C(9)	-82.2
O(46)-C(2)	1.45500	O(46)-C(10)-N(15)	115.4	C(10)-N(15)-C(9)-N(8)	88.7
C(10)-N(15)	1.43600	C(10)-O(46)-C(2)	119.9	N(15)-C(9)-N(8)-C(1)	-85.2
C(2)-N(7)	1.44200	N(15)-C(9)-N(8)	116.2	C(9)-N(8)-C(1)- N(7)	77.5
N(15)-C(9)	1.47100	C(10)-N(15)-C(9)	118.7	N(8)- C(1)-N(7)-C(2)	-79.5
N(7)-C(1)	1.47300	C(9)-N(8)-C(1)	120.1	O(46)-C(2)-N(7)-C(16)	-77.0
C(9)-N(8)	1.46100	N(7)-C(1)-N(8)	118.1	O(46)-C(10)-N(15)-C(36)	76.2
C(1)-N(8)	1.45800	C(10)-N(15)-C(36)	119.0	N(8)-C(1)- N(7)-C(16)	84.9
C(2)-H(6)	1.08200	(9)-N(15)-C(36)	118.7	N(8)-C(9)-N(15)-C(36)	-69.8
C(2)-H(3)	1.07600	C(9)-N(8)-C(26)	117.7	C(2)-O(46)-C(10)-H(12)	-39.5
C(10)-H(11)	1.07500	C(1)-N(8)-C(26)	121.2	C(2)-O(46)-C(10)-H(11)	-156.9
C(10)-H(12)	1.08200	C(1)-N(7)-C(16)	121.1	C(10)-O(46)-C(2)-H(3)	150.1
C(9)-H(13)	1.08100	C(2)-N(7)-C(16)	118.2	C(10)-O(46)-C(2)-H(6)	32.6
C(9)-H(14)	1.07600	O(46)-C(2)-H(3)	104.4	H(12)-C(10)-N(15)-C(36)	-161.7
C(1)-H(5)	1.07500	O(46)-C(2)-H(6)	108.7	H(11)-C(10)-N(15)-C(36)	-41.1
C(1)-H(4)	1.08200	O(46)-C(10)-H(11)	104.3	C(10)-N(15)-C(9)-H(13)	-32.9
N(15)-C(36)	1.42200	O(46)-C(10)-H(12)	108.3	C(10)-N(15)-C(9)-H(14)	-149.6
N(7)-C(16)	1.41800	N(7)-C(2)-H(3)	109.4	C(26)-N(8)-C(9)-H(13)	-155.9
N(8)-C(26)	1.43400	N(7)-C(2)-H(6)	109.0	C(26)-N(8)-C(9)-H(14)	-38.9
		N(7)-C(1)-H(4)	6.4	C(26)-N(8)-C(1)-H(5)	32.9
		06.4 N(7)-C(1)-H(5)	108.8	C(26)-N(8)-C(1)-H(4)	149.3
		N(8)-C(1)-H(4)	107.5	C(16)-N(7)-C(1)-H(5)	-37.9
		N(8)-C(1)-H(5)	107.5	C(16)-N(7)-C(1)-H(4)	-154.3
		N(8)-C(9)-H(13)	108.6	C(16)-N(7)-C(2)-H(3)	40.2
		N(8)-C(9)-H(14)	107.8	C(16)-N(7)-C(2)-H(6)	160.6
		N(15)-C(9)-H(13)	107.2		
		N(15)-C(9)-H(14)	108.6		
		N(15)-C(10)-H(11)	109.6		
		N(15)-C(10)-H(12)	108.9		

TABLE-3
CALCULATED GEOMETRICAL PROPERTIES FOR
ADDLE CONFORMER OF **2** AT HF/3-21+G(d,p)

Bond length (Å)		Bond angles (º)		Torsion angles (º)	
O(46)-C(10)	1.455	O(46)-C(2)-N(7)	115.1	O(46)-C(2)-N(7)-C(1)	105.1
O(46)-C(2)	1.455	C(2)-N(7)-C(1)	118.1	O(46)-C(10)-N(15)-C(9)	105.1
C(10)-N(15)	1.442	O(46)-C(10)-N(15)	115.1	C(10)-N(15)-C(9)-N(8)	-113.6
C(2)-N(7)	1.442	C(10)-O(46)-C(2)	121.1	N(15)-C(9)-N(8)-C(1)	36.7
N(15)-C(9)	1.458	N(15)-C(9)-N(8)	112.1	C(9)-N(8)-C(1)-N(7)	36.6
N(7)-C(1)	1.458	C(10)-N(15)-C(9)	118.1	N(8)-C(1)-N(7)-C(2)	-113.6
C(9)-N(8)	1.466	C(9)-N(8)-C(1)	118.3	O(46)-C(2)-N(7)-C(16)	-73.1

Bond length (Å)		Bond angles (º)		Torsion angles (º)	
C(1)-N(8)	1.466	N(7)-C(1)-N(8)	112.1	O(46)-C(10)-N(15)-C(36)	-73.2
C(2)-H(6)	1.076	C(10)-N(15)-C(36)	121.0	N(8)-C(1)- N(7)-C(16)	64.63
C(2)-H(3)	1.077	C(9)-N(15)-C(36)	120.8	N(8)-C(9)-N(15)-C(36)	64.6
C(10)-H(11)	1.076	C(9)-N(8)-C(26)	120.8	C(2)-O(46)-C(10)-H(12)	-153.0
C(10)-H(12)	1.077	C(1)-N(8)-C(26)	120.8	C(2)-O(46)-C(10)-H(11)	90.2
C(9)-H(13)	1.080	C(1)-N(7)-C(16)	120.8	C(10)-O(46)-C(2)-H(3)	-153.1
C(9)-H(14)	1.079	C(2)-N(7)-C(16)	121.0	C(10)-O(46)-C(2)-H(6)	90.1
C(1)-H(5)	1.080	O(46)-C(2)-H(3)	104.0	H(12)-C(10)-N(15)-C(36)	44.7
C(1)-H(4)	1.079	O(46)-C(2)-H(6)	108.1	H(11)-C(10)-N(15)-C(36)	165.6
N(15)-C(36)	1.405	O(46)-C(10)-H(11)	108.1	C(10)-N(15)-C(9)-H(13)	126.3
N(7)-C(16)	1.405	O(46)-C(10)-H(12)	104.0	C(10)-N(15)-C(9)-H(14)	8.7
N(8)-C(26)	1.398	N(7)-C(2)-H(3)	111.1	C(26)-N(8)-C(9)-H(13)	-21.8
		N(7)-C(2)-H(6)	108.5	C(26)-N(8)-C(9)-H(14)	96.7
		N(7)-C(1)-H(4)	107.2	C(26)-N(8)-C(1)-H(5)	-21.8
		[N(7)-C(1)-H(5)	110.5	C(26)-N(8)-C(1)-H(4)	96.7
		N(8)-C(1)-H(4)	111.2	C(16)-N(7)-C(1)-H(5)	-55.4
		N(8)-C(1)-H(5)	107.7	C(16)-N(7)-C(1)-H(4)	-173.1
		N(8)-C(9)-H(13)	107.7	C(16)-N(7)-C(2)-H(3)	44.7
		N(8)-C(9)-H(14)	111.2	C(16)-N(7)-C(2)-H(6)	165.6
		N(15)-C(9)-H(13)	110.4		
		N(15)-C(9)-H(14)	107.2		
		N(15)-C(10)-H(11)	108.5		
		N(15)-C(10)-H(12)	111.1		

TABLE-4
CALCULATED GEOMETRICAL PROPERTIES FOR
BOAT CHAIR CONFORMER OF **2** AT HF/3-21+G(d,p)

Bond length (Å)		Bond angles (º)		Torsion angles (º)	
O(1)-C(2)	1.45765	O(1)-C(2)-N(4)	113.4	O(1)-C(2)-N(4)-C(6)	65.3
O(1)-C(3)	1.43185	C(2)-N(4)-C(6)	117.7	O(1)-C(3)-N(5)-C(7)	-20.5
C(2)-N(4)	1.44040	O(1)-C(3)-N(5)	115.1	C(10)-N(4)-C(6)-N(8)	75.3
C(3)-N(5)	1.46652	C(3)-O(1)-C(2)	121.1	C(10)-N(4)-C(2)-O(1)	-105.2
N(4)-C(6)	1.45455	N(5)-C(7)-N(8)	112.1	C(10)-N(4)-C(2)-H(35)	16.1
N(5)-C(7)	1.45613	C(3)-N(5)-C(7)	118.1	C(10)-N(4)-C(2)-H(36)	139.0
C(6)-N(8)	1.48580	C(9)-N(8)-C(1)	118.3	C(10)-N(4)-C(6)-H(38)	-162.6
C(7)-N(8)	1.47668	N(4)-C(6)-N(8)	115.0	C(10)-N(4)-C(6)-H(37)	-45.2
C(2)-H(35)	1.07647	C(6)-N(8)-C(7)	117.4	C(21)-N(8)-C(7)-H(39)	-101.9
C(2)-H(36)	1.07616	N(8)-C(7)-N(5)	112.3	C(21)-N(8)-C(7)-H(40)	17.7
C(6)-H(37)	1.07783	N(5)-C(3)-O(1)	110.2	C(21)-N(8)-C(6)-H(38)	82.8
C(6)-H(38)	1.08553	C(2)-N(4)-C(10)	120.8	C(21)-N(8)-C(6)-H(37)	-35.2
C(3)-H(41)	1.07961	C(6)-N(4)-C(10)	120.8	N(4)-C(6)-N(8)-C(7)	55.7
C(3)-H(46)	1.08141	C(6)-N(8)-C(21)	115.6	C(6)-N(8)-C(7)- N(5)	-75.9
C(7)-H(39)	1.07789	C(7)-N(8)-C(21)	118.9	N(8)- C(7)-N(5)-C(3)	103.0
C(7)-H(40)	1.07781	C(7)-N(5)-C(9)	120.8	O(1)-C(3)-N(5)-C(9)	161.6
N(4)-C(10)	1.42080	C(3)-N(5)-C(9)	120.3	C(9)-N(5)-C(7)-H(39)	157.9
N(5)-C(9)	1.39204	O(1)-C(2)-H(35)	108.4	C(9)-N(5)-C(7)-H(40)	39.8
N(8)-C(21)	1.42490	O(1)-C(2)-H(36)	103.0	C(9)-N(5)-C(3)-H(41)	-81.4
		O(1)-C(3)-H(41)	105.4	C(9)-N(5)-C(3)-H(46)	40.5

Bond length (Å)	Bond angles (º)		Torsion angles (º)
	O(1)-C(3)-H(46)	110.2	
	N(4)-C(2)-H(35)	109.7	
	N(4)-C(2)-H(36)	111.5	
	N(4)-C(6)-H(37)	109.1	
	N(4)-C(6)-H(38)	106.9	
	N(8)-C(6)-H(37)	107.2	
	N(8)-C(6)-H(38)	109.8	
	N(8)-C(7)-H(39)	111.4	
	N(8)-C(7)-H(40)	107.6	
	N(5)-C(7)-H(39)	107.5	
	N(5)-C(7)-H(40)	108.8	
	N(5)-C(3)-H(41)	111.9	
	N(5)-C(3)-H(46)	109.1	

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(*Received*: 13 September 2007; *Accepted*: 10 March 2008) AJC-6445