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ORIGINAL RESEARCH

Synthesis, 1D and 2D NMR spectral assignments, and stereochemical studies of some 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-one oximes

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Abstract

A series of 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-one oximes (**4a-4e**) have been synthesized. ^{1}H and ^{13}C NMR spectra of these oximes were recorded. Chemical shifts have been assigned and the stereochemistry of the compounds was established using 1D and 2D NMR spectral data. A detailed spectral investigation was carried out for one of the representative compounds (**4a**) with COSY, NOESY, HMQC, HMBC, DEPT-135, and N NMR spectral data. The NMR result clearly indicated the twin chair conformation of the two piperidine rings. The NMR results proved the axial orientation of two aryl groups (C4 and C10) in one piperidine ring and equatorial orientation of two aryl groups (C8 and C9) in another piperidine ring. The effect of allylic ($A^{1,3}$) interaction between the oxime hydroxyl group and H-5e has been observed. Long-range coupling between H-10e and H-2 which are in 'W' arrangement is noted.

Keywords 2D NMR · ^{15}N NMR · Oxime · Tricyclic compound · Conformation · W arrangement

Introduction

The chemistry of bicyclic and tricyclic compounds containing piperidine nucleus is of great interest due to their stereochemical behavior and biological activities [1–5]. Synthesis, stereochemistry, and biological activities of azabicyclononanone and diazaadamantane derivatives have been widely reported [6–13]. Introduction of oxime functional group in the cyclic compounds have been used for some important pharmaceutical and synthetic chemistry applications, and often act as chemical building blocks for the synthesis of agrochemicals and pharmaceuticals [14, 15]. The Oximes show important biological activities such as antidepressants, analgesic, anti-inflammatory, fungicidal, antitumor, herbicides, and antimicrobial activity [16–22]. Besides, oximes being electron donor groups, they can be used as ligands which are effective in the DNA binding and cleavage activity of heterocyclic bases [23, 24]. The biological activity of the organic compounds depends primarily on the stereochemistry of the molecules and hence, it is essential to establish the configuration and conformation of the synthesized molecules [25, 26]. The oxime of diazabicyclic ketones have shown antimicrobial and antifungal activities and the stereochemistry of these compounds have been studied using 1D and 2D NMR spectroscopic techniques [27]. In continuation with our earlier work on 1,3-diazaadamantanan-6-ones [7], we report here the synthesis and stereochemical study of oximes of 4,8,9,10-tetraaryl substituted 1,3-diazaadamantan-6-ones using 2D-NMR spectroscopic techniques such as ^{1}H-^{1}H COSY, NOESY, TOCSY, HMQC, and HMBC.

Experimental

General procedure for the synthesis of compound 1a-1e and 2a-2e

Compounds 2,4,6,8-tetraaryl-3,7- diazabicyclo [3.3.1] nonan-9-ones (**1a-1e**) were synthesized as one-pot synthesis by double Mannich condensation of acetone, substituted benzaldehyde and ammonium acetate in 1:4:2 ratio in ethanol [9]. The bicyclic compounds (**1a-1e**) were converted into 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-ones by literature methods [7, 28] Scheme 1. Numbering and structure of the newly synthesized compounds shown in Scheme 2.

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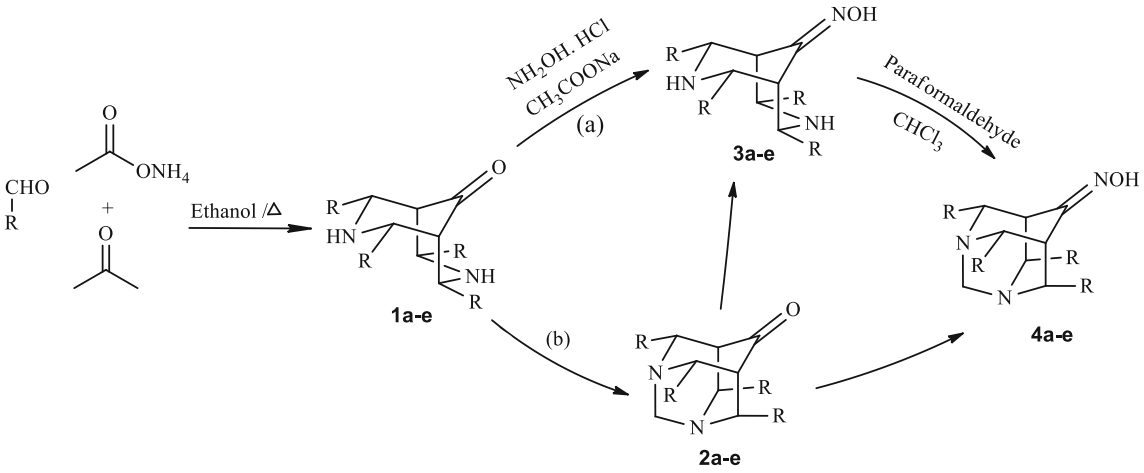


Compound **1-4**

a **b** **c** **d** **e**

R = C_6H_5, *p*-OCH_3 C_6H_5, *p*-Cl C_6H_5, *p*-CH_3 C_6H_5, *p*-F C_6H_5

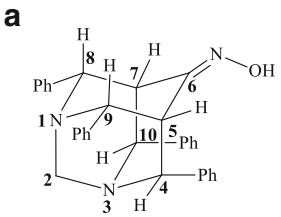
Scheme 1 Synthesis of 2,4,6,8-Tetraaryl-3,7- diazabicyclo [3.3.1] nonan-9-one (**1a-1e**), 4,8,9,10-Tetraaryl-1,3-diazatricyclo [3.3.1.1] decan-6-one (**2a-2e**), 4,8,9,10-Tetraaryl-1,3-diazabicyclo [3.3.1] nonan-9-one oxime (**3a-3e**), and 4,8,9,10-Tetraaryl-1,3-diaazaadamantane-6-one oxime (**4a-4e**)

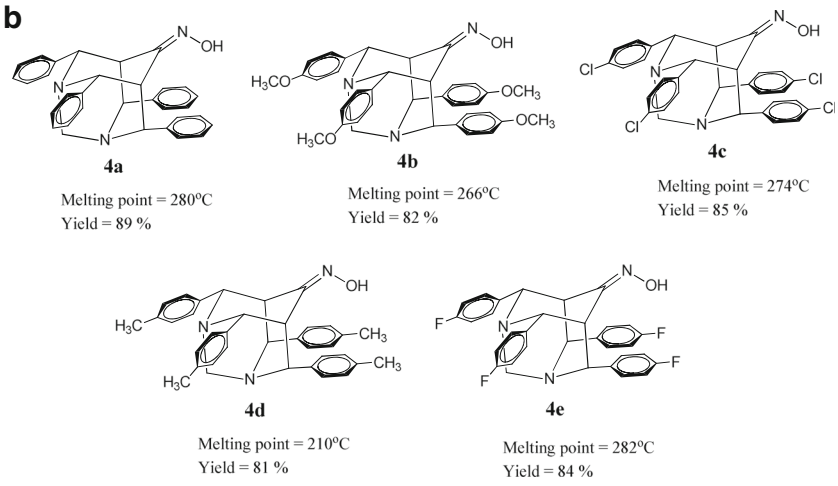
General procedure for the synthesis of Oximes (4a-4e)

Oximes (**4a-4e**) were synthesized by two methods:

a) Oximes of 2,4,6,8-tetraaryl-3,7- diazabicyclo [3.3.1] nonan-9-ones (**3a-3e**) were prepared by using the method already reported [9]. These oximes (**3a-3e**) were refluxed with paraformaldehyde in chloroform solvent for 3 h. After completion of the reaction, the solvent was removed and the resulting diazaadamantanone oximes were recrystallized using chloroform solvent.

Scheme 2 **a**) Numbering for 1D and 2D NMR spectral analysis of Compound **4a-4e**. **b**) Structure of the newly synthesized compounds (**4a-e**)





b) An attempt was made to synthesis the oximes (**4a-4e**) from 1,3-diazaadamantanones (**2a-2e**). Interestingly, the reaction yielded a mixture of oximes of diazabiclononanones (**3a-3e**) (predominantly) and oximes of diazaadamantanones (**4a-4e**).

Spectral measurements

General

Melting points were determined by the open capillary method. FT-IR spectra were recorded on a JASCO FT/IR-4700 instrument. All the NMR spectra were recorded on a Bruker AVANCE III HD 400 MHz spectrometer.

NMR spectra

Recording of one-dimensional NMR spectra

NMR spectra of all the synthesized compounds were recorded at 295–298 K. The 1D ^{1}H and ^{13}C NMR spectra were measured using 3 mg and 20 mg of compound dissolved in 0.5 ml of $CDCl_3$ solution respectively; TMS was used as internal standard, in ^{15}N NMR spectrum reference using formamide. The pulse conditions were as follows: **H NMR** spectra: number of data points (TD) 65,536, number of scans (NS) 16, dummy scans (DS) 2, spectra with (SWH) 8012.8 Hz, acquisition time (AQ) 4 s, spectrometer operating frequency 400.23, line broadening (LB) 0.30 Hz, Recycle Delay (D1) 1.0 s. **^{15}N NMR** spectra: TD 3276, NS 885, DS 4, SWH 20380.4 Hz, AQ 0.80 s, SF 40.554, LB 0.25 Hz, D1 10.0 s. **^{15}C NMR** spectra: TD 65536, NS 1024, DS 4, SWH 24038.4 Hz, AQ 1.3 s, SF 100.63, LB 1.00 Hz, D1 2.0 s. **DEPT 135**: TD 65536, NS 256, DS 8, SWH 16129 Hz, AQ 2.0 s, SF 100.63, LB 1.00 Hz, D1 2.0 s.

Recording of two-dimensional NMR spectra

All the 2D NMR spectra were recorded on the same instrument using 5 mg and 20 mg of compound dissolved in $CDCl_3$ solution. The pulse conditions were as follows: **^{1}H-^{1}H COSY**: TD 2048 (F2), TD 128 (F1) NS 1, DS 16, SWH 3571.4 Hz, AQ 0.28 s, SF 400.23, LB 0 Hz, D1 1.90 s. **NOESY**: TD 2048 (F2), TD 256 (F1) NS 4, DS 32, SWH 4132.2 Hz, AQ 0.24 s, SF 400.23, LB 0 Hz, D1 2.00 s. **TOCSY**: TD 2048 (F2), TD 256 (F1) NS 8, DS 16, SWH 4310.3 Hz, AQ 0.23 s, SF 400.23, LB 0 Hz, D1 2.01 s. **HMQC**: TD 1024 (F2), TD 128 (F1) NS 4, DS 16, SWH 3937 Hz, AQ 0.13 s, SF 400.23 (F2), SF 100.63 (F1), LB 0 Hz, D1 1.46 s. **HMBC**: the parameters were very similar to those used in the HMQC experiment, TD 2048 (F2), TD 128 (F1) NS 4, DS 16, SWH 3937 Hz, AQ 0.26 s, SF 400.23 (F2), SF 100.63 (F1), LB 0 Hz, D1 1.43 s.

Result and discussion

FT-IR

The FT-IR spectral values of the compounds **4a-4e** are shown in Table 1 and **4a** is considered as the representative compound. Formation of the product initially confirmed by FT-IR spectroscopy, which shows the disappearance of the carbonyl group stretching frequency and appearance of –OH and C=N stretching frequencies. The weak band at 3431 cm^{-1} corresponding to the oxime hydroxy group. The aromatic C–H and C=C frequency band appeared at 3031–3062 and 1492 cm^{-1} respectively. The aliphatic C–H deformation bands appeared at 2847–2955 cm^{-1}, refer to the methylene bridge and piperidine CH groups. The oxime C=N band is present at 1655 cm.

Proton NMR chemical shift analysis of 4,8,9,10-tetraphenyl-1,3-diazaadamantan-6-one oxime (4a)

In the proton NMR spectrum of **4a**, each of the benzylic protons (H-4,8,9 and 10) and bridged-head protons (H-5 and 7) gives rise to a distinct singlet. The bridge-head protons H-5 and H-7 appear as a broad singlet at δ 4.73 ppm with the half-with, $W_{1/2}$ of 6.28 Hz and at δ 3.85 ppm with the $W_{1/2}$ of 5.59 Hz respectively. The H-5 proton shows up in the downfield region due to $A^{1,3}$ allylic interaction (Fig. 1) of the oxime group [29]. The chemical shift differences between the two bridge-head protons $\Delta_{5,7}$ is δ 0.88 ppm,

Table 1 IR spectral data (cm^{-1}) of **4a–4e**

Entry	OH	C=N	Aromatic C–H stretching	Aliphatic C–H stretching	Aromatic C=C
4a	3431	1655	3059, 3031, 3062	2955, 2917, 2847	1492
4b	3413	1643	3174, 3050, 3027	2945,2921, 2868	1512
4c	3429	1631	3183, 3054	2947, 2878	1493
4e	3420	1611	3069	2996, 2947, 2833	1510
4d	3430	1604	3198, 3076	2947, 2884	1507

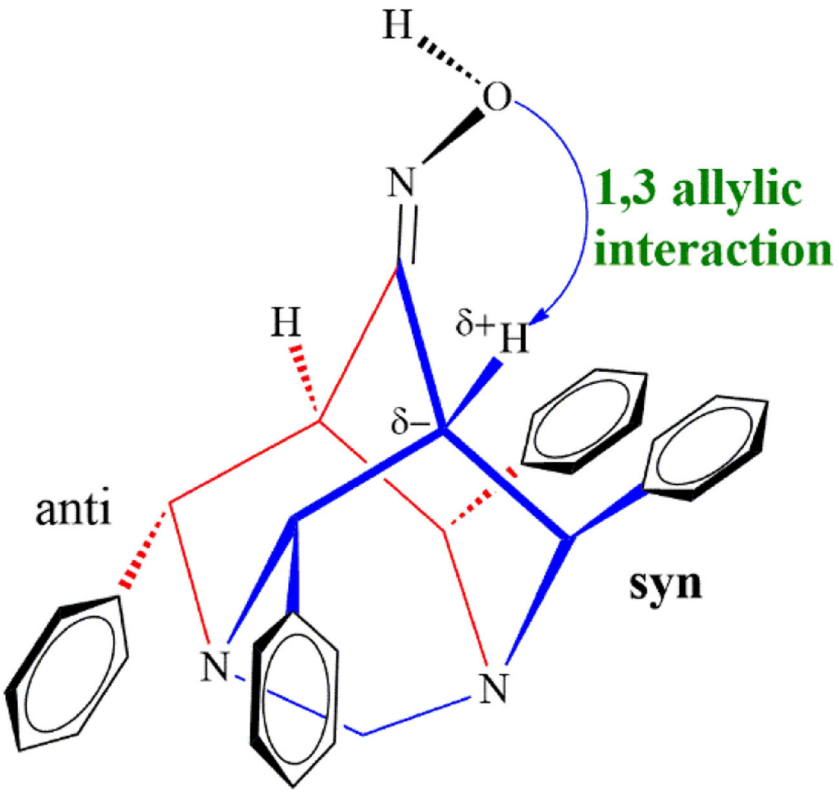


Fig. 1 Oxime hydroxy group and H-5 $A^{1,3}$ allylic interaction of compound **4a**

obviously by the allylic interaction present in the –C=N–O and H-5 proton. Due to this interaction, the H-5 and C-5 have acquired positive and negative charges respectively. Benzylic protons H-4 and H-9, adjacent to C5-H appear as a singlet at δ 4.66 ($W_{1/2}$ of 4.83 Hz) and at δ 4.70 ppm ($W_{1/2}$ of 5.92 Hz) respectively. Other two benzylic protons H-8 and H-10 resonate at δ 4.75 ($W_{1/2}$ of 7.03 Hz) and at δ 4.60 ppm ($W_{1/2}$ of 4.77 Hz) respectively. The signal at δ 7.75 ppm is due to oxime OH and it is confirmed by D_2O exchange analysis. ^{1}H NMR chemical shift values of five new oximes are given in Table 2. All the proton positions and chemical shift values are assigned and confirmed by ^{1}H-^{1}H COSY, NOESY, and TOCSY techniques. For better understanding, the ^{1}H-^{1}H COSY, TOCSY, and NOESY correlations are presented in Table 3. COSY and NOESY spectra are reproduced in Figs. 2 and 3 respectively.

Table 2 H NMR data of (δ, ppm) of **4a-4e**

Entry	H-2	H-4	H-5	H-7	H-8	H-9	H-10	N–OH[a]	Others
4a	4.37	4.66	4.73	3.85	4.75	4.70	4.60	7.75	–
4b	4.29	4.60[b]	4.65	3.73	4.60[b]	4.60[b]	4.54	7.75	3.62, 3.81
4c	4.26	4.51	4.66	3.71	4.61	4.58	4.45	7.58	–
4d	4.31	4.62[c]	4.56	3.78	4.67	4.66	4.62[c]	7.88	2.09, 2.35
4e	4.27	4.55	4.67	3.72	4.62	4.61	4.49	7.43	–
Entry	Aryl group protons attached at C4 and C10					Aryl group protons attached at C8 and C9			
	Ortho	Meta		Para		Ortho	Meta		Para
4a	7.14–7.16	6.80–6.83 (m)		6.76		7.64–7.70 (m)	7.38–7.43 (m)		7.30
4b	6.91–6.94 (m)	6.36 (d)		–		7.52–7.58 (m)	7.01–7.03		–
4c	6.99 (d)	6.82 (d)		–		7.50–7.56 (m)	7.37–7.40 (m)		–
4d	6.97 (d)	6.60 (d)		–		7.50–7.55 (m)	7.19 (t)		–
4e	7.05–7.08 (m)	6.54 (t)		–		7.55–7.62 (m)	7.10–7.13 (m)		–

[a] OH proton of the oxime is confirmed by identified by D_2O exchange

[b] Merged with H-9 and H-10

[c] Merged with H-8 and H-9

Table 3 Correlation in the ^{1}H-^{1}H COSY and NOESY chemical shift value of compound **4a**

Signal (in ppm)	Correlation in COSY	Correlation in NOESY	Correlation in TOCSY
4.37 (H-2)	–	4.60, 4.66, 7.64–7.70	4.60, 4.66, 4.70, 4.75
4.66 (H-4)	3.85, 4.60, 7.14–7.16	4.37, 7.14–7.16, 7.64–7.70	4.60, 4.70, 4.73, 6.80–6.83, 7.14–7.16
4.73 (H-5)	4.70, 4.75 (w)	–	3.85, 4.66, 4.70
3.85 (H-7)	4.60, 4.66, 4.75 (s)	4.60, 4.75, 7.14–7.16, 7.64–7.70	4.37, 4.60, 4.66, 4.75
4.75 (H-8)	3.85, 7.64–7.70	3.85, 7.14–7.16, 7.64–7.70	3.85, 4.37, 7.30, 7.38–7.43, 7.64–7.70
4.70 (H-9)	4.70, 7.64–7.70	7.14–7.16, 7.64–7.70	4.73, 7.30, 7.38–7.43, 7.64–7.70
4.60 (H-10)	3.85 (w), 7.14–7.16	3.85, 7.14–7.16, 7.64–7.70	3.85, 4.66, 4.75, 6.80–6.83, 7.14–7.16

w, weak correlation; *s*, strong correlation

In COSY, one of the bridge-head protons, H-7, is correlated with the two equatorial protons, H-4 and H-10, and one axial proton, H-8. Another bridge-head proton H-5 has COSY correlation with adjacent axial proton H-8 and H-9. There is a correlation of H-8 and H-9 with ortho protons of the C-8 and C-9 phenyl groups at δ 7.64–7.70 ppm. A similar observation is noted for another two benzylic protons at H-4, 10 and ortho protons of the C-4, 10 phenyl groups at δ 7.14–7.16 ppm. The long-range correlation is further assigned using TOCSY spectrum.

In the NOESY spectrum, H-5 and 7 protons have a correlation with all the ortho protons of the phenyl groups at C-4, 10, 8, and 9. H-7 proton has NOESY correlation with H-8, 10 protons. H-2 has a correlation with H-4, 10 and ortho protons of C-8, 9 phenyl groups. NOESY studies unequivocally proved the equatorial orientation of H-4,10 protons and axial orientation of H-8, 9 protons.

^{15}N NMR exhibit two signals, one at δ 199.98 ppm due to piperidine nitrogen and another at δ 406.94 ppm due to oxime nitrogen.

Carbon NMR chemical shift analysis of 4,8,9,10-tetraphenyl-1,3-diazaadamantan-6-one oxime (4a)

The ^{13}C NMR analysis for all the synthesized compounds have been carried out with the aid of DEPT-135, ^{1}H-^{13}C one bond correlations (HMQC) and ^{1}H-^{13}C multiple bond

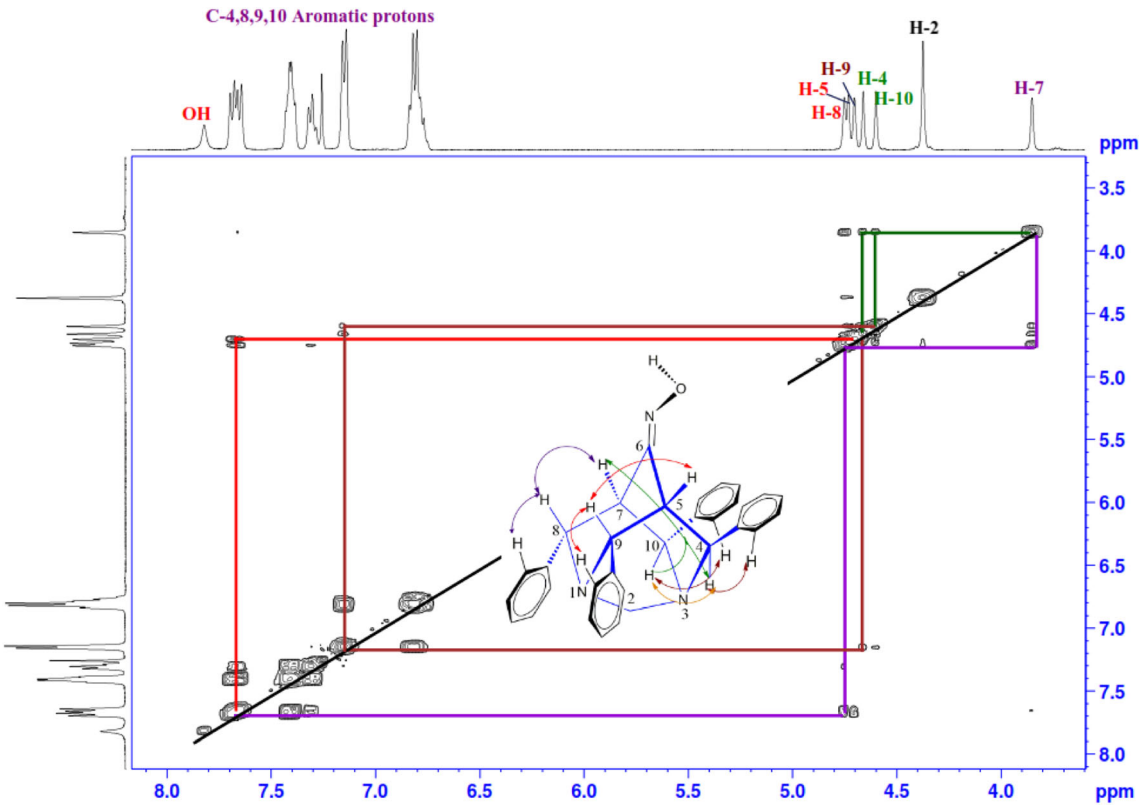


Fig. 2 COSY spectrum of 4,8,9,10-tetraphenyl-1,3-diaazaadamantane-6-one oxime **(4a)**

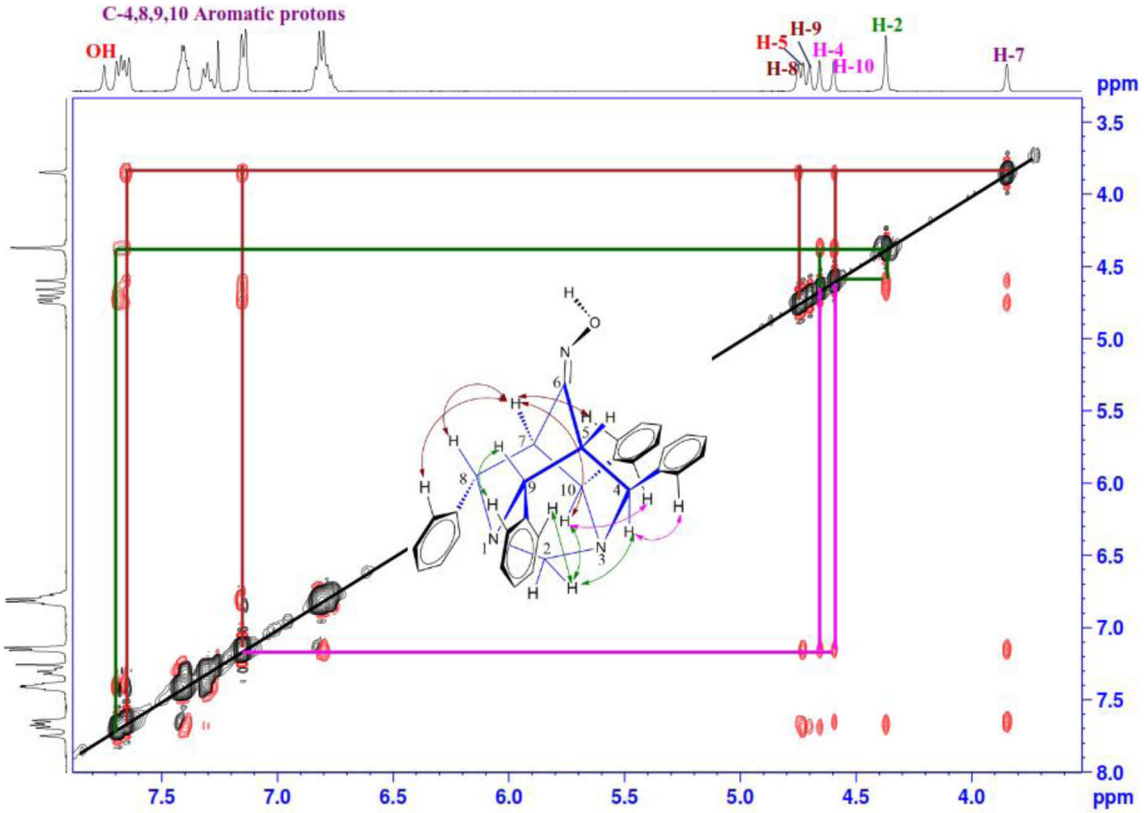


Fig. 3 NOESY Spectrum of 4,8,9,10-tetraphenyl-1,3-diaazaadamantane-6-one oxime **(4a)**

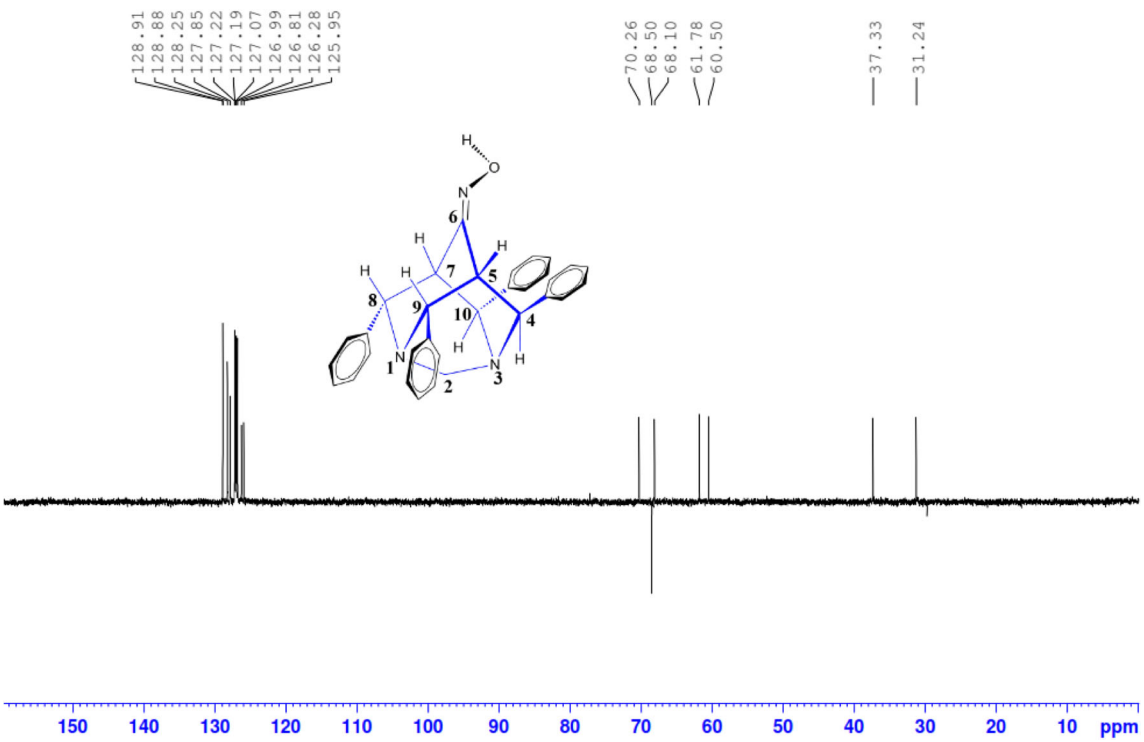


Fig. 4 DEPT-135 spectrum of 4,8,9,10-tetraphenyl-1,3-diaazaadamantane-6-one oxime **(4a)**

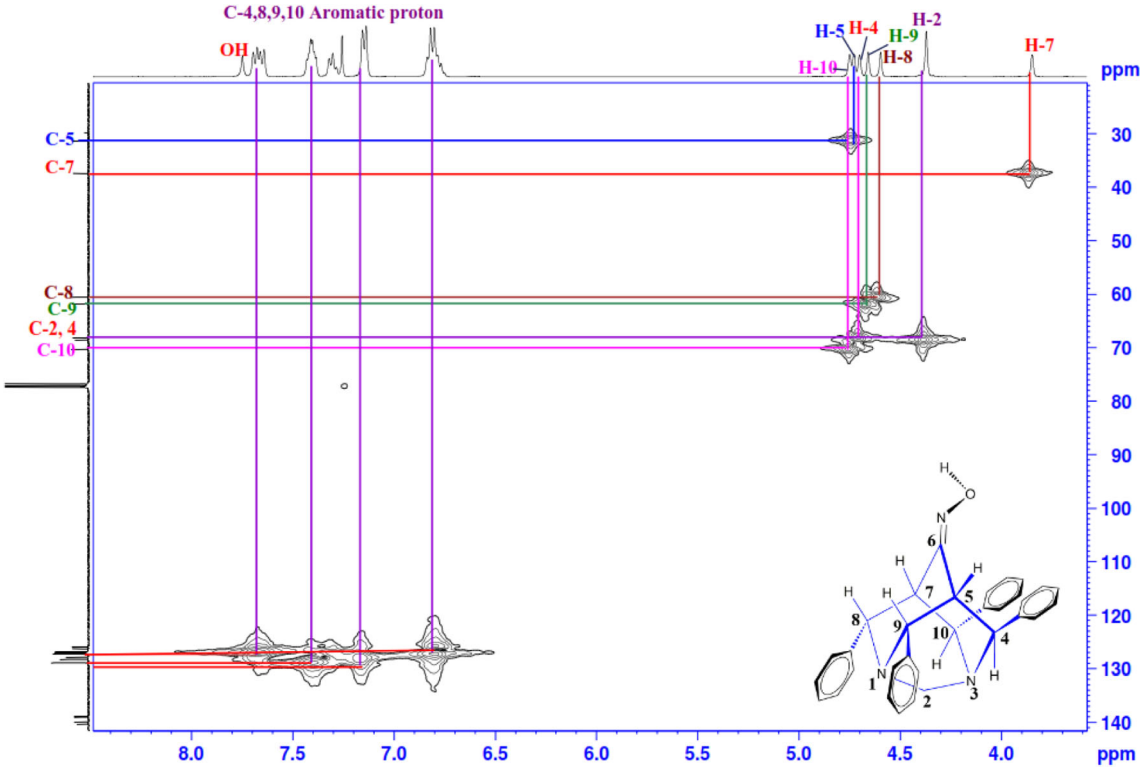


Fig. 5 HMQC spectrum of 4,8,9,10-tetraphenyl-1,3-diaazaadamantane-6-one oxime **(4a)**

correlations (HMBC) of representative compound **4a** and they are presented in Figs. 4, 5, and 6. Complete carbon chemical shift assignments of compounds **4a**–**4e** are presented in Table 4. A careful analysis of Table 4 provides information about the effect of oxime group in the chemical shift of heterotricyclic ring carbons. In the DEPT-135 spectrum of

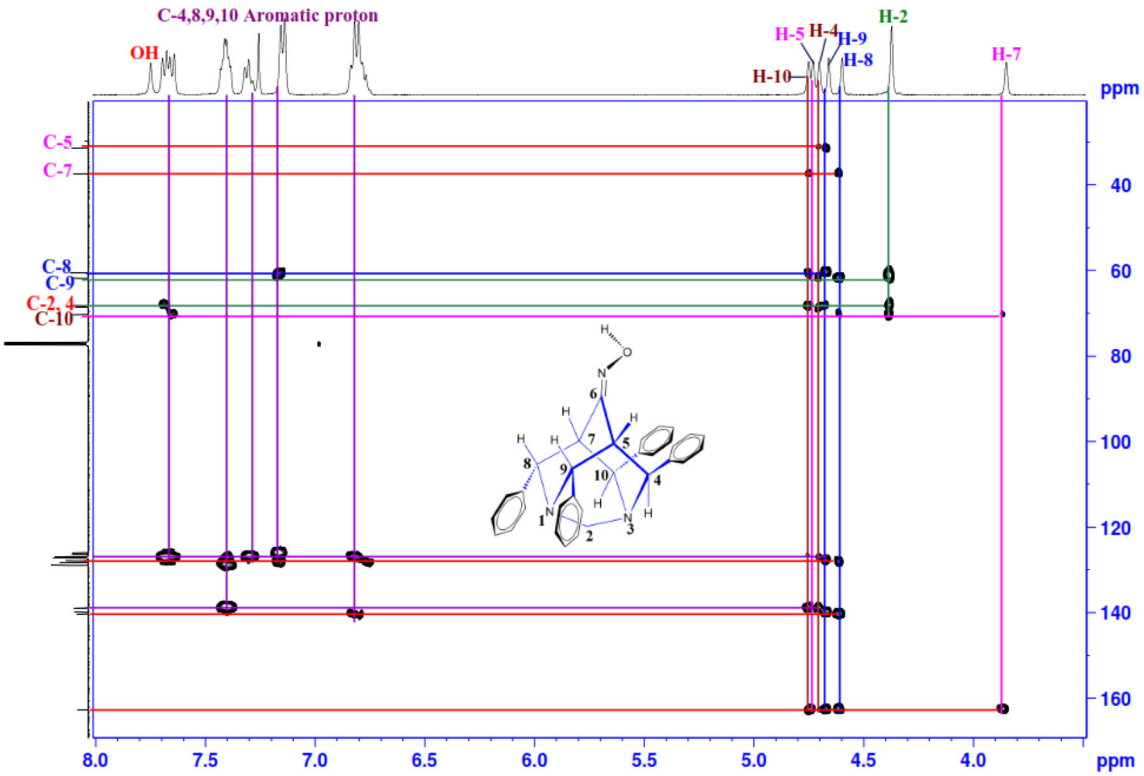


Fig. 6 HMBC spectrum of 4,8,9,10-tetraphenyl-1,3-diaazaadamantane-6-one oxime **(4a)**

Table 4 ^{13}C NMR data of (δ, ppm) of **4a-4e**

Entry	C-2	C-4	C-5	C-6	C-7	C-8	C-9	C-10	Others
4a	68.50	61.78	31.23	162.63	37.33	70.26	68.11	60.50	–
4b	67.82	61.07	31.54	162.85	37.64	69.78	67.62	59.86	55.14
4c	68.06	60.98	30.68	159.24	36.97	69.34	67.17	59.74	–
4d	68.20	61.55	31.52	162.89	37.59	70.10	67.96	60.24	20.79
4e[a]	72.64	65.55	35.55	163.88	41.86	74.05	71.87	64.28	–
Entry	Aryl group chemical shift attached at C4 and C10				Aryl group chemical shift attached at C8 and C9				
	Ipso	Ortho	Meta	para	Ipso	Ortho	Meta	para	
4a	139.89, 140.31	127.85, 128.25	125.95, 126.27	138.89, 138.98	126.81–127.07	128.88, 128.91	127.22	138.89, 138.98	
4b	132.64, 133.00	128.92, 129.33	112.69, 112.85	130.97, 131.07	127.93, 128.11	114.16, 114.19	158.59	130.97, 131.07	
4c	132.02, 132.31	129.31, 129.76	127.07, 127.26	132.02, 132.31	128.11, 128.31	129.02, 129.08	133.02	132.02, 132.31	
4d	136.01, 136.11	127.82	126.75, 126.93	135.10, 135.45	127.67–128.18	129.50, 129.54	136.67	135.10, 135.45	
4e[a]	140.51, 141.02	134.29–134.78	118.22–118.60	139.26, 139.35	133.08–133.34	120.27–120.53	165.26–167.03	139.26, 139.35	

[a] ^{13}C NMR spectrum of **4e** is run by mixture of solvent ($CDCl_3$ and DMSO)

4a, the aliphatic region signals at δ 31.23, 37.33 ppm (assigned due to C-5 and C-7) and δ 70.26, 68.16, 61.83, and 60.56 ppm (assigned due to C-8, C-9, C-4 and C-10 benzylic carbons) exhibit in the upward direction. The signal at δ 68.50 ppm exhibit in the downward direction is assigned due to C-2 carbon (–N–CH_2–N–). The signal at δ 125.95–128.91 ppm are assigned due to aromatic carbons and signal at δ 162.63 ppm is assigned due to C-6 carbon. Four ipso carbons of the aryl groups and C-6 carbon, which are quaternary carbon could not be seen in the DEPT-135 spectrum.

In HMQC, ^{13}C NMR signal at δ 68.50 ppm (C-2) is correlated to H-2 at δ 4.37 ppm confirming N–CH_2–N protons. In HMQC spectrum, the proton signals at δ 3.85 (H-7) and 4.73 (H-5) ppm correlation with the carbon signal at 37.33 ppm and 31.23 ppm, which lead to the assignment of this signals to the C-7 and C-5 carbon respectively. Similarly, four benzylic protons at 4.75 (H-8), 4.70 (H-9), 4.66 (H-4), and 4.60 (H-10) are correlated with the corresponding carbon signal at 70.26 (C-8), 68.16 (C-9), 61.83 (C-4), and 60.56 (C-10) respectively.

HMBC spectrum of **4a** showed the correlation of the aliphatic proton signal at δ 3.85 (H-7), 4.75 (H-8), 4.70 (H-9), 4.66 (H-4), 4.73 (H-5), and 4.60 (H-10) ppm with carbon signal at 162. 63 (C-6), which led to the assignment of this signal to the oxime carbon (C-6). Since the proton signal at δ 4.37 ppm (H-2) does not correlation with carbon signal at δ 162.63 ppm, this could be assigned to N–CH_2–N group. Other HMQC and HMBC correlations are shown in Table 5.

Conformation and "*W*" arrangement

In order to understand the conformational analysis of cyclic ring, vicinal coupling constants are a more important parameter. However, in the present oximes, coupling constants values could not be resolved because all the protons exhibit separate singlet. Therefore, conformation of the two piperidine

Table 5 Correlation in the HMQC and HMBC spectra data of compound **4a**

Signal (δ in ppm)	HMQC correlations	HMBC correlations
4.37 (H-2)	68.50	61.78, 68.11, 70.26
4.66 (H-4)	61.78	31.23, 60.50, 68.11, 127.85, 139.89, 162.63
4.73 (H-5)	31.23	162.63
3.85 (H-7)	37.33	70.26, 162.63
4.75 (H-8)	70.26	31.23, 60.50, 68.11, 126.98, 138.98, 138.89, 162.63
4.70 (H-9)	68.11	37.33, 61.78, 68.50, 127.07, 127.19, 138.89, 138.98, 162.63
4.60 (H-10)	61.78	31.23, 61.78, 70.26, 127.85, 139.89, 162.63
6.75–6.84 (para and meta proton of the Ph at C-4/C-10)	125.95, 127.19, 127.22	127.07, 126.98, 128.25, 139.89, 140.31
7.14–7.16 (ortho proton of the Ph at C-4/C-10)	127.85, 128.25	60.50, 125.95, 126.81, 127.85, 128.25
7.29–7.32 (para proton of the Ph at C-8/C-9)	–	126.81
7.38–7.43 (meta proton of the Ph at C-8/C-9)	128.88, 128.91	127.19, 127.22, 128.88, 128.91, 138.89, 138.98
7.64–7.70 (ortho proton of the Ph at C-8/C-9)	126.81–127.07	68.11, 70.26, 126.98, 127.07

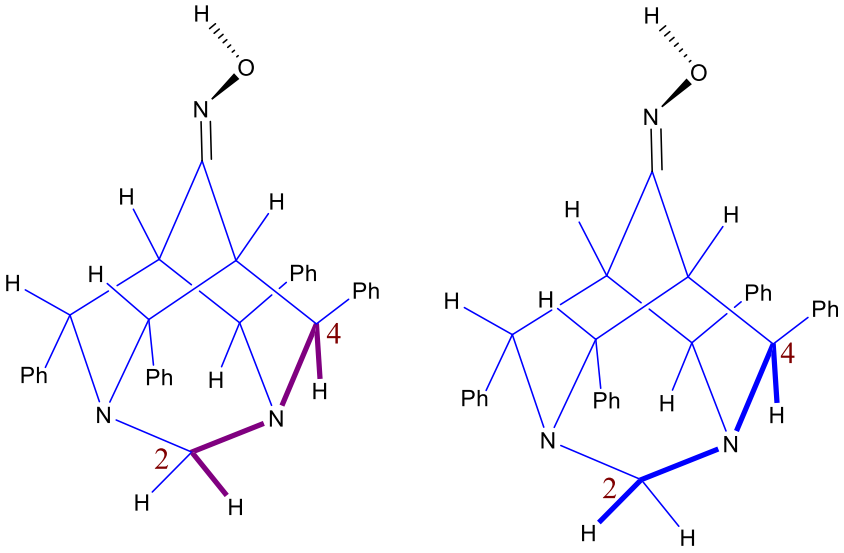


Fig. 7 Correlations between the protons that are in "W" arrangements, from the NOESY spectrum of (**4a**)

rings in oximes were successfully achieved with the help of half-with ($W_{1/2}$) and NOESY analysis. The precursor 4,8,9,10-tetraarylpiperidin-4-ones adopts twin-chair conformation with the axial and equatorial orientation of aryl groups [33]. The observed $W_{1/2}$ of benzylic protons H-4 = 4.83 Hz and H-10 = 4.77 Hz are closely related to the parent ketone (H-4, 10 = 4.12 Hz). In the other benzylic protons, $W_{1/2}$ of H-8 = 7.03 and H-8 = 5.92 Hz are also closely related to the ketone (H-8, 9 = 5.30 Hz). In the precursor, bridge-head protons (H-5, 7) have strong NOESY correlation with the benzylic protons (H-4, 8, 9, 10). The similar correlation occurring in oximes and the bridged-head proton H-7 (δ 3.85 ppm) NOESY are correlated with H-8 (δ 4.75 ppm) and H-10 (δ 4.60 ppm). Besides, the piperidine nitrogen bridging CH_2 group NOESY correlation with H-4 and H-10 protons is also similar to that of its precursor. Hence, these suggestions confirm that the tricyclic oxime also adopts the twin-chair conformation with axial and equatorial orientation of aryl groups.

Long-range coupling in the saturated bicyclic and tricyclic system occur through a rigid arrangement of the bonds in the form of W (^{4}J), with hydrogen occupying the end position [30–32]. The strong correlation of the NOESY spectrum implies the presence of long-range coupling (W arrangement). The W arrangement of studied compounds is shown in Fig. 7.

Oximation effect

The oximation effect of the two piperidine rings has been calculated from ^{1}H and ^{13}C NMR chemical shift of oxime and their respective parent ketones. In the studied oximes **4a-4e**, the proton chemical shift value of *syn* α-proton H-5 (Fig. 1) is deshielded by 0.75 to 0.81 ppm and the *anti*-α-proton H-7 (Fig. 1) is shielded by 0.12 to 0.15 ppm. The benzylic protons H-4, 10 are comparatively more shielded than other two benzylic protons (H-8, 9). The shielding values of these protons are shown in Table 6. This shielding effect confirms the oxime group oriented in equatorial position (H-4, 10 proton side). During oximation, the chemical shift value of N–CH_2–N does not produce any significant change. In general, in the decrease in electronegativity of a particular group in the ring skeleton, the α-carbon is more shielded and the β- and γ-carbons are less shielded (Table 7) [33]. Accordingly, in oximes **4a-4d**, the carbon chemical shift value of *syn* α-carbon C-5 is shielded by 14–19 ppm and *anti*-α-carbon C-7 is shielded by 8–12 ppm. The benzylic C-4 and C-10 carbons are also shielded. The

Table 6 Effect of oximation on ^{1}H chemical shifts (ppm) of **4a-4e**

Entry	H-4	H-5	H-7	H8	H-9	H-10
	δ_{Oxime}–δ_{Ketone} position					
4a	− 0.19	0.75	− 0.13	− 0.01	− 0.06	− 0.25
4b	− 0.21	0.78	− 0.14	− 0.07	− 0.07	− 0.27
4c	− 0.22	0.81	− 0.14	− 0.08	− 0.11	− 0.28
4d	− 0.19	0.66	− 0.12	− 0.01	− 0.02	− 0.19
4e	− 0.23	0.80	− 0.15	− 0.08	− 0.09	− 0.29

Table 7 Effect of oximation on ^{13}C chemical shifts (ppm) of **4a-4e**

Entry	C2	C-4	C-5	C-7	C-8	C-9	C-10
	δ_{Oxime}–δ_{Ketone} position						
4a	− 0.05	− 2.47	− 18.94	− 12.84	0.84	− 1.31	− 3.75
4b	− 0.07	− 2.50	− 18.94	− 12.84	0.81	− 1.35	− 3.71
4c	− 0.09	− 2.58	− 19.08	− 12.79	0.76	− 1.41	− 3.82
4d	− 0.05	− 2.38	− 18.90	− 12.83	0.75	− 1.39	− 3.69
4e[a]	4.62	2.08	− 14.45	− 8.14	5.53	3.25	0.81

[a] ^{13}C NMR spectrum of **4e** is run by mixture of solvent ($CDCl_3$ and DMSO)

remaining ^{13}C chemical shift values are compared with ketones (**2a-2d**) and oximes (**4a-4d**) and listed in Table 7.

Conclusion

In this study, a series of five new oximes of 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-one (**4a-4e**) were synthesized and characterized by FT-IR, NMR spectral data to assign the structure of the compounds. The chemical shift and conformation of the compound are further confirmed by 2D NMR correlation of a representative oxime **4a**. On the basis of the ^{1}H-^{1}H COSY, NOESY, and TOCSY spectral data, it is found that piperidine rings exist in a twin-chair conformation with an axial orientation of the two aryl groups at C-4 and C-10 and equatorial orientation of other two aryl groups (C-8 and C-9). In addition, the stereochemistry is not altered by the introduction of an oxime group in the parent ketone. However, due to allylic A strain in C=N–OH group and due to the proximity of the oxime hydroxy and C5-H, the chemical shift values of C-5 and H-5 are shielded and deshielded respectively. The long-range NOESY and TOCSY correlation further confirms the structural framework of the oxime.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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