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Unprecedented synthesis, 1D and 2D NMR spectral studies of 2,4,6,11-tetraaryl-9-oxa-1,5-diazatricyclo [5.3.1.$0^{3.8}$] undecane via a novel rearrangement

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Abstract

A novel rearrangement of a methylene group from nitrogen to oxygen has been observed during sodium borohydride or lithium aluminium hydride reduction of 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-one. Resulting new compounds, 2,4,6,11-tetraaryl-9-oxa-1,5-diazatricyclo [5.3.1.$0^{3.8}$] undecane, containing an oxaquinuclidine skeleton, is characterized along with its stereochemistry by 2D-NMR and single crystal XRD techniques.

Keywords: ^{1}H NMR; ^{13}C NMR; ^{15}N NMR; 2D NMR; reduction; ^{13}C–^{19}F coupling; diazaadamantanone; bispidine; quinuclidine; conformation

Introduction

Piperidine ring-containing cyclic compounds are key structural fragments of many valuable medicinally active compounds. Some of them are well-known pharmacophores, present in numerous naturally occurring alkaloids and biologically active molecules such as drugs and pharmaceutical ingredients.[1] Derivatives of bispidines, containing two piperidine rings are also of great interest in drug synthesis due to their presence in a variety of naturally occurring lupin alkaloids and various biologically active molecules. [2] Bispidine with aromatic substituents enhances the biological property of the molecules. [3] A huge number of these cyclic compounds have been found to possess useful medicinal and biological properties such as anti-inflammatory, sedative, [4] cytotoxicity, [5] and anti-photoaging activity. [6] Quinuclidine is an interesting [2.2.2] bridged bicyclic nitrogen heterocycle with a nitrogen atom placed at the bridgehead. The natural products quinine [7] and quinidine are without a doubt the most recognized members of the quinuclidine family, with a long history in traditional medicine and in recent decades as privileged chiral organic ligands in catalysis [8]. Synthesis of new bispidine derivatives and their conformational analysis have provided a valuable interest in the field of medicinal chemistry because the biological properties are strongly related to the conformation of the molecule [9]. Hence, it is imperative to establish the stereochemistry and conformation of the bioactive molecules [10]. The bioactive bicyclic derivatives exist in chair, chair-boat, twin chair or twin boat conformations with interesting stereochemistry. [11-13] Hence, this methodology will be useful for the development of new biologically active molecules. Herein, we report the synthesis, ^{1}H and ^{13}C NMR spectral assignment of five new 2,4,6,11-tetraaryl-9-oxa-1,5-diazatricyclo [5.3.1.$0^{3.8}$] undecanes through solution 2D NMR spectral techniques.

Results and discussion

The starting bicyclic compounds (**1a-e**) exist in chair-boat conformation with all aryl groups oriented equatorially.[14] Bicyclic compounds 2,4,6,8-tetraaryl-3,7-diazabicyclo [3.3.1] nonan-9-ones (**1a-e)** were prepared through one-pot synthesis from ammonium acetate, acetone and aryl aldehydes in ethanol medium.[15] Bicyclic compounds (**1a-e**) were refluxed with paraformaldehyde for 3 h in chloroform medium and yielded 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-ones (**2a-e**). In these compounds, two aryl groups, in the β-position with respect to the carbonyl group are in equatorial position in one piperidine ring. Two aryl groups in the β-positions with respect to the carbonyl group, are in axial positions in other piperidine ring. [16] Hence, we wanted to study the stereochemistry of the reduction reaction of these ketones (**2a-e**) using either $NaBH_4$ or LAH as a reducing agent. It is reported that in 4-

substituted cyclohexanone, hydride ion transfer will take place from the less hindered side to yield an axial alcohol. [17]

Synthesis of oxa quinuclidine ring-containing compounds is a novel and efficient synthetic method that has been developed by $NaBH_4$ or LAH reduction of 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-one (Scheme 1), and the details are presented in this manuscript. This method has advantages, such as readily available substrates, mild reaction conditions and good yields. The reduction of a ketone would normally yield on alcohol, and we expected 6-hydroxy-4,8,9,10-tetraaryl-1,3-diazaadamantane from the above reduction reaction. But, to our surprise, the product on analysis by FT-IR, 1D and 2D NMR spectral studies was found to be 2,4,6,11-tetraaryl-9-oxa-1,5-diazatricyclo [5.3.1.$0^{3.8}$] undecane (**3)** (Scheme 1).

The ^{1}H and ^{13}C NMR chemical shifts of compounds **3a-e** are given in **Table 1** and **2**, respectively. The NMR spectrum of **3e** is used as the representative compound. In a ^{1}H NMR spectrum, initially, we assigned a singlet at 1.80 ppm to the -OH proton, expected in the reduction product of a ketone. A singlet at 4.12 ppm, integrated for two protons, confirmed the presence of a -CH_2-group. The ^{13}C and DEPT-135 NMR spectra indicated the absence of the carbonyl group in **3e** and the presence of -CH_2-group. The compound is further characterized by two−dimensional and ^{15}N NMR spectra. The COSY/NOESY and HSQC/HMBC correlations of compounds **3e** are given in **Table 3** and **4**, respectively. Important ^{1}H-^{1}H COSY, NOESY and HMBC correlations are shown in Fig. 1. The broad singlet at 1.80 ppm shows a strong COSY correlation with the broad signal at 4.15 ppm (H-4 and H-6 protons of the newly assigned structure). It also shows a NOESY correlation with the same signal. If the signal at 1.80 ppm were due to a hydroxy group, then the above correlations could not be possible, because the -OH and H-4/H-6 protons would be far separated, and hence, it is concluded that this signal is not due to a hydroxy group. The triplet at 2.76 (2H) ppm shows COSY, NOESY correlations with four benzylic (H-4,6=4.15 and H-2,11=4.39 ppm) protons and H-8 (4.07 ppm) proton, hence this signal is unambiguously assigned to bridgehead protons (H-3 and H-7). In the HMBC spectrum, the triplet at 4.07 ppm (H-8; 1H; J = 3.84 Hz) correlates with C-10 at 72.18 ppm. This shows the proximity of C8-H and at C-10. Had it been due to the -CH_2-group bridging the two piperidine nitrogens as in **2e,** diazaadamantanone, then the above correlation would not be possible. Similarly, the -CH_2- hydrogens are correlating with only the two benzylic carbons at C-2 and C-11. This confirms that the -CH_2- group is not bridging the two piperidine nitrogens.

In the ^{1}H-^{15}N HSQC correlation spectra, the nitrogen signal at 49.79 ppm correlates with the proton signal at 1.80 ppm, and it confirms that this proton signal is due to the presence of an NH group, not an OH group. All these facts/results confirm that the -CH_2- group is bridging the nitrogen and oxygen atoms. Besides, the presence of an N-H group is further confirmed by the ^{15}N NMR spectrum. Finally, the structure of **3e** is unambiguously confirmed by single crystal X-ray analysis (Fig. 2). Recently we have published the crystal structure and Hirshfeld surface analysis of compound **3e** in Acta Cryst E.[18]

The ^{13}C-^{19}F coupling of compound **3e** is explained based on XRD numbering pattern (Fig. 2). F1/F4 couples with C3/C30 appeared as a doublet at 160.6 ppm (^{1}J = 207.0 Hz). A two-bond coupling with C2,C4/C29,C31 appear as a doublet at 114.6 ppm (^{2}J = 80 Hz). A three-bond coupling with C1,C5/C28,C32 appear as a doublet at 129.0 ppm (^{3}J = 32 Hz). A four-bond coupling with C6/C27 appear as a doublet at 135.9 ppm (^{4}J = 16 Hz). In the same way F2/F3 couples with C13/C21 as well as C10/C18 and appear as a doublet at 163.0 ppm (^{1}J = 211 Hz) and 137.0 ppm (^{4}J = 12 Hz), respectively. F2/F3 also coupled with C11,C15/C19,C23 and C12,C14/C20,C22 appear as a doublet at 115.6 ppm (^{2}J = 84 Hz) and 127.9 ppm (^{3}J = 32 Hz), respectively.

Two piperidine rings are in chair-boat conformations, and the four fluorophenyl groups are equatorially oriented based on ^{1}H NMR, COSY and NOESY spectra. The bridgehead protons, H-3 & H-7, appeared as a triplet at 2.76 ppm (t, J=5.04 Hz) and they couple with H-8 at 4.07 ppm (t, J= 3.84 Hz). H_{3e} couples with H_{2e} (4.40 ppm, d, J= 4.88 Hz) and also with H_{4a} (4.15 ppm, t, J= 3.84 Hz). H_{7e} couples with H_{11e} (4.40 ppm, d, J= 4.88 Hz) and also with H_{6a} (4.15 ppm). It leads to the conclusion that all aryl groups at C-2, 11 and C-4, 6 are equatorially oriented. The 3 & 7 bridgehead protons have COSY and NOESY correlation with the neighbouring benzylic protons and also with H-8 at 4.07 ppm. The N-H proton, appearing as a broad singlet at 1.80 ppm, has strong COSY and NOESY correlation with the benzylic hydrogens at positions 4 & 6 but not with benzylic hydrogens at positions 2 & 11. It leads to the conclusion that the piperidine ring, C3-C4-N5-C6-C7-C8, exists in a chair conformation. Had this ring been in a boat conformation, then we would have expected flag pole-bow spirit interactions of piperidine-NH with H-8, which is absent in the compounds studied. A sharp singlet at 4.12 ppm (H-10; CH_2) shows NOESY and COSY correlation with benzylic hydrogens 2 & 11 and also with H-8. It is evidence for a boat conformation of another piperidine ring (C8-C7-C11-N1-C2-C3) and for an presence of a six-membered ring (N1-C10-O-C8-C7/C3-C11/C2) which constituted part of a oxaquiniclidine ring system.

Long-range coupling in the saturated bicyclic and tri-cyclic compounds occur through a rigid arrangement of the bonds in the form of W (^{4}J), with hydrogen occupying the end position. [19] This long-range coupling strongly supports the conformation of the ring. The W arrangements of the studied compounds are shown in Fig. 3. "W" arrangements between H-3,7 and NH (Fig. 3a & 3b) is evidenced from COSY correlation, which proves the chair conformation of C3-C4-N5-C6-C7-C8 six membered ring in chair conformation. "W" arrangements also present in H-2,11 and CH_2 (Fig. 3c & 3d), which is evidenced for the formation of oxaquiniclidine ring (CH_2 bridging the N1 and O9).

A plausible mechanism for this unusual rearrangement from the 1,3-diazaadamantan-6-one into a oxaquinuclidine skeleton is presented in Scheme 2. In-line with the stereochemistry of metal hydride reduction (structure **2−>4**), the hydride ion transfer takes place through the less hindered side of piperidine ring **A**, where two aryl groups at C-8 & C-9 in structure **2** are equatorially oriented. A hydride ion transfer through piperidine ring **B** is prevented by two axially oriented aryl groups at C-4 & C-10 in structure **2**. Obviously, the newly formed -OH group in structure **5** exerts two severe 1,3-diaxial steric interactions with two diaxially oriented aryl groups at C-4 & C-10 in piperidine ring **B**. This might be the driving force for the spontaneous ring opening from the N-CH_2-N group to produce iminium ion **6**. Severe 1,3-diaxial interactions are now relieved when the piperidine ring **B** undergoes conformational flipping from a chair to a boat conformation in **7**. Two aryl groups at C2 & C11 in structure **8** are now oriented equatorially. Cyclisation of **7** to **8** could take place easily due to the proximity of the hydroxy group and iminium carbon. This nitrogen to oxygen migration of a methylene group forms a new oxaquinuclidine skeleton. The reaction was carried in a different sequence as shown in scheme 3. Here, bicyclic ketone **1e** was first reduced with $NaBH_4$ in a chloroform-ethanol medium. Hydroxy compound **4e**, thus formed, was heated with paraformaldehyde in chloroform medium and yielded compound **3e** exclusively. This leads to the conclusion that tetraaryl hydroxy adamantane, once formed, undergoes spontaneous rearrangement to yield **3e**.

Conclusion

A novel rearrangement involving migration of a methylene group from nitrogen to oxygen to form a stable oxaquinuclidine skeleton is reported. 4,8,9,10-Tetraaryl-1,3-diazaadamantan-6-one on reduction either with $NaBH_4$ or with $LiAlH_4$ yielded 2,4,6,11-tetraaryl-9-oxa-1,5-diazatricyclo [5.3.1.0$^{3.8}$] undecane. In the new compounds, containing an oxaquinuclidine skeleton, two piperidine rings are in chair-boat conformation with all the aryl

groups oriented equatorially. The reaction condition is mild, and excellent yields are obtained in short reaction times. A mechanism for the unusual rearrangement is proposed.

Experimental section

General Method

Melting points were determined by the open capillary method. FT-IR spectra were recorded on a JASCO FT/IR-4700 instrument. All NMR spectra were recorded on a Bruker AVANCE III HD 400 MHz spectrometer and recorded at 295-297 K in $CDCl_3$ as the solvent with TMS as an internal standard. Chemical shifts are reported in ppm (δ) and referenced to TMS (δ_H = 0 ppm) in ^{1}H NMR spectra, residual $CDCl_3$ (δ_H = 7.2 ppm, δ_C = 77 ppm). Three mg of compound dissolved in 0.5 ml of $CDCl_3$ was used for the assignment of ^{1}H and D_2O exchange chemical shift. Thirty mg of compound dissolved in 0.5 ml of $CDCl_3$ was used for ^{13}C NMR, DEPT-135, ^{1}H - ^{1}H COSY, NOESY, HSQC, HMBC, ^{1}H-^{15}N HSQC and ^{15}N NMR analysis.

Recording of one-dimensional NMR spectra

The pulse conditions were as follows: **^{1}H NMR** spectra: number of data points (TD) 65536, number of scans (NS) 16, dummy scans (DS) 2, spectra with (SWH) 8012.8 Hz, acquisition time (AQ) 4 sec, spectrometer operating frequency 400.23 MHz, line broadening (LB) 0.30 Hz, Recycle Delay (D1) 1.0 sec. **^{13}C NMR** spectra: TD 65536, NS 1274, DS 4, SWH 24038.4 Hz, AQ 1.3 sec, SF 100.63 MHz, LB 1.00 Hz, D1 2.0 sec. **^{15}N NMR** spectra: TD 32768, NS 1528, DS 4, SWH 20380.4 Hz, AQ 0.80 sec, SF 40.554 MHz, LB 0.25 Hz, D1 10.0 sec.

Recording of two-dimensional NMR spectra

H-H COSY: TD 2048 (F2), TD 128 (F1) NS 1, DS 16, SWH 3289 Hz, AQ 0.31 sec, SF 400.23 MHz, LB 0 Hz, D1 1.88 sec. **NOESY**: TD 2048 (F2), TD 256 (F1) NS 4, DS 32, SWH 3875.9 Hz, AQ 0.26 sec, SF 400.23 MHz, LB 0 Hz, D1 1.99 sec, mixing time 0.30 sec. **HSQC**: TD 1024 (F2), TD 128 (F1) NS 4, DS 16, SWH 3875.9 Hz, AQ 0.13 sec, SF 400.23 (F2) MHz, SF 100.63 (F1) MHz, LB 0 Hz, D1 1.46 sec, one bond coupling 145.0 Hz. **HMBC**: The parameters were very similar to those used in the HSQC experiment only change in TD 2048 (F2), TD 128 (F1), long-range coupling 10.0 Hz. **^{1}H-^{15}N HSQC**: TD 2048 (F2), TD 256 (F1) NS 8, DS 16, SWH 5597 Hz, AQ 0.18 sec, SF 400.23 MHz, LB 0 Hz, D1 2.00 sec, one bond coupling 90.0 Hz.

Typical experimental procedure

The compound (**2e**) 4,8,9,10-tetra(4-fluorophenyl)-1,3-diazaadamantan-6-one (2 mmol, 1.05 g) dissolved in chloroform (5 ml) and $NaBH_4$ (4 mmol, 0.15 g) dissolved in ethanol (5 ml) were mixed and transferred to a closed container and stirred at 10^o C. The reaction was monitored by TLC, and after complete disappearance of the ketone the resulting mixture was filtered. The solvent was evaporated and washed with cold water and recrystallised from chloroform: ethanol to obtain the compound **3e**.

2.4,6,11-tetra(4-fluorophenyl)-9-oxa-1,5-diazatricyclo [5.3.1.$0^{3.8}$] undecane **3e**; Colorless power, 90 % yield (0.95 g); IR (KBr): 3316, 3078, 2987, 2955, 2930, 1508, 1222, 1158; ^{1}H-NMR ($CDCl_3$ / TMS, 400.22 MHz) 1.80 (1H, s), 2.76 (2H, t, J=5.04 Hz), 4.07 (1H, t, J=3.84 Hz), 4.12 (2H, s), 4.15 (2H, s) 4.40 (2H, d, J=4.88 Hz), 6.80 (4H, t, J=8.68 Hz), 6.97-7.01 (8H, m) 7.46-7.50 (4H, s). D_2O Exchange ($CDCl_3$ / D_2O / TMS, 400.22 MHz) 2.76 (2H, t, J=5.28 Hz), 4.07 (1H, d, J=6.12 Hz), 4.13 (4H, d, J=5.24 Hz), 4.40 (2H, d, J=3.76 Hz), 6.79 (4H, t, J=8.32 Hz), 6.97-7.00 (8H, m), 7.46-7.49 (4H, m). ^{13}C-NMR ($CDCl_3$ / TMS, 100.63 MHz) 44.1, 58.2, 60.9, 69.4, 72.1, 114.5, 114.7, 115.5, 115.7, 127.8, 127.9, 129.0, 129.1, 135.9, 135.9, 136.9, 137.0, 160.3, 160.8, 162.7, 163.3. DEPT-135 ($CDCl_3$ / TMS, 100.63 MHz) (44.1, 58.2, 60.9, 69.4, 114.5, 114.7, 115.5, 115.7, 127.8, 127.9, 129.0, 129.1 = Upward direction), 72.19 (Downward direction) ^{15}N NMR (CDCl3 / Formamide, 40.55) 49.79, 200.35. HRMS (TOP MS ES) m/z: [M-^{12}C+3] calcd. for $C_{31}H_{26}F_4N_2O$ 521.198; found 521.048.

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Supplementary Material

Copies of ^{1}H NMR, ^{13}C NMR and FT-IR spectra of compounds **3a-e** have been provided. Copies of 2D NMR (COSY, NOESY, HSQC, HMBC), D_2O treated, ^{15}N, ^{1}H-^{15}N HSQC and HRMS spectra for the compound **3e** is given. The supplementary material also contains X-ray data of compound **3e** and this data (CCDC 1854381) can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Table 1. ^{1}H NMR chemical shift (δ, ppm) of **3a-3e**

Entry	H-10	H-4,6	H-3,7	H-2,11	H-8	NH	Others
3a	4.19	4.17	2.85 (t, 5.32 Hz)	4.51 (d, 4.72 Hz)	4.08 (t, 3.54 Hz)	1.85	–
3b	4.17	4.08	2.74 (t, 4.40 Hz)	4.42 (d, 4.00 Hz)	4.01 (t, 3.60 Hz)	1.73	3.72, 3.75
3c	4.08	4.13	2.76 (t, 5.12 Hz)	4.38 (d, 5.12 Hz)	4.06 (t, 3.86 Hz)	1.80	–
3d	4.17	4.09	2.76 (t, 4.84 Hz)	4.47 (d, 4.96 Hz)	4.01 (t, 3.82 Hz)	1.76	2.28, 2.22
3e	4.12	4.15	2.76 (t, 5.04 Hz)	4.40 (d, 4.88 Hz)	4.07 (t, 3.84 Hz)	1.80	–

Entry	Ortho H at C2 & C11	Ortho H at C4 & C6	Meta H	Para H
3a	7.29 (t, 7.42 Hz)	7.54 (d, 7.56 Hz)	7.06, 7.08, 7.19 (t, 7.24 Hz)	7.01, 7.02
3b	6.96 (d, 8.00 Hz)	7.41 (d, 8.00 Hz)	6.63 (d, 7.60 Hz), 6.82 (d, 8.00 Hz)	–
3c	7.10 (d, 8.60 Hz)	7.27 (d, 5.36 Hz)	6.95 (d, 8.44 Hz), 7.45 (d, 8.44 Hz)	–
3d	7.10 (d, 7.88 Hz)	7.40 (d, 8.00 Hz)	6.87-6.92 (dd)	–
3e	6.99-7.01 (m)	7.46-7.50 (dd)	6.80 (t, 8.68 Hz), 6.97-6.99 (m)	–

Table 2. ^{13}C NMR chemical shift (δ, ppm) of **3a-3e**

Entry	C-10	C-4,6	C-3,7	C-2,11	C-8	Others	Ipso	Ortho	Meta	Para
3a	72.6	61.9	44.5	58.7	69.8	–	140.7,	127.5,	128.7	126.3,
3b	72.3	61.3	44.6	58.2	69.9	55.1,	141.6	127.4	113.0,	126.5
3c	72.3	61.0	43.9	58.2	69.3	55.3	133.1,	127.5,	114.0	157.9,
3d	72.6	61.8	44.8	58.4	70.0	20.9,	133.9	128.7	128.0,	158.8
3e	72.1	60.9	44.1	58.2	69.4	21.1	138.6,	129.0,	127.7	132.5,
						–	139.6	128.8	129.3,	133.3
						–	138.8,	127.5,	128.3	136.8,
							138.0	126.5	114.6,	135.6
							135.9,	127.9,	115.6	160.6,
							137.0	129.0		163.0

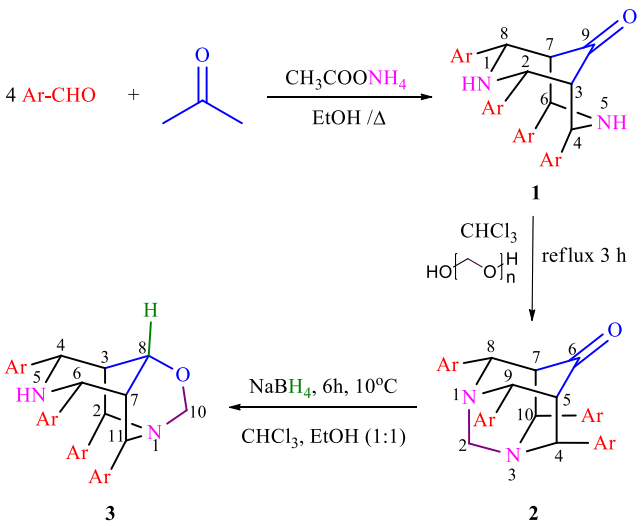
Table 3. Correlation in the ^{1}H - ^{1}H COSY and NOESY spectra data of compound **3e**

Signal (δ in ppm)	COSY Correlation	Correlation in NOESY
1.80 (1H, NH)	2.76 (w), 4.15	4.15, 4.40 (w), 7.46-7.50
2.76 (2H, H-3,7)	4.07, 4.15, 4.40	4.07, 4.15, 4.40, 7.46-7.50, 6.80 (w), 6.99-7.01
4.07 (1H, H-8)	2.76	2.76
4.12 (2H, H-10)	4.40, 4.07	2.76, 4.40
4.15 (2H, H-4,6)	2.76, 1.80, 7.46-7.50	1.80 (w), 7.46-7.50, 6.99-7.01
4.40 (2H, H-2,11)	2.76, 4.12, 6.99-7.01	1.80, 2.76, 7.46-7.50, 6.99-7.01
6.80 (meta proton of the Ph at C-2/C-11)	6.99-7.01	6.99-7.01
6.97-7.01 (meta proton of the Ph at C-4/C-6 and ortho proton of the Ph at C-2/C-11)	6.80, 7.46-7.50	2.76, 4.12, 4.40, 6.80
7.46-7.50 (ortho proton of the Ph at C-4/C-6)	6.97-7.01	1.80, 2.76, 4.15, 4.30, 6.99-7.01

w: weak correlation

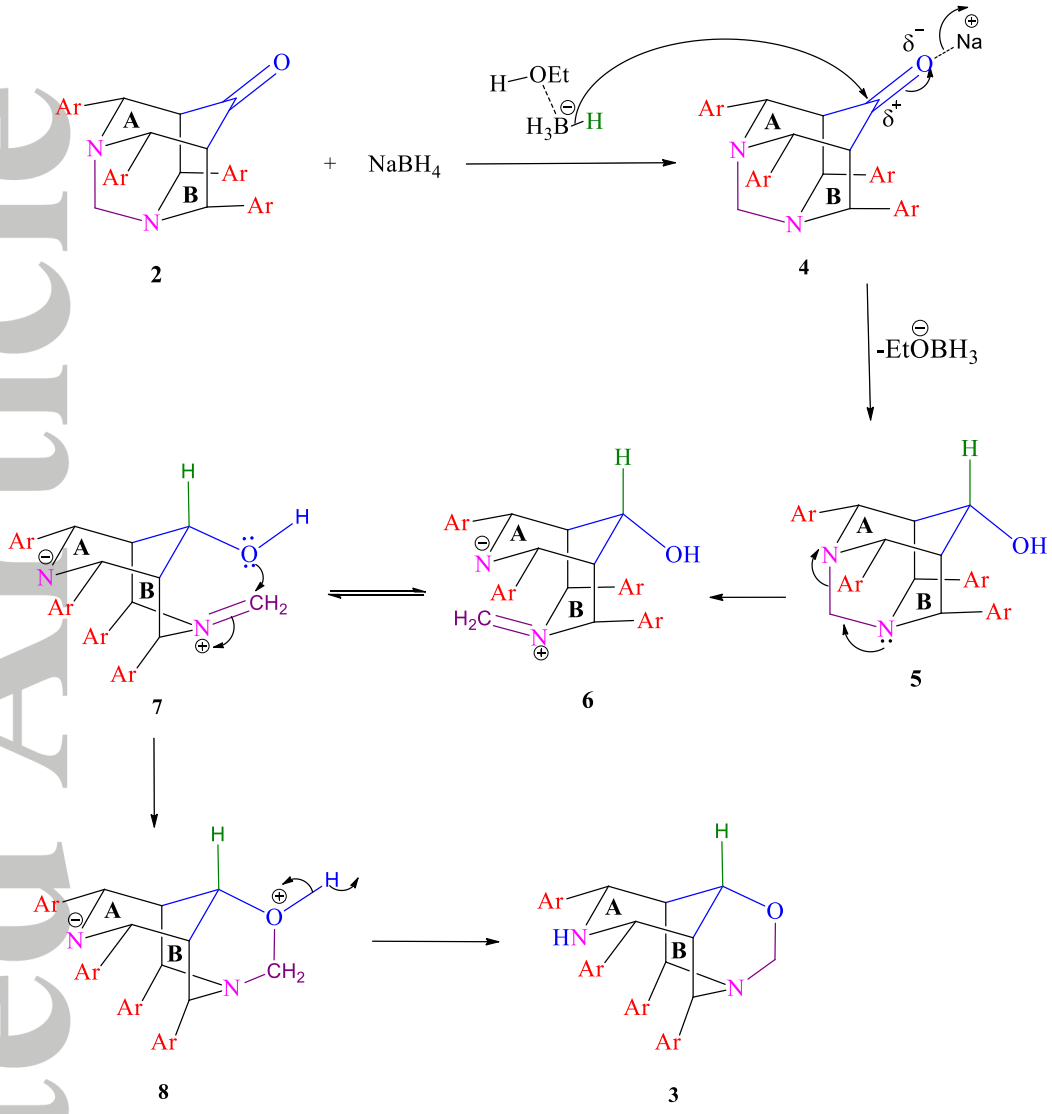
Table 4. Correlation in the HSQC and MMBC spectra data of compound **3e**

Signal (δ in ppm)	HSQC Correlations	HMBC Correlations
1.80 (1H, NH)	-	44.1 (C-3,7)
2.76 (2H, H-3,7)	44.1	69.4 (C8), 135.9 (w), 135.9
4.07 (1H, H-8)	69.4	44.1 (C-3,7), 58.2 (C-2,11), 72.1 (C-10)
4.12 (2H, H-10)	72.1	58.2, 69.4 (w)
4.15 (2H, H-4,6)	60.9	44.1 (C-3,7), 58.2 (C-2,11), 69.4, 127.8,
4.40 (2H, H-2,11)	58.2	127.9, 136.9, 137.0
		44.1 (C-3,7), 58.2 (C-2,11), 60.9 (C-4,6),
6.80 (meta proton of the Ph	114.5,	72.1 (C-10), 114.5 (w), 129.0, 129.1,
at C-2/C-11)	114.7	135.9, 135.9
6.97-7.01 (meta proton of	115.5,	114.5, 114.7, 129.0, 129.1, 135.9,
the Ph at C-4/C-6 6.99-7.01	115.7	135.9,160.3-163.3
ortho proton of the Ph at C-	129.0,	58.2 (C-2,11), 115.5, 115.7, 129.0,
2/C-11)	129.1	129.1, 136.9, 137.0, 160.3-163.3
7.46-7.50 (ortho proton of	127.8,	60.9 (C-4,6), 115.5, 115.7, 127.8, 126.9,
the Ph at C-4/C-6)	127.9	160.3-163.3

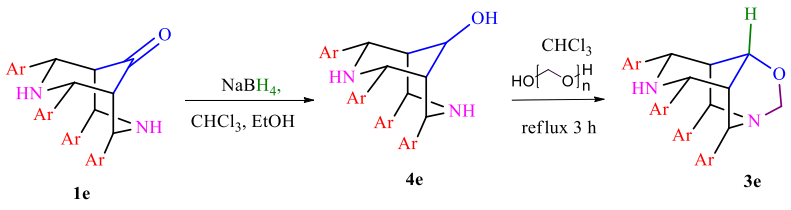


Compounds	Ar	Compounds **3a-e**	
		Melting point °C	% Yield
a	C_6H_5	232	91
b	*p*-OCH_3 C_6H_4	230	94
c	*p*-Cl C_6H_4	238	89
d	*p*-CH_3 C_6H_4	244	92
e	*p*-F C_6H_4	242	90

Scheme 1. Synthesis of 2,4,6,8-tetraaryl-3,7- diazabicyclo [3.3.1] nonan-9-one (**1**), 4,8,9,10-tetraaryl-1,3-diazaadamantan-6-one (**2**) and 2,4,6,11-tetraaryl-9-oxa-1,5-diazatricyclo [5.3.1.$0^{3.8}$] undecane (**3**).



Scheme 2. Plausible reaction mechanism for the formation of compounds **3a-e**.



Scheme 3 Reduction of **1e** and cyclization of **4e** yielded **3e**.

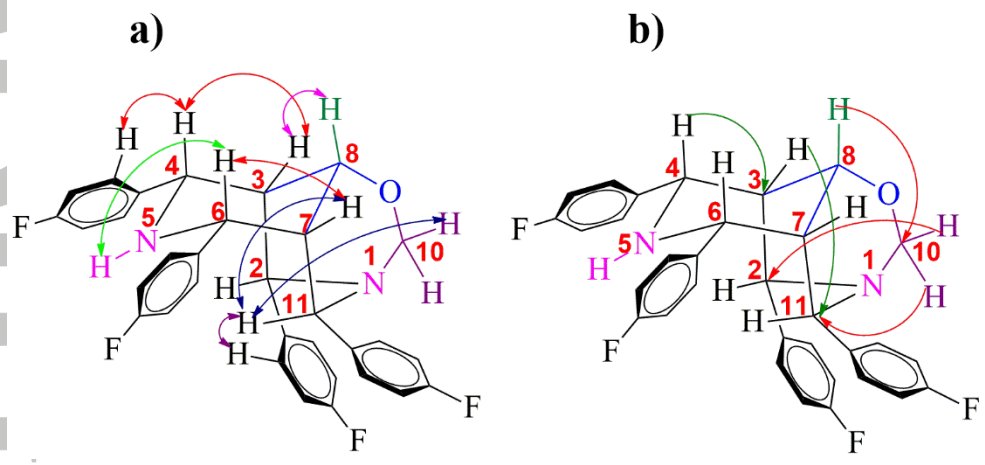


Figure 1. a) Selected 1H - 1H COSY and NOESY correlation of 3e. b) Selected HMBC correlation of 3e.

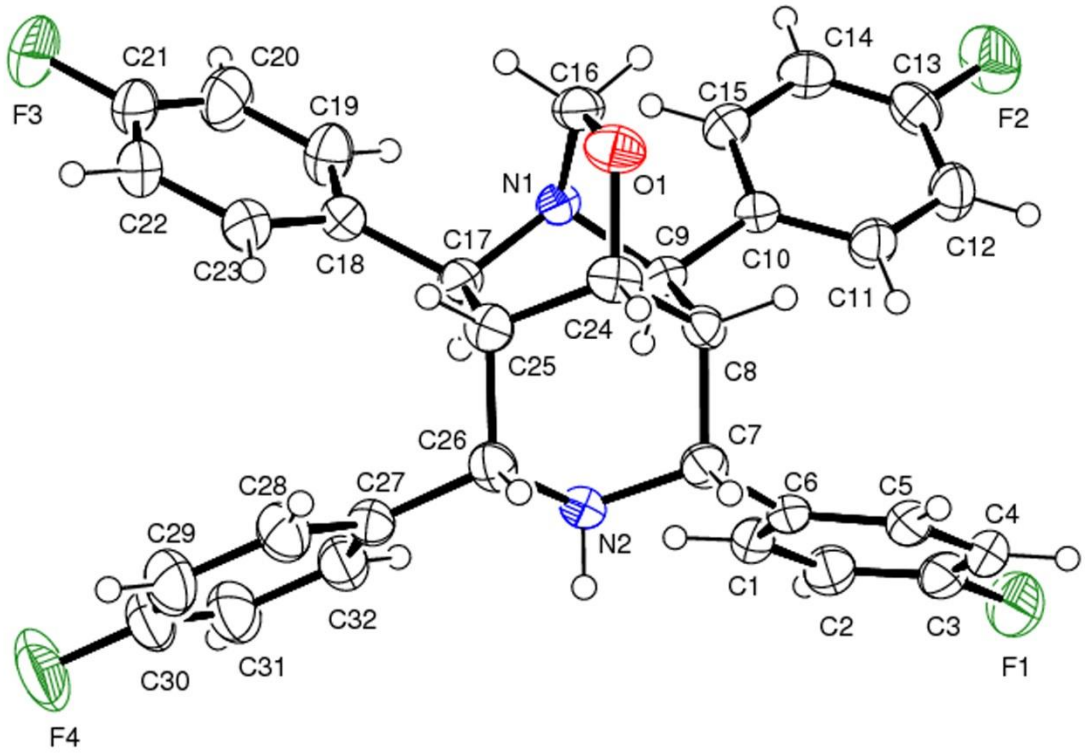


Figure 2. ORTEP diagram of 3e

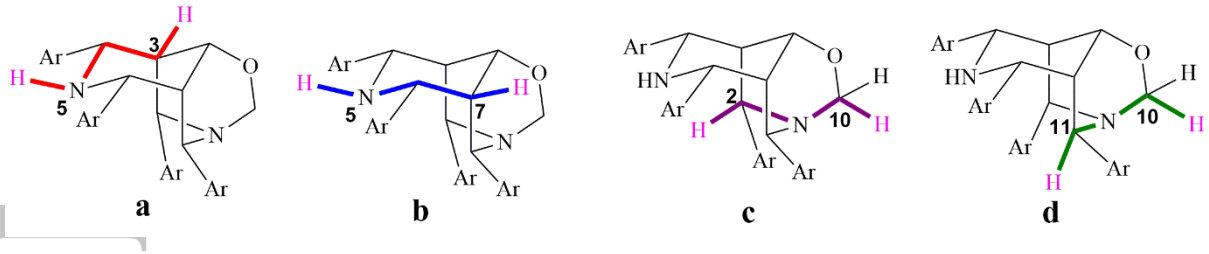


Fig. 3. Correlation between the protons that are in "W" arrangements, from the COSY spectrum of 3e.