Struct Chem
DOI 10.1007/s11224-013-0297-y

ORIGINAL RESEARCH

A theoretical and experimental study to unequivocal structural assignment of tetrahydroquinoline derivatives

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Received: 11 February 2013 / Accepted: 10 June 2013

Abstract The tetrahydroquinoline derivatives can be easily synthesized through Povarov reaction and have several important biological activities. This work describes a comparative study for the unequivocal assignment of molecular structure of different tetrahydroquinoline derivatives, through a complete analysis of NMR 1D and 2D NMR spectra (^{1}H, ^{13}C, COSY, HSQC, and HMBC), and the correlation this data with theoretical calculations of energy-minimization and chemical shift (δ), employing the theory level of DFT/B3LYP with set of the cc-pVDZ basis. For these derivatives the experimental analyses and the theoretical model adopted were sufficient to obtain a good description of its structures, and these results can be used to assign the structure of various others tetrahydroquinoline derivatives.

Keywords Tetrahydroquinoline derivatives · Theoretical study · NMR · Chemical shifts calculations · Poravov adducts

Introduction

As an important class of natural products, the tetrahydroquinolines derivatives are compounds that have the basic structure of quinolines and have several important biological activities [1–5], among them: psychotropic [6], antiallergic [7], anti-inflammatory [8], and estrogenic activity [9]. The pyranquinolines and furanquinolines derivatives exhibit a pharmacological potential [10]. Recently published studies demonstrated that quinoline derivatives also show good applications in solar cells, due to the high number of conjugated π electrons in its structure [11–15].

The tetrahydroquinoline derivatives can be easily synthesized through Povarov's reaction (single or multi-step) using several kinds of catalysts, such as: $NbCl_5$, $InCl_3$, $LiBF_4$, and $BF_3{\cdot}Et_2O$ [16–29]. The Povarov's reaction is derived from aza-Diels–Alder reaction and it is an excellent tool for the synthesis of natural products and heterocyclic. In this reaction, imines react with dienophiles to obtain the tetrahydroquinolines derivatives through of a concerted mechanism (Fig. 1).

Povarov's reaction for obtaining the tetrahydroquinoline derivatives generally lead to the formation of a pair of diastereoisomers, with stereochemistry *cis* and *trans* between the hydrogens H-1 and H-2, providing different proportions between these isomers, depending on the conditions used [16–29]. However, even with the wide variety of these catalysts used to the obtention of these derivatives, we did not find, at the literature, more detailed studies about the structure determination of these compounds. Therefore, this work had an objective to realize a theoretical and experimental study, in order to determine unequivocally the structure assignment and the conformation of the different tetrahydroquinoline derivatives, using *ab initio* calculations and nuclear magnetic resonance experiments, and then correlating these two methods. This was achieved by the use of several techniques, such as COSY, HMQC, HMBC analysis, associated with theoretical calculations.

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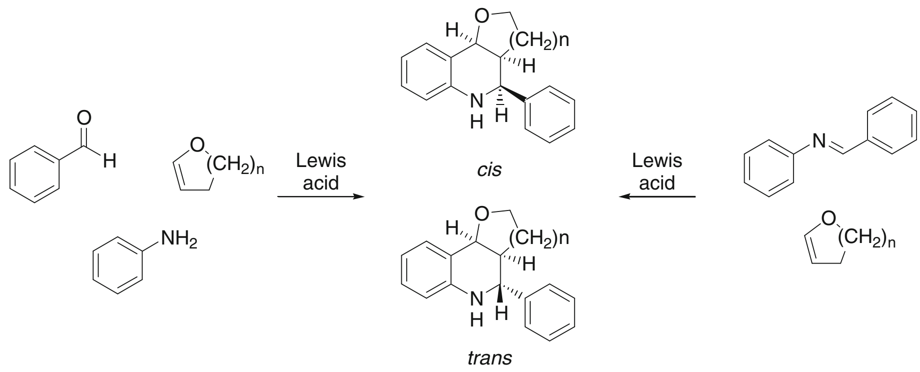
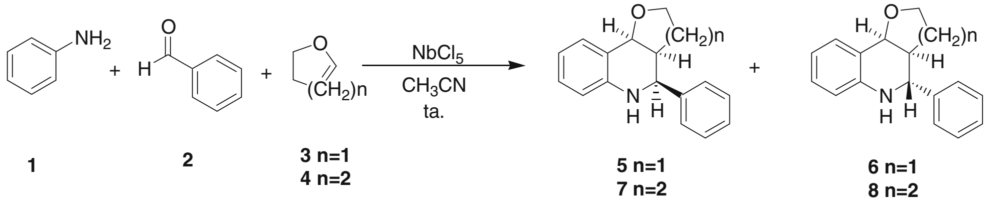


Fig. 1 Preparation of tetrahydroquinoline derivatives through Povarov's reaction



Scheme 1 Reaction of preparation of tetrahydroquinolines derivatives studied

The nuclear magnetic resonance (NMR) has been one of the most powerful methods in structural elucidation, and it is proving to be a versatile technique to solve a lot of chemical problems. The data obtained from NMR spectra are largely used to characterize chemical environment of the individual atoms [30–32].

However, the correct attribution of signal, as well as the understanding of the relationship between chemical shifts and molecular structure, can be difficult problems to solve. *Ab initio* calculations are increasingly precise, being possible to use them as tool to help in the solution of many problems. Thus, the use of two techniques together can be very useful to make correct assignment, and to understand the molecule chemical structure [33–38].

Experimental and theoretical methods

All reactions were performed under an atmosphere of N_2, unless otherwise specified. Acetonitrile was distilled with calcium hydride. All commercially available reagents were used without further purification. Thin-layer chromatography was performed on Aldrich® silica gel aluminum sheets, which were visualized with a vanillin/methanol/water/sulfuric acid mixture. Aldrich® silica gel 60 was employed for column chromatography.

Synthesis of tetrahydroquinoline derivatives

The tetrahydroquinolines (**5**, **6**, **7** and **8**) were prepared, through Povarov multicomponent reaction, among aniline (**1**), benzaldehyde (**2**), 2,3-dihydrofuran (**3**) or 3,4-dihydropyran (**4**), using $NbCl_5$ -as Lewis acid (Scheme 1) [16–18].

To a solution of niobium pentachloride (10 or 25 mol%) in 2.0 mL of anhydrous Acetonitrile, maintained at room temperature under a nitrogen atmosphere, we added a solution of the benzaldehyde (**2**) (1.0 mmol), 2,3-dihydrofuran (**3**) or 3,4-dihydropyran (**4**) (1.0 mmol), and aniline (**1**) (1.0 mmol) in 3.0 mL of anhydrous acetonitrile. After completion of the addition, stirring was continued at room temperature. The reaction mixture was quenched with water addition (3.0 mL). The mixture was extracted with

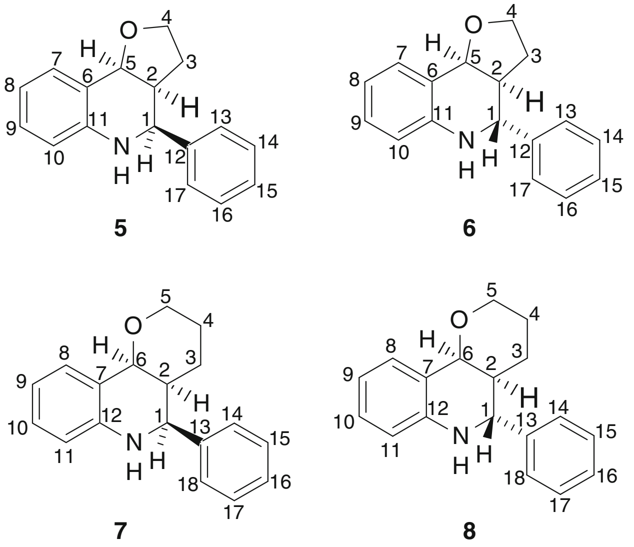


Fig. 2 Structure of tetrahydroquinoline derivatives **5**, **6**, **7** and **8**

Table 1 Attribution of 1D and 2D NMR data for compound **5**

Attribution	δ_C (ppm)	HSQC	δ_H (ppm)	Multiplicity	J (Hz)	COSY	HMBC
C1	56.5	**H1**	4.71	d	$J_1 = 3.0$	H2	H2, H3′, H13, H17
C2	44.8	**H2**	2.80	dddd	$J_1 = 10.4$; $J_2 = 8.1$; $J_3 = 8.0$; $J_4 = 3.0$	H1, H3′, H3″, H5	H1, H3′, H3″, H4′, H4″, H5
C3	23.7	**H3′**	2.21	dddd	$J_1 = 11.9$; $J_4 = 10.4$; $J_3 = 8.8$; $J_4 = 8.6$	H2, H3″, H4′, H4″	H1, H2, H4′, H4″, H5
		H3″	1.55	dddd	$J_1 = 11.9$; $J_2 = 8.1$; $J_3 = 7.5$; $J_4 = 3.4$	H2, H3′, H4′, H4″	
C4	65.8	**H4′**	3.84	ddd	$J_1 = 8.8$; $J_2 = 8.3$; $J_3 = 3.4$	H3′, H3″, H4″	H3′, H5
		H4″	3.74	ddd	$J_1 = 8.6$; $J_2 = 8.3$; $J_3 = 7.5$	H3′, H3″, H4′	
C5	74.9	**H5**	5.29	d	$J_1 = 8.0$	H2	H1, H2, H3″, H4′, H4″, H10
C6	121.7	**–**	**–**	**–**	**–**	**–**	H2, H5, H8, H9, H10
C7	129.1	**H7**	7.47	d	$J_1 = 7.6$	H8	H5, H8, H9
C8	118.2	**H8**	6.82	dd	$J_1 = 7.6$; $J_2 = 7.0$	H7, H9	H9, H10
C9	127.3	**H9**	7.10	dd	$J_1 = 8.0$; $J_2 = 7.0$	H8, H10	H5, H7, H8, H10
C10	113.9	**H10**	6.61	d	$J_1 = 8.0$	H9	H7, H8, H9
C11	143.9	–	–	–	–	–	H1, H5, H7, H8, H9, H10
C12	141.2	–	–	–	–	–	H1, H13, H17
C13	127.6	**H13**	7.36	m	–	H14	–
C14	125.5	**H14**	7.36	m	–	H13, H15, H16	–
C15	126.6	**H15**	7.36	m	–	H14, H16	–
C16	125.5	**H16**	7.36	m	–	H14, H15, H17	–
C17	127.6	**H17**	7.36	m	–	H16	–

Table 2 Attribution of 1D and 2D NMR data for compound **6**

Atribuition	δ_C (ppm)	HSQC	δ_H (ppm)	Multiplicity	J (Hz)	COSY	HMBC
C1	58.2	**H1**	3.74	d	$J_1 = 11.2$	H2	H2, H3′, H3″, H5, H13, H17
C2	43.8	**H2**	2.40	dddd	$J_1 = 11.2$; $J_2 = 7.7$; $J_3 = 4.9$; $J_4 = 2.1$	H1, H3′, H3″ H5	H1, H3′, H3″, H4′, H4″
C3	29.7	**H3′**	1.95	dddd	$J_1 = 13.2$; $J_2 = 8.3$; $J_3 = 6.0$; $J_4 = 2.1$	H2, H3″, H4′, H4″	H2, H4′, H4″, H5
		H3″	1.65	dddd	$J_1 = 13.2$; $J_2 = 9.2$; $J_3 = 7.7$; $J_4 = 6.2$	H2, H3′, H4′, H4″	
C4	65.6	**H4′**	3.96	ddd	$J_1 = 8.8$; $J_2 = 8.3$; $J_3 = 6.2$	H3′, H3″, H4″	H2, H3′, H3″
		H4″	3.77	ddd	$J_1 = 9.2$; $J_2 = 8.8$; $J_3 = 6.0$	H3′, H3″, H4′	
C5	76.6	**H5**	4.54	d	$J_1 = 4.9$	H2	H3″, H4′, H4″, H7, H10
C6	120.5	–	–	–	–	–	H5, H7, H8, H9, H10
C7	131.6	**H7**	7.37	d	$J_1 = 7.0$	H8	H5, H8, H9, H10
C8	118.8	**H8**	6.73	dd	$J_1 = 8.3$; $J_2 = 7.7$	H7, H9	H7, H9, H10
C9	129.6	**H9**	7.06	dd	$J_1 = 8.3$; $J_2 = 7.0$	H8, H10	H1, H7, H8
C10	115.1	**H10**	6.56	d	$J_1 = 7.7$	H9	H7, H8, H9
C11	145.8	–	–	–	–	–	H1, H5, H7, H8, H9
C12	142.1	–	–	–	–	–	H1, H2, H13, H17
C13	129.1	**H13**	7.31	m	–	H14	–
C14	128.7	**H14**	7.31	m	–	H13, H15, H16	–

Table 2 continued

Atribuition	δ_C (ppm)	HSQC	δ_H (ppm)	Multiplicity	J (Hz)	COSY	HMBC
C15	128.6	**H15**	7.31	m	–	H14, H16	–
C16	128.7	**H16**	7.31	m	–	H14, H15, H17	–
C17	129.1	**H17**	7.31	m	–	H16	–

ethyl acetate (10.0 mL). The organic layer was separated and washed with saturated sodium bicarbonate solution (3 × 10.0 mL), saturated brine (2 × 10.0 mL), and then dried over anhydrous magnesium sulfate. The solvent was removed under vacuum, and the products were purified by column chromatography through silica gel using mainly a mixture of hexane and ethyl acetate (9.0:1.0) as eluent.

NMR spectra

For obtaining spectra the NMR 1D (^{1}H and ^{13}C) and 2D (COSY, HSQC and HMBC) of synthesized compounds, was used an equipment Bruker AVANCE DRX 500 spectrometer (5 mm z-gradient BBI probe) operating at 500.13 MHz (^{1}H) or 125.78 MHz (^{13}C), using as internal standard the tetramethylsilane (TMS), using $CDCl_3$ as solvent.

Computational calculations

The structure of tetrahydroquinolines derivatives studied was optimized with the chloroform solvent effect by IE-FPCM method on the level B3LYP with the set of functions of cc-pVDZ basis [39]. The chemical shifts were calibrated with values calculated to TMS, using the GIAO

Table 3 Attribution of 1D and 2D NMR data for compound **7**

Atribuition	δ_C (ppm)	HSQC	δ_H (ppm)	Multiplicity	J (Hz)	COSY	HMBC
C1	59.7	**H1**	4.69	d	$J_1 = 2.3$	H2	H2, H3′, H3″, H6, H14, H18
C2	39.3	**H2**	2.16	dddd	$J_1 = 11.9$; $J_2 = 5.6$; $J_3 = 4.0$; $J_4 = 2.3$	H1, H3′, H3″, H6	H1, H3′, H3″, H4′, H4″, H6
C3	25.8	**H3′**	1.46	m	–	H2, H3″, H4′, H4″	H1, H2, H4′, H4″, H5′, H5″
		H3″	1.43	m	–	H2, H3′, H4′, H4″, H5′	
C4	18.4	**H4′**	1.55	m	–	H3′, H3″, H4″, H5′, H5″	H1, H2, H3′, H3″, H5′, H5″, H6
		H4″	1.31	dddd	$J_1 = 10.4$; $J_2 = 5.0$; $J_3 = 3.5$; $J_4 = 2.5$	H3′, H3″, H4′, H5″	
C5	61.0	**H5′**	3.58	dddd	$J_1 = 11.4$; $J_2 = 4.3$; $J_3 = 2.0$; $J_4 = 2.0$	H3″, H4′, H4″, H5″	H2, H3′, H4′, H6
		H5″	3.43	td	$J_1 = 11.4$; $J_2 = 11.4$; $J_3 = 2.5$	H4′, H4″, H5′	
C6	73.2	**H6**	5.33	d	$J_1 = 5.6$	H2	H1, H3′, H5′, H5″, H8, H9
C7	120.3	–	–	–	–	–	H6, H8, H9, H11
C8	129.2	**H8**	7.30	dd	$J_1 = 7.7$; $J_2 = 1.0$	H9, H10	H7, H9, H10, H11
C9	118.7	**H9**	6.79	ddd	$J_1 = 7.7$; $J_2 = 7.1$; $J_3 = 0.8$	H8, H10, H11	H8. H10, H11
C10	128.8	**H10**	7.09	ddd	$J_1 = 8.0$; $J_2 = 7.1$; $J_3 = 1.0$	H8, H9, H11	H8, H9, H11
C11	114.8	**H11**	6.60	dd	$J_1 = 8.0$; $J_2 = 0.8$	H9, H10	H8, H9, H10
C12	145.6	–	–	–	–	–	H1, H6, H8, H9, H10
C13	141.5	–	–	–	–	–	H1, H14, H18
C14	128.7	**H14**	7.40	m	–	H15, H16	–
C15	128.0	**H15**	7.40	m	–	H14, H16. H17	–
C16	127.2	**H16**	7.40	m	–	H14, H15, H17, H18	–
C17	127.9	**H17**	7.40	m	–	H15, H16, H18	–
C18	128.5	**H18**	7.40	m	–	H16, H17	–

Table 4 Attribution of 1D and 2D NMR data for compound **8**

Atribuition	δ_C (ppm)	HSQC	δ_H (ppm)	Multiplicity	J (Hz)	COSY	HMBC
C1	55.2	**H1**	4.72	d	$J_1 = 10.9$	H2	H3′, H3″, H6, H14, H18
C2	39.3	**H2**	2.11	ddt	$J_1 = 10.9$; $J_2 = 4.8$, $J_3 = 2.8$; $J_4 = 2.8$	H1, H3′, H3″, H6	H1, H3′, H3″, H4′, H4″
C3	24.5	**H3′**	1.65	ddt	$J_1 = 13.6$; $J_2 = 13.4$; $J_3 = 4.8$; $J_4 = 4.8$	H2, H3″, H4′, H4″	H2, H4′, H4″, H5′, H5″
		H3″	1.47	dtdd	$J_1 = 13.6$; $J_2 = 4.3$; $J_3 = 4.3$; $J_4 = 2.8$; $J_5 = 2.3$	H2, H3′, H4′, H4″, H5′	
C4	22.4	**H4′**	1.84	tddd	$J_1 = 13.4$; $J_2 = 13.4$; $J_3 = 11.4$, $J_6 = 4.3$; $J_5 = 2.3$	H3′, H3″, H4″, H5′, H5″	H1, H2, H3′, H3″, H5′, H5″, H6
		H4″	1.33	dddd	$J_1 = 13.4$; $J_2 = 4.8$; $J_3 = 4.3$; $J_4 = 2.5$	H3′, H3″, H4′, H5″	
C5	69.0	**H5′**	4.10	ddt	$J_1 = 11.4$; $J_2 = 4.3$; $J_3 = 2.3$; $J_4 = 2.3$	H3″, H4′, H4″, H5″	H2, H3′, H4′
		H5″	3.72	td	$J_1 = 11.4$; $J_2 = 11.4$; $J_3 = 2.5$	H4′, H4″, H5′	
C6	74.9	**H6**	4.39	d	$J_1 = 2.8$	H2	H1, H3′, H5′, H5″, H8, H9
C7	121.0	–	–	–	–	–	H6, H9, H11
C8	131.3	**H8**	7.22	dd	$J_1 = 7.7$; $J_2 = 1.3$	H9, H10	H9, H10, H11
C9	117.9	**H9**	6.71	ddd	$J_1 = 7.7$; $J_2 = 7.3$; $J_3 = 0.7$	H8, H10, H11	H10, H11
C10	129.8	**H10**	7.09	ddd	$J_1 = 8.1$; $J_1 = 7.3$; $J_1 = 1.3$	H8, H9, H11	H8, H9
C11	114.5	**H11**	6.53	dd	$J_1 = 8.1$; $J_2 = 0.7$	H9, H10	H8, H9, H10
C12	145.1	–	–	–	–	–	H1, H6, H8, H9, H10
C13	142.7	–	–	–	–	–	H1, H2, H14, H18
C14	129.0	**H14**	7.37	m	–	H15, H16	–
C15	128.3	**H15**	7.37	m	–	H14, H16. H17	–
C16	128.2	**H16**	7.37	m	–	H14, H15, H17, H18	–
C17	128.3	**H17**	7.37	m	–	H15, H16, H18	–
C18	129.0	**H18**	7.37	m	–	H16, H17	–

method and same level of theory. All the calculations were made using the Gaussian09 program [40]. The graphics and the correlation coefficients between the theoretical and experimental data were obtained with the aid of the Origin^{TM} program [41].

To analyze the ring conformation, the parameters were calculated using the standards of Cremer and Pople [42], for implementation CONFORM [43]. The input data was the same of calculated by GIAO level, without shifts, which caused an extrapolation of the data.

Results and discussion

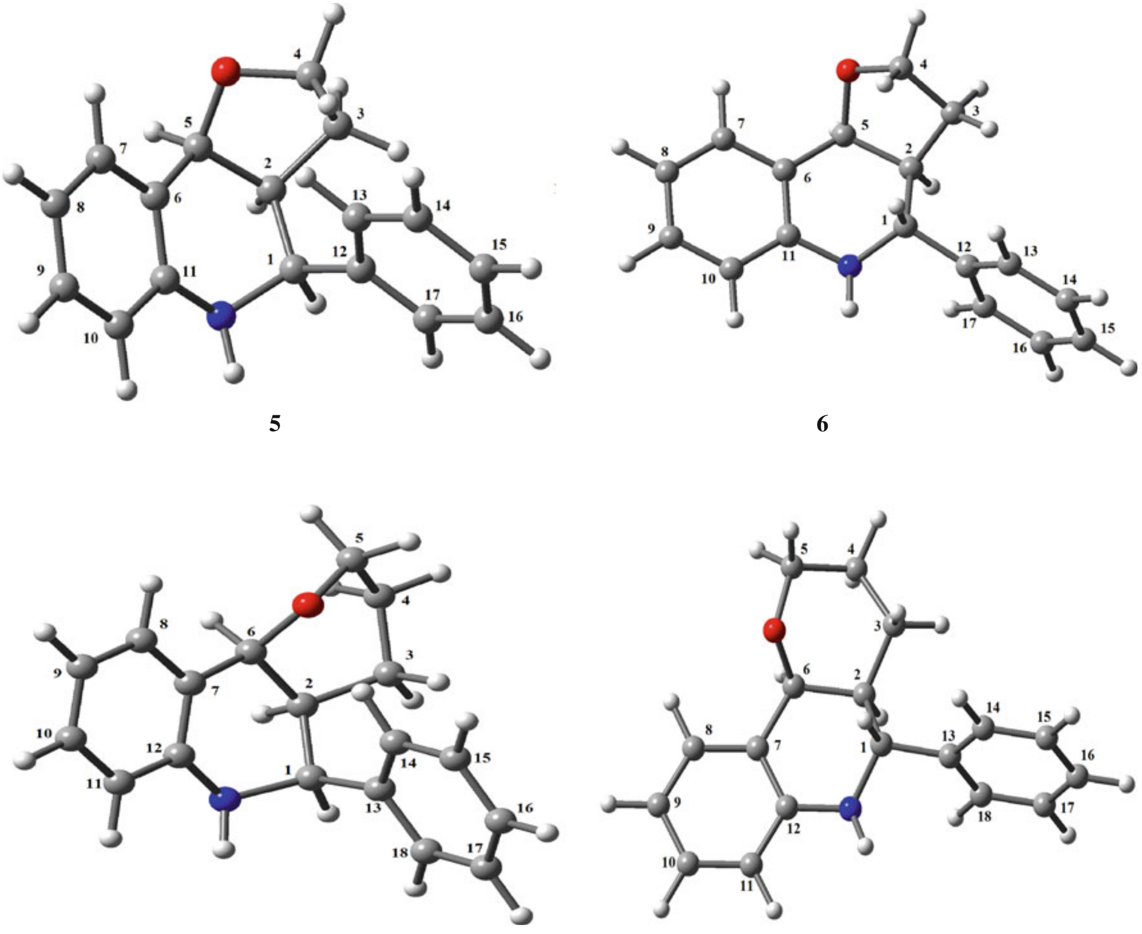
The unequivocal assignment of all chemical shifts of carbons and hydrogens, and measured hydrogen coupling constants to the tetrahydroquinoline derivatives **5**, **6**, **7**, and **8**, are shown in Fig. 2 and Tables 1, 2, 3, and 4, respectively.

Through NMR analysis, it was possible to determinate all chemical shifts for carbons and hydrogens, and another important information obtained by NMR analysis was the determination of the relative stereochemistry of the hydrogens H1 and H2, by determination of its coupling constants. The *cis* adducts, compounds **5** and **7**, show smaller coupling constants ($J_{1/2} = 3.0$ and 2.3 Hz, respectively), typical for a *cis* conformation between this hydrogens. In *trans* adducts, compounds **6** and **8**, the coupling constants are significantly higher ($J_{1/2} = 11.2$ and 10.9 Hz, respectively), indicative of the *trans* orientation of H-1 and H-2.

To confirm the correct attribution of all chemical shifts obtained experimentally, a theoretical study was realized for calculation of all ^{1}H and ^{13}C NMR chemical shifts of the tetrahydroquinoline derivatives studied. The structure of tetrahydroquinolines was initially optimized using B3LYP level of theory and with the basis set functions cc-pVTZ as input, and the minimum energy obtained for all structures are shown in Fig. 3.

The optimized structures of the tetrahydroquinoline derivatives show that the pyran ring, in compounds **7** and **8**, take on twist-boat conformation, due to the rigidity of the quinolinic ring and the "*syn*" addition mechanism of the aza-Diels–Alder reaction, that occur on the multicomponent Povarov reaction. The bond length and the bond angles between the atoms oxygen and nitrogen obtained in calculated structures for compound **5** (Table 5), are similar with the experimental data values obtained through of X-ray crystallography [44], which proves that the theory utilized for the simulation of these compounds was adequate, and the data obtained are near of the real compounds. The calculated dihedral angles, between the hydrogens H2/H5 to compounds **5** and **7**, and H2/H6 to compounds **6** and **8**, near the 0° justified the values of coupling constant measured for this hydrogens, because they are in accordance to Karplus equations, that correlate the relationship between the dihedral angle and the vicinal coupling constant $_{3}J$ [45–47] (Table 6).

About the ring conformation, in the calculated compounds **5** and **6**, the furan ring adopts a twist conformation with puckering parameters $q_2 = 20.875$ (3) Å and $\Phi_2 = 314.984$ (9)° for compound **5**, and $q_2 = 19.755$ (6) Å and $\Phi_2 = 164.92$ (1)° for molecule **6**; and the piperidine ring exists in a half-boat conformation for both structures [$\theta = 43.323$ (1)° and $\Phi = 240.046$ (1)° for compound **5**, and $Q = 5150.372$ (4) Å, $\theta = 136.774$ (1)° and $\Phi = 60.022$ (1)° for compound **6**]. For the calculated compounds **7** and **8**, the pyran rings adopts a half-boat conformation [$Q = 3990.713$ (4) Å, $\theta = 136.546$ (1)° and $\Phi = 59.574$ (1)° for compound **7**, and $Q = 3990.713$ (4) Å, $\theta = 136.546$ (1)° and $\Phi = 59.574$ (1)° for compound **8**], like the piperidine rings for the same compounds [$Q = 1813.727$ (6) Å, $\theta = 136.396$ (1)° and $\Phi = 59.983$ (1)° for compound **7**, and $Q = 582.962$ (6) Å, $\theta = 44.159$ (1)° and $\Phi = 239.887$ (1)° for compound **8**].



5 **6**

7 **8**

Fig. 3 Structure optimized for the tetrahydroquinoline derivatives

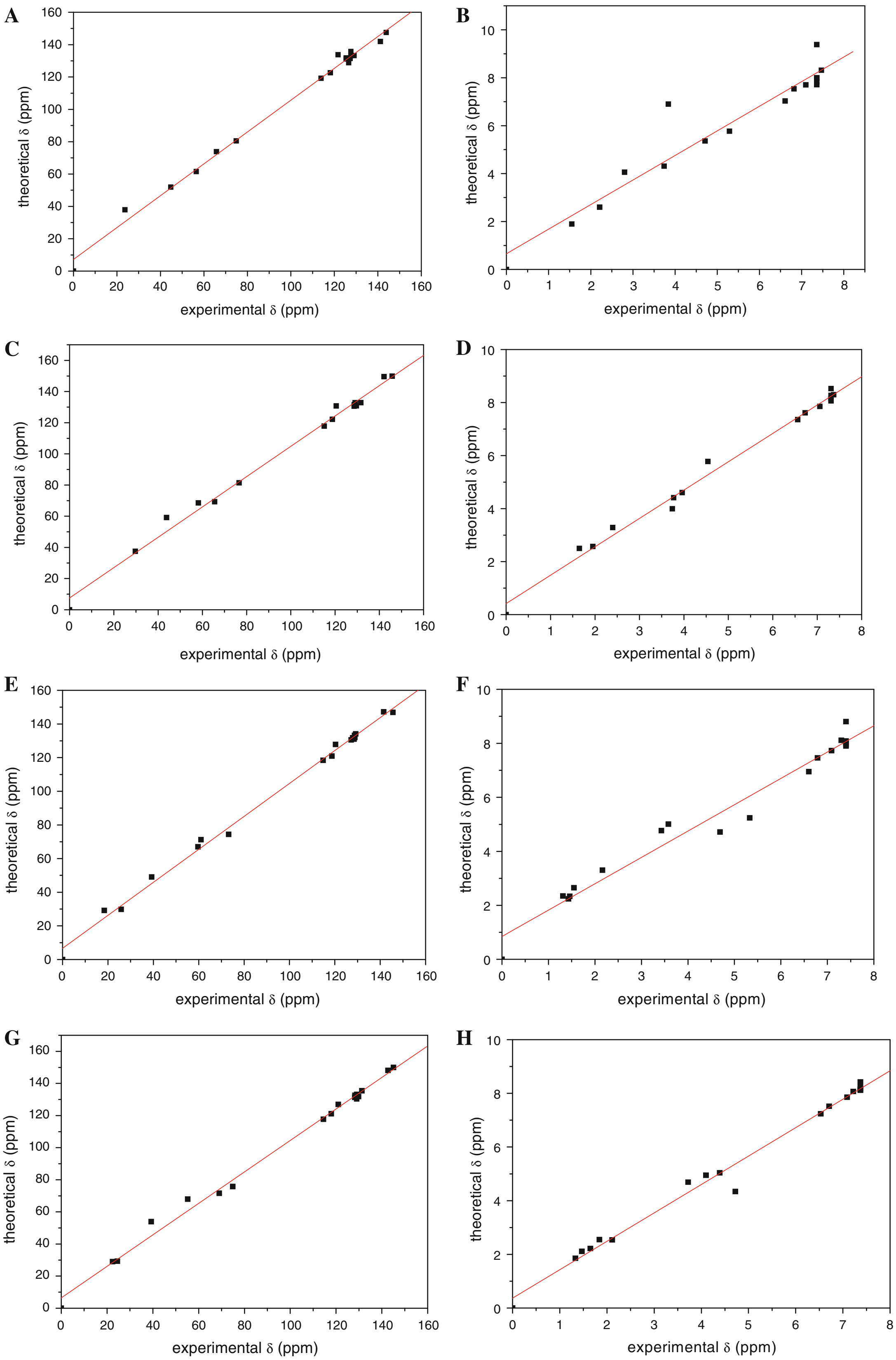


Fig. 4 Correlation graphics for: **a** (compound **5**—NMR ^{13}C); **b** (compound **5**—NMR ^{1}H); **c** (compound **6**—NMR ^{13}C); **d** (compound **6**—NMR ^{1}H); **e** (compound **7**—NMR ^{13}C); **f** (compoundo **7**—NMR ^{1}H); **g** (compound **8**—NMR ^{13}C)e; **h** (compound **8**—NMR ^{1}H)

Table 5 Calculated and experimental bond length (Å) and bond angle (°) for the tetrahydroquinoline derivatives

Compound	Bond	Calculated bond length (Å)	Experimental bond length (Å)*		Calculated bond angle (°)	Experimental bond angle (°)*
5	O–C_4	1.42	1.425	C_4–O_5–C_5	108.15	107.84
	O–C5	1.44	1.429			
	N–C_1	1.47	1.457	C_1–N_5–C_{11}	114.92	120.02
	N–C_{11}	1.40	1.386			
6	O–C_4	1.42	–	C_4–O_6–C_5	108.15	–
	O–C_5	1.44	–			–
	N–C_1	1.47	–	C_1–N_6–C_{11}	114.92	–
	N–C_{11}	1.40	–			–
7	O7–C_5	1.43	–	C_5–O_7–C_6	112.48	–
	O7–C_6	1.44	–			–
	N7–C_1	1.47	–	C_1–N_7–C_{12}	118.20	–
	N7–C_{12}	1.40	–			–
8	O–C_5	1.43	–	C_5–O_8–C_6	111.90	–
	O–C_6	1.43	–			–
	N–C_1	1.46	–	C_1–N_8–C_{12}	116.92	–
	N–C_{12}	1.40	–			–

* Ref [44]

Table 6 Calculated dihedral angle for the tetrahydroquinoline derivatives

Compound	Hydrogens	Diedral angle (°)	J_{exp} (Hz)
5	H1/H2	26.0	3.0
	H2/H5	−10.1	8.0
6	H1/H2	166.2	11.2
	H2/H5	−10.1	7.7
7	H1/H2	46.5	2.3
	H2/H6	−27.7	5.6
8	H1/H2	−180.0	10.9
	H2/H6	−34.1	2.8

The calculated NMR shielding tensors were converted into chemical shifts, considering the isotropic values of the shielding tensors of ^{1}H and ^{13}C of TMS ($\delta_C = 196.70$ and $\delta_H = 32.23$), calculated at the same levels of theory. The values obtained from chemical shifts for the four structures are shown in Tables 7, 8, 9, and 10.

Analyzing the Tables 7, 8, 9, and 10, it is verified that there is a good agreement between experimental and theoretical data, thus, the theoretical level utilized for the simulation of the compounds was appropriate, and provided us a more precise analysis in relation to the chemical shifts, However, a comparison between experimental and theoretical data was realized from the graphics (Fig. 4) and correlation coefficients (Table 11) to confirm a good correlation existing between the two methods utilized.

Table 7 Theoretical and experimental ^{1}H and ^{13}C chemical shifts (ppm) for compound **5**

C	δ_C[a]	δ_C[b]	H	δ_H[a]	δ_H[b]
1	56.5	61.54	**1**	4.71	5.36
2	44.8	51.90	**2**	2.80	4.05
3	23.7	37.93	**3′**	2.21	2.60
			3″	1.55	1.89
4	65.8	73.82	**4′**	3.84	6.89
			4″	3.74	4.31
5	74.9	80.45	**5**	5.29	5.76
6	121.7	133.75	**–**	–	–
7	129.1	133.21	**7**	7.47	8.31
8	118.2	122.61	**8**	6.82	7.53
9	127.3	131.40	**9**	7.10	7.69
10	113.9	119.19	**10**	6.61	7.02
11	143.9	147.52	**–**	–	–
12	141.2	141.94	**–**	–	–
13	127.6	135.70	**13**	7.36	9.38
14	125.5	131.13	**14**	7.36	7.71
15	126.6	128.79	**15**	7.36	7.99
16	125.5	131.80	**16**	7.36	7.98
17	127.6	133.21	**17**	7.36	7.82

[a] Experimental values

[b] Theoretical values

The analysis of Fig. 4 and Table 11 allows us to confirm the excellent concordance between the results, since all the correlation coefficients are close to 1, which indicates that

Table 8 Theoretical and experimental ^{1}H and ^{13}C chemical shifts (ppm) for compound **6**

C	δ_{C}[a]	δ_{C}[b]	H	δ_{H}[a]	δ_{H}[b]
1	58.2	68.50	**1**	3.74	3.99
2	43.8	59.22	**2**	2.40	3.28
3	29.7	37.48	**3′**	1.95	2.57
			3″	1.65	2.49
4	65.6	69.31	**4′**	3.96	4.60
			4″	3.77	4.41
5	76.6	81.44	**5**	4.54	5.78
6	120.5	130.72	–	–	–
7	131.6	132.84	**7**	7.37	8.29
8	118.8	122.14	**8**	6.73	7.61
9	129.6	130.84	**9**	7.06	7.85
10	115.1	117.80	**10**	6.56	7.35
11	145.8	149.87	–	–	–
12	142.1	149.55	–	–	–
13	129.1	132.77	**13**	7.31	8.52
14	128.7	131.29	**14**	7.31	8.26
15	128.6	130.61	**15**	7.31	8.17
16	128.7	131.49	**16**	7.31	8.12
17	129.1	132.74	**17**	7.31	8.06

[a] Experimental values

[b] Theoretical values

Table 9 Theoretical and experimental ^{1}H and ^{13}C chemical shifts (ppm) for compound **7**

C	δ_{C}[a]	δ_{C}[b]	H	δ_{H}[a]	δ_{H}[b]
1	59.7	67.04	**1**	4.69	4.71
2	39.3	49.09	**2**	2.16	3.30
3	25.8	29.80	**3′**	1.46	2.33
			3″	1.43	2.24
4	18.4	29.16	**4′**	1.55	2.65
			4″	1.31	2.34
5	61.0	71.25	**5′**	3.58	5.01
			5″	3.43	4.76
6	73.2	74.39	**6**	5.33	5.23
7	120.3	127.85	–	–	–
8	129.2	134.11	**8**	7.30	8.11
9	118.7	120.94	**9**	6.79	7.46
10	128.8	131.97	**10**	7.09	7.73
11	114.8	118.37	**11**	6.60	6.95
12	145.6	146.90	–	–	–
13	141.5	147.21	–	–	–
14	128.7	133.22	**14**	7.40	7.89
15	128.0	131.76	**15**	7.40	8.02
16	127.2	130.55	**16**	7.40	8.80
17	127.9	131.68	**17**	7.40	8.08
18	128.5	130.93	**18**	7.40	7.95

[a] Experimental values

[b] Theoretical values

all the experimental data are in good agreement with the theoretical data, for both the chemical displacements (carbon and hydrogen).

Table 10 Theoretical and experimental ^{1}H and ^{13}C chemical shifts (ppm) for compound **8**

C	δC[a]	δC[b]	H	δH[a]	δH[b]
1	55.2	67.99	**1**	4.72	4.33
2	39.3	53.97	**2**	2.11	2.53
3	24.5	29.29	**3′**	1.84	2.11
			3″	1.33	1.85
4	22.4	28.99	**4′**	1.65	2.55
			4″	1.47	2.21
5	69.0	71.57	**5′**	4.10	4.94
			5″	3.72	4.69
6	74.9	75.75	**6**	4.39	5.03
7	121.0	126.96	–	–	–
8	131.3	135.46	**8**	7.22	8.06
9	117.9	121.10	**9**	6.71	7.51
10	129.8	131.82	**10**	7.09	7.85
11	114.5	117.71	**11**	6.53	7.23
12	145.1	149.97	–	–	–
13	142.7	148.11	–	–	–
14	129.0	133.11	**14**	7.37	8.42
15	128.3	132.60	**15**	7.37	8.22
16	128.2	131.30	**16**	7.37	8.15
17	128.3	131.48	**17**	7.37	8.11
18	129.0	130.41	**18**	7.37	8.11

[a] Experimental values

[b] Theoretical values

Table 11 Correlation coefficient (*R*) for ^{1}H and ^{13}C chemical shifts

Compound	*R*–^{13}C	*R*–^{1}H
5	0.99682	0.96042
6	0.99610	0.99576
7	0.99794	0.98581
8	0.99706	0.99437

Therefore, we can to conclude that the theoretical level adopted in our studies to describe the structure of tetrahydroquinolines derivatives was appropriate, showing a good theoretical–experimental correlation, which helped us in the determining the structure of studied derivatives.

The correlation between the experimental and theoretical data show to be an excellent tool to help the structural elucidation and unequivocally attribution of all

NMR signals of tetrahydroquinolines studied. Other point to be detached in this work is that the values of NMR chemical displacement obtained with the theoretical level B3LYP/cc-pVDZ allows the association of a computational cost not so high and an accurate precision of results obtained.

Conclusion

Based on the results mentioned above, we can conclude that the theoretical data showed an excellent correlation with the experimental data and reinforce the structural elucidation and assignments of all NMR signals for Povarov adducts treated in this work. For these derivatives, the experimental analyses and the theoretical model adopted were sufficient to obtain a good description of its structures, and these results can be used to assign the structure of various others tetrahydroquinoline derivatives synthetized by Povarov reaction. The theory-level B3LYP/cc-pVDZ proved to be an effective model to perform the calculation of the chemical shift of ^{1}H and ^{13}C-NMR.

Acknowledgments The authors would like to thank Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) (Procs. N° 2010/18022-2; 2011/15186-7 and 2011/04006-8), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenadoria de Aperfeiçoamento de Pessoal do Nível Superior (CAPES), and Pró-Reitoria de Pesquisa da UNESP (PROPe-UNESP) for their financial support.

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