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Article

NMR Structural Analysis of #Braznitidumine: A New Indole Alkaloid with 1,2,9-Triazabicyclo[7.2.1] System, Isolated from *Aspidosperma nitidum* (Apocynaceae)

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O estudo fitoquímico das cascas do cerne de *Aspidosperma nitidum* permitiu o isolamento de um novo tipo de alcalóide indólico, contendo um sistema 1,2,9-triazabiciclo[7.2.1], que foi denominado braznitidumina **1**. A caracterização de sua estrutura química foi realizada pela análises dos dados de IV, UV, ESI-EM e RMN de ^{1}H, ^{13}C e ^{15}N, empregando experimentos 1D e 2D (^{1}H ^{1}H COSY, ^{1}H ^{1}H NOESY, ^{1}H ^{13}C HSQC e ^{1}H ^{13}C HMBC). Pela análise do experimento ^{1}H ^{1}H NOESY, verificou-se que **1** apresenta uma conformação dobrada com aproximação entre os grupos indólico e imidazolidino-di-hidropirano. Essa configuração foi investigada por cálculos teóricos envolvendo otimizações de geometria (DFT/BLYP/6-31G*) para análise conformacional desse alcalóide, pela qual a distância entre os dois grupos mostrou-se compatível com as informações obtidas pelo experimento NOESY.

The phytochemical study of the stem bark of *Aspidosperma nitidum* led to the isolation of a new type of indole alkaloid with a 1,2,9-triazabicyclo[7.2.1] system, which has been called braznitidumine **1**. The characterization of its chemical structure was carried out by IR, UV, ESIMS, and ^{1}H, ^{13}C, and ^{15}N NMR by using 1D and 2D (^{1}H ^{1}H COSY, ^{1}H ^{1}H NOESY, ^{1}H ^{13}C HSQC and ^{1}H ^{13}C HMBC) experiments. ^{1}H ^{1}H NOESY results showed that **1** presents a folded conformation with the approximation of the indole and the imidazolidine di-hydropyran groups. This configuration was investigated by theoretical calculations involving geometry optimization (DFT/BLYP/6-31G*) for the conformational analysis of this alkaloid. It confirmed the distance between the two groups in agreement with the NOESY experimental data.

Keywords: Apocynaceae, *Aspidosperma nitidum*, indole alkaloid, 1,2,9-triazabicyclo[7.2.1] system

Introduction

The *Aspidosperma* Mart. (Apocinaceae) genus is native to Americas and is found from Mexico to Argentina.[1] The literature reports the presence of alkaloids in species of this genus, mainly indole ones.[2] *Aspidosperma nitidum*, popularly known as *carapanaúba*, is widely distributed in the Amazonas State, Brazil. The stem barks of this species are largely employed in folk medicine as a contraceptive, antimalarial, antiinflammatory (uterus and ovary), anticarcinogenic, antidiabetic, antileprosy, and for stomach upsets.[3] Nevertheless, just one report has been found in literature on its chemical components.[4] In that work the only reported alkaloid from this species was 10-methoxydihydrocorynantheol.

In this paper, we report the results of the phytochemical study of the *Aspidosperma nitidum* species. From the ethanolic extract was isolated the indole alkaloid (**1**) named braznitidumine, which has a very interesting bridged chemical structure containing a 1,2,9-triazabicyclo[7.2.1] system. The structure was determined by means of spectroscopic techniques, mainly ESIMS, IR and 1D and 2D NMR spectra.

Results and Discussion

Purification of the stem bark ethanol extract of *Aspidosperma nitidum* by silica gel column

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This name is an homage to Professor Raimundo Braz-Filho. This article was submitted to the special issue dedicated to Professor Raimundo Braz-Filho on the occasion of his 70th birthday.

Table 1. ^{1}H (400 MHz), ^{13}C (100 MHz), and ^{15}N (40.55 MHz) NMR data (including ^{1}H ^{15}N and ^{1}H ^{13}C HSQC and ^{1}H ^{13}C HMBC correlations) of braznitidumine (**1**) in DMSO-d_6

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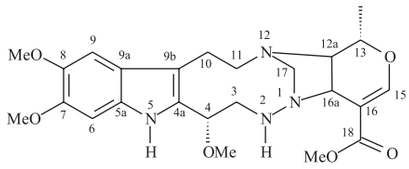

	HSQC			HMBC		
Atom	δ_N	δ_C	δ_H	$^{2}J_{C,H}^{a,b}$	$^{3}J_{C,H}^{a,b}$	$^{4}J_{C,H}^{b}$
2	55.0		2.00	H-3#	H-16a#	-
3		32.3	2.64	-	-	
4		64.0	4.90	MeO-4	-	
4a		127.3		H-4	H-10	-
5	127.4		11.13	-	H-6#	-
5a		130.8		H-6	H-9	
6		95.4	6.90	-	-	H-9; MeO-7
7		146.9		-	H-9; MeO-7	-
8		144.6		-	H-6; MeO-8	-
9		101.1	7.01	-	-	H-6; MeO-8
9a		118.2		-	H-6; H-10	-
9b		102.1		H-10	H-9; H-4; H-11*	-
10		17.8	2.98	H-11	-	-
11		54.3	3.84	-	-	-
12a		35.7	2.26	-	Me-13	-
13		71.3	4.55	Me-13	H-16a**	-
15		155.0	7.53	-	-	-
16		107.6	-	-	-	
16a		27.6	3.00	-	-	-
17		61.4	4.03	-	-	-
18		166.4		-	MeO-18; H-16a**	-
Me-13		17.9	1.44	-	-	-
MeO-4		49.6	3.26	-	H-4**	-
MeO-7		56.1	3.76	-	-	-
MeO-8		55.8	3.76	-	-	-
MeO-18		51.1	3.66	-	-	-

[a]delay = 65 ms; [b]delay = 130 ms; [#]delay = 125 ms; *correlation observed only in a; **correlation observed only in b.

chromatography resulted in the isolation of the new indole alkaloid (**1**). Its molecular formula, $C_{24}H_{32}N_4O_6$, was deduced from the precisely determined mass of the molecular ion peak [M$^+$] at *m/z* 472.682 in the positive mode ESIMS. This molecular formula has 11 degrees of unsaturations, which is in agreement with ^{1}H (1D and 2D COSY), ^{13}C (1D and 2D HSQC, HMBC) NMR spectral data. 1D ^{1}H and ^{13}C ({^{1}H} and DEPT) and 2D (^{1}H ^{13}C HSQC, ^{1}H ^{15}N HSQC, ^{1}H ^{13}C HMBC, ^{1}H ^{15}N HMBC) NMR experiments led to the elucidation of a very interesting new indole alkaloid, name braznitidumine, as yet unreported in the literature.

A NH and a conjugated carbonyl group were identified by absorption bands at 3430 and 1697 cm^{-1}, respectively, observed in the IR spectrum of **1**.[5] The UV spectral data of **1** in methanol, λ_{max} 208.80, 217.37, 272.20, and 305.50 nm, were characteristic of indole systems.[6]

Tables 1 and 2 show ^{1}H, ^{13}C, and ^{15}N NMR data of compound **1**. The ^{1}H NMR spectrum showed most of the hydrogen resonance as unresolved broad signals (290 to 300 K). This spectrum revealed the presence of an indole group by singlets at δ_H 7.01 (H-9) and 6.90 (H-6), which show correlations in the ^{1}H ^{13}C HSQC with the ^{13}C signals at δ_C 101.1 (C-9) and 95.4 (C-6), respectively. It also displayed long range correlations in the ^{1}H ^{13}C HMBC of the signal at δ_H 7.01 with the ^{13}C signals at δ_C 95.4 (C-6), 102.1 (C-9b), 130.8 (C-5a), and 146.9 (C-7); of the signal at δ_H 6.90 with the ^{13}C signals at δ_C 101.1 (C-9), 118.2 (C-9a), and 144.6 (C-8); of the signal at δ_H 3.76, relative to six hydrogens of methoxyl groups (MeO-7 and MeO-8), with the ^{13}C signals at δ_C 95.4 (C-6), 101.1 (C-9), 144.6 (C-8), and 146.9 (C-7) (Figure 1). These last correlations indicate the phenyl moiety of an indole group, with two *orto* methoxyl substituents. The ^{1}H NMR spectrum also shows a singlet at δ_H 11.13 (H-5), which is not correlated to any signal either by ^{1}H ^{1}H COSY or ^{1}H ^{13}C HSQC, but that is correlated with the ^{15}N signal at δ_N 127.4 (N-5) by ^{1}H ^{15}N HSQC. Through these last data, it was identified

Table 2. ^{1}H (400 MHz) NMR data (including ^{1}H ^{1}H COSY and ^{1}H ^{1}H NOESY correlations) of braznitidumine (**1**) in DMSO-d_6

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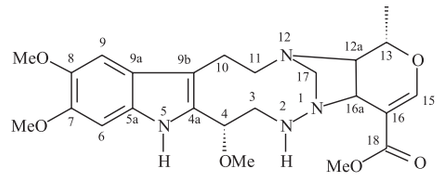

Atom	δ_H (multiplicity)	^{1}H ^{1}H COSY	^{1}H ^{1}H NOESY	
			Experiment 1[a]	Experiment 2[b]
2	2.00 (b)	H-3; H-4; H-16a	H-16a	
3	2.64 (bd, *J* 15.0 Hz)	H-2; H-4	H-4; H-10	H-5; H-10
4	4.90 (dd, *J* 7.5 and 2.0 Hz)	H-2; H-3	H-3; MeO-4	H-5; MeO-4; MeO-18
5	11.13 (b)			H-3; H-4; H-6; MeO-18
6	6.90 (s)			H-5; MeO-7; MeO-18
9	7.01 (s)			MeO-8
10	2.98 (b)	H-11	H-3	H-3
11	3.84 (m)	H-10		Me-13
12a	2.26 (b)	H-13; H-17; H-16a		Me-13; MeO-4
13	4.55 (m)	H-12a; Me-13	Me-13	Me-13; MeO-18
15	7.53 (s)			MeO-18
16a	3.00 (b)	H-12a; H-2	H-2	
17	4.03 (b)	H-12a	MeO-4	
Me-13	1.44 (d, *J* 5.8 Hz)	H-13	H-13	H-12a; H-11; H-13
MeO-4	3.26 (s)	H-4; H-17	H-4; H-12a	
MeO-7	3.76 (s)			H-6
MeO-8	3.76 (s)			H-9
MeO-18	3.66 (s)			H-4; H-5; H-6; H-13; H-15

[a]in experiment 1, mixing time = 350 ms; [b]in experiment 2, mixing time = 700 ms; b = broad; bd = broad doublet; d = doublet; dd = double doublet.

an NH by the indole group. Finally, a correlation was observed of the ^{1}H signal at δ_H 6.90 (H-6) with the ^{15}N signal at δ_N 127.4 (N-5) by ^{1}H ^{15}N HMBC.

The connectivity of the indole group with the rest of the molecule was deduced from the following ^{1}H ^{13}C HMBC correlations: the signal at δ_H 2.98 (H-10) with the ^{13}C signals at δ_C 102.1 (C-9b) *via* ^2J, 127.3 (C-4a) *via* ^3J, and 118.2 (C-9a) *via* ^3J; the signal at δ_H 3.84 (H-11) with the ^{13}C signal at δ_C 102.1 (C-9b) *via* ^3J; the signal at δ_H 4.90 (H-4) with the ^{13}C signals at δ_C 102.1 (C-9b) *via* ^3J and 127.3 (C-4a) *via* ^2J.

The homonuclear spin-spin couplings of H-10 with H-11 and of H-4 with both hydrogens having signals at δ_H 2.00 (H-2) and 2.64 (H-3) were revealed by 2D ^{1}H ^{1}H COSY and so was the coupling between H-2 and H-3. Other ^{1}H ^{13}C HSQC correlations were observed: H-3 with the ^{13}C signal at δ_C 32.3 (C-3); H-10 with the ^{13}C signal at δ_C 17.8 (C-10); H-11 with the ^{13}C signal at δ_C 54.3 (C-11); H-4 with the ^{13}C signal at δ_C 64.0 (C-4). No HSQC correlation was observed to the H-2 signal. In addition, ^{1}H ^{13}C HMBC long range ^2J and ^3J correlations were observed for the H-11 signal and the MeO-4 signal at δ_H 3.26 with the ^{13}C signals at δ_C 17.8 (C-10) and 64.0 (C-4), respectively. ^{1}H ^{15}N HSQC shows correlation of the ^{1}H signal at δ_H 2.00 (H-2) with the ^{15}N signal at δ_N 55.0 (N-2), which shows long range correlations with the signals at δ_H 2.64 (H-3), 3.00 (H-16a), and 3.26 (MeO-4) in ^{1}H ^{15}N HMBC.

Some broad and relatively very small signals characteristic of nitrogen-bonded aliphatic carbons[7] were observed in the ^{13}C NMR spectrum at δ_C 27.6 (CH-16a), 32.3 (CH_2-3), 35.7 (CH-12a), 54.3 (CH_2-11), and 61.4 (CH_2-17). The ^{1}H ^{13}C HMQC and ^{1}H ^{13}C HSQC experiments confirmed these signals were due to hydrogenated carbons.

The substituted indole fragment shown in Figure 1 was inferred from all the data discussed above. In this fragment, the proximity of the NH indole and the oxygen of MeO-4 may lead to the formation of a hydrogen bond and thus explain the deshielding at δ_H 11.13 observed for H-5.

In addition, the combination of ^{1}H and ^{13}C NMR data with the IR spectrum revealed a molecular fragment of dihydropyran methyl ester (Figure 2). All the three signals of both non-hydrogenated ^{13}C at δ_C 107.6 (C-16) and 166.4 (C-18) as well as the one of ^{13}C at δ_C 155.0 (C-15), show correlations by ^{1}H ^{13}C HSQC with the ^{1}H signal at δ_H 7.53 (H-15), and are therefore compatible with the conjugated carbonyl system deduced from the IR spectrum. The ^{1}H signals at δ_H 3.66 (MeO-18) and at δ_H 3.00 (H-16a) are both correlated with the carbonyl ^{13}C signal at δ_C 166.4

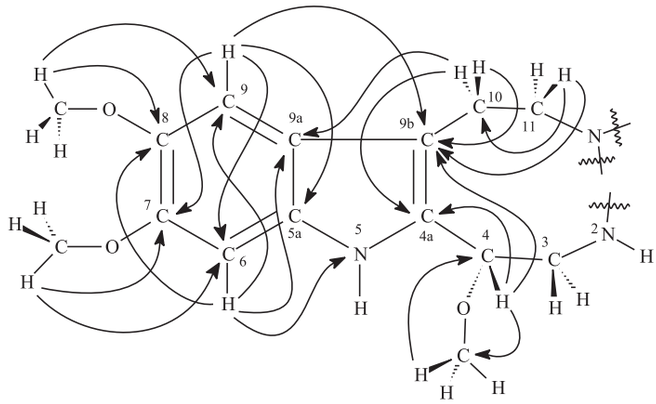

Figure 1. Important ^{1}H ^{13}C HMBC (*via* ^{2}J, ^{3}J, and ^{4}J) and ^{1}H ^{15}N HMBC (*via* ^{3}J) correlations for indole fragment of braznitidumine (**1**).

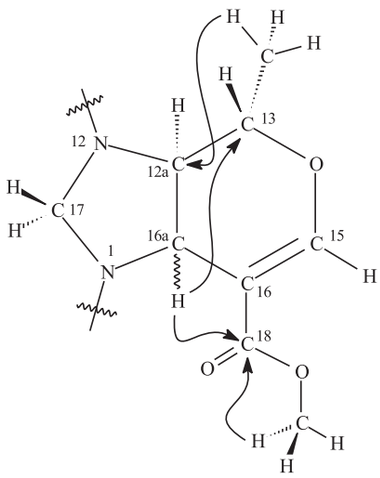

Figure 2. Substituted-fused imidazolidine-pyran system fragment of braznitidumine (**1**), and ^{1}H ^{13}C HMBC correlations.

(C-18) in ^{1}H ^{13}C HMBC. On the other hand, H-16a is correlated with the nitrogenated ^{13}C signal at δ_C 27.6 (C-16a) in ^{1}H ^{13}C HSQC and with the ^{13}C signal at δ_C 71.3 (C-13) in ^{1}H ^{13}C HMBC. H-16a is coupled with a hydrogen with a signal at δ_H 2.26 (H-12a) in ^{1}H ^{1}H COSY (Table 2). The latter shows spin-spin coupling with hydrogens presenting signals at δ_H 4.55 (H-13) and 4.03 (H-17) in ^{1}H ^{1}H COSY and it correlates with the nitrogenated ^{13}C signal at δ_C 35.7 (C-12a) in ^{1}H ^{13}C HSQC. The spin-spin coupling between H-12a and H-17 is weak and is only detected by ^{1}H ^{1}H COSY, possibly due to a W ^{4}J coupling.

The methyl signal at δ_H 1.44 (Me-13), which is correlated with the ^{13}C signal at δ_C 17.9 (Me-13) in ^{1}H ^{13}C HSQC, is correlated with the signal at δ_H 4.55 (H-13) in ^{1}H ^{1}H COSY and with the ^{13}C signal at δ_C 35.7 (C-12a) in ^{1}H ^{13}C HMBC. Finally, in ^{1}H ^{13}C HSQC, the ^{13}C signal at δ_C 61.4 (C-17) is correlated with the signal at δ_H 4.03 and so must be the remaining of the cited aliphatic nitrogenated CH_2 detected in the DEPT experiment. As its attached hydrogen shows weak coupling with H-12a in the ^{1}H ^{1}H COSY and also because of its chemical shift, this CH_2 group is thought to be linked to two nitrogen atoms in a fused 5-6 ring system, *i.e.* a substituted fused imidazolidine-pyran system fragment of **1**, as shown in Figure 2. The literature reports some other indole alkaloids isolated from *Aspidosperma* species as isomitrafiliane, 3-isoajamalicine, mitrafiline, and isomitrafilinic acid with a substituted pyran fragment, but none with the fused imidazolidine-pyran system shown in Figure 2.[8] Taking into account the molecular formula and the deduced structure of both the indole (Figure 1) and the imidazolidine-pyran (Figure 2) fragments, one of the aliphatic nitrogen atoms of each of these fragments must be shared to connect them. Hence, the structure containing the bridgehead-nitrogen bridged-bicyclic system shown in Figure 3 is proposed for braznitidumine **1**. In accord with this, ^{1}H ^{15}N HMBC shows long range correlation of the signal at δ_N 55.0 (N-2) with the signal at δ_H 2.64 (H-3, *via* ^{2}J), with the signal at δ_H 3.00 (H-16a, *via* ^{3}J), and with the signal at δ_H 3.26, showing weak coupling (MeO-4, *via* ^{5}J). No other correlations were observed in the NMR experiments performed (^{1}H ^{1}H COSY, ^{1}H ^{13}C HMBC, ^{1}H ^{15}N HMBC) *via* scalar homonuclear or heteronuclear spin-spin coupling of imidazolidine-pyran system atoms with indole fragment atoms. However, the proposed structure **1** was confirmed by dipolar interaction due to spatial proximity observed as correlations in ^{1}H ^{1}H NOESY experiment (Table 2). Figure 3 shows the ^{1}H ^{1}H NOESY correlations detected for braznitidumine **1**.

No correlation of the signal at δ_H 2.26 (H-12a) with the signal at δ_H 3.00 (H-16a) in ^{1}H ^{1}H NOESY was observed. The correlations of H-12a with both Me-13 and H-17 show that they are on the same side of the molecule. The latter correlates also with OMe-4. Thus, the relative configuration of H-12a is established relatively to those

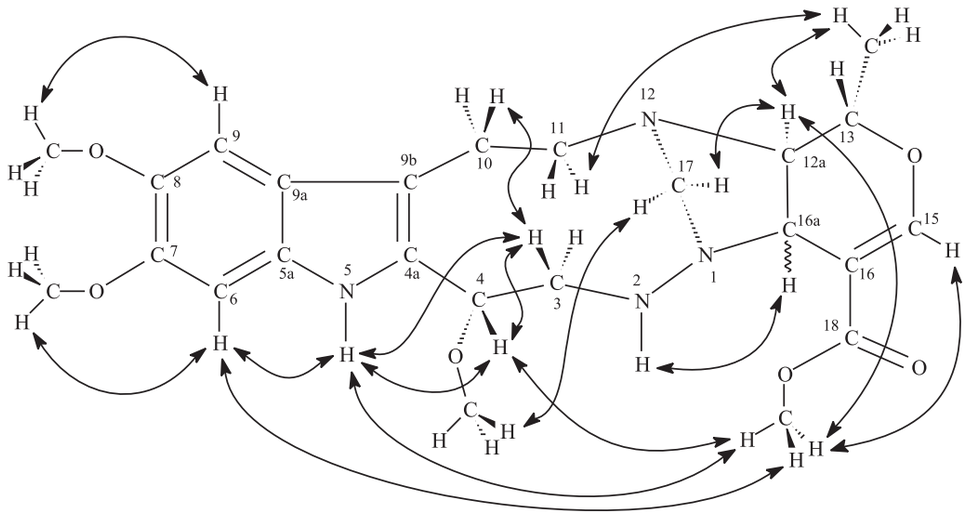

Figure 3. Structure of braznitidumine (**1**) and principal ^{1}H ^{1}H NOESY correlations.

groups in the molecule. However, nothing may be deduced for H-16a configuration, because the only correlation it presents is with the NH-2 (Figure 3). Therefore, H-16a may be *cis* or *trans* relatively to H-12a.

The correlations of MeO-18 with H-4, H-5, and H-6, as well as the correlation of Me-13 with H-11 indicates their spatial proximity, which could be explained if braznitidumine show a folded conformation. This conformation may be accounted for if the imidazolidine-pyran ring fusion is *trans* or *cis* as may be seen by the Dreiding model as well by the DFT/BLYP/6-31G* optimized geometry (Figures 4a and 4b, respectively).

Figure 4 shows the DFT/BLYP/6-31G* optimized geometry of **1** considering the solvent (DMSO) effect by PCM method. By single bond rotations of this geometry, the folding could be verified from spatial proximity of Me-13 with H-11, as well as of MeO-18 with H-4, H-6, and H-5. In the folded *trans* configuration (Figure 4a), the hydrogen interatomic distances are: C$\underline{H}_3$O-18 – H-5 = 2.470 Å; C$\underline{H}_3$O-18 – H-6 = 4.326 Å; C$\underline{H}_3$O-18 – H-4 = 1.210 Å; C$\underline{H}_3$O-4 – H-17 = 3.140 Å; C$\underline{H}_3$-13 – H-17 = 4.320 Å. In the folded *cis* configuration (Figure 4b), the hydrogen interatomic distances are: C$\underline{H}_3$O-18 – H-5 = 2.241 Å; C$\underline{H}_3$O-18 – H-6 = 2.594 Å; C$\underline{H}_3$O-18 – H-4 = 1.192 Å; C$\underline{H}_3$O-4 – H-17 = 2.792 Å; C$\underline{H}_3$-13 – H-17 = 2.464 Å.

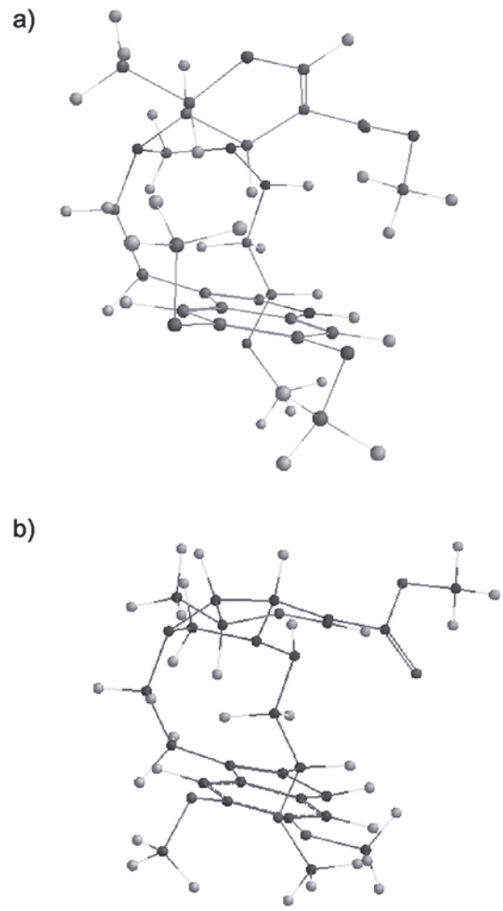

Figure 4. DFT/BLYP/6-31G* optimized geometry of braznitidumine (**1**) obtained from ^{1}H ^{1}H NOESY correlations: (a) *trans* and (b) *cis* configurations.

Experimental

General Procedures

Melting point was obtained on a Mettler FP82 HT and was uncorrected. FTIR spectrum was determined in KBr disk

on an FTIR Perkin Elmer Spectrum 200 spectrometer. ESI-MS spectrum was obtained in positive mode in a Q-TOF Micro™ MICROMASS spectrometer. UV spectrum was obtained in 1% methanol solution in a Perkin Elmer 202 spectrometer. Chromatographic purification was carried out on silica gel (70-230 mesh). In the thin layer chromatography analysis was used silica gel 60F254 and 60G mixture (1:3).

^{1}H and ^{13}C NMR spectra were measured on a Bruker DRX400 – *AVANCE* spectrometer, with inverse probes and field gradient, operating at 400.129 and 100.613 MHz, respectively. DMSO-d_6 was used as a solvent (the sample was dissolved in 0.75 mL of solvent and transferred to a 5 mm NMR tube), with TMS as an internal reference (δ = 0). ^{15}N spectra were measured on a Bruker DRX400 – *AVANCE* spectrometer with inverse probe and field gradient, operating at 40.549 MHz, at Centro Nacional de Ressonância Magnética Nuclear (CNRMN), UFRJ. DMSO-d_6 was used as a solvent with urea as external reference (78 ppm in DMSO-d_6). Chemical shifts are given in the δ-scale (ppm) and coupling constants *J* in Hz. Experiments were carried out using pulse sequence and programs provided by the manufacturer. One dimensional (1D) ^{1}H and ^{13}C NMR spectra were acquired under standard conditions by using a direct detection 5 mm ^{1}H/^{13}C dual probe. Standard pulse sequences were used for two dimensional (2D) homonuclear and heteronuclear shift correlation spectra by using a multinuclear inverse detection 5 mm probe with field gradient at z axis. For ^{1}H ^{13}C HMBC, three delays for evolution of long range coupling [1/($^{n}J_{C-H}$)] 65, 125, and 130 ms] were used. For the 2D ^{1}H ^{1}H NOESY experiment two mixing times (350 and 700 ms) were pre-optimized by a specific Bruker computer program.

Theoretical calculations

Theoretical studies were carried out using the software package GAUSSIAN03.[9] Spatial arrangements determined through NOESY experiments were used as initial models for geometry optimization calculations by the semi-empirical PM3 method in the gaseous state.[10] Geometries obtained by PM3 method were optimized again by the Density Functional Theory (DTF)[11] method with BLYP functionals[12] with a 6-31G*[13] basis set (DFT/BLYP/6-31G*). All structures obtained by theoretical calculations were characterized as true energy minima in PES through frequency calculations (when the frequencies are real, they correspond to a true minimal energy structure). Calculations of solvent effects were performed for optimized geometries in the DFT/BLYP/6-31G* level by using the Polarizable Continuum Model (PCM) at the same calculation level.[14]

*Material and isolation of **1***

Stem of *A. nitidum* was collected near Manaus City, Amazon State in June 2000. A voucher specimen (181832) is deposited in the Herbarium of Instituto Nacional de Pesquisas da Amazônia (INPA). The dried and powered stem barks (1.5 kg) of *A. nitidum* were extracted with EtOH and yielded 173 g of crude ethanol extract after the removal of the solvent. This extract was chromatographed on silica gel column and eluted with methylene chloride, acetyl acetate, and ethanol. The ethanol solution evaporated under vacuum yielded 40.20 g of a residue, which was rechromatographed on silica gel with ethyl acetate:methanol 9:1 as an eluent. Compound **1** (120.0 mg) was obtained as a yellow solid; mp 272.9-273.1 °C; Dragendorff positive test for alkaloids (orange-yellow color); IR (KBr) ν_{max}/cm^{-1}: 3430, 2949, 1697, 1485, 1442, 1308, 1285. MS (ESI+) *m/z*: 472.682 (M^+; 0.3), 427.214 ($[M–C_2H_6O]^+$; 1). For NMR data see Tables 1 and 2.

Conclusions

The structure of alkaloid braznitidumine (**1**) could be elucidated through the analysis of its 1D and 2D ^{1}H, ^{13}C, and ^{15}N NMR spectra. It showed a new and interesting framework including a 1,2,9-triazabicyclo[7.2.1] system in a folded molecule. The new compound may show either a *trans* or a *cis* fused imidazolidine-pyran system fragment in its structure. Geometry optimization calculations (DFT/BLYP/6-31G*) are compatible with nOe data and corroborate ^{1}H ^{1}H NOESY results.

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Supplementary Information

Supplementary data are available at free of charge at http://jbcs.sbq.org.br, as PDF file.

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NMR Structural Analysis of #Braznitidumine: A New Indole Alkaloid with 1,2,9-Triazabicyclo[7.2.1] System, Isolated from *Aspidosperma nitidum* (Apocynaceae)

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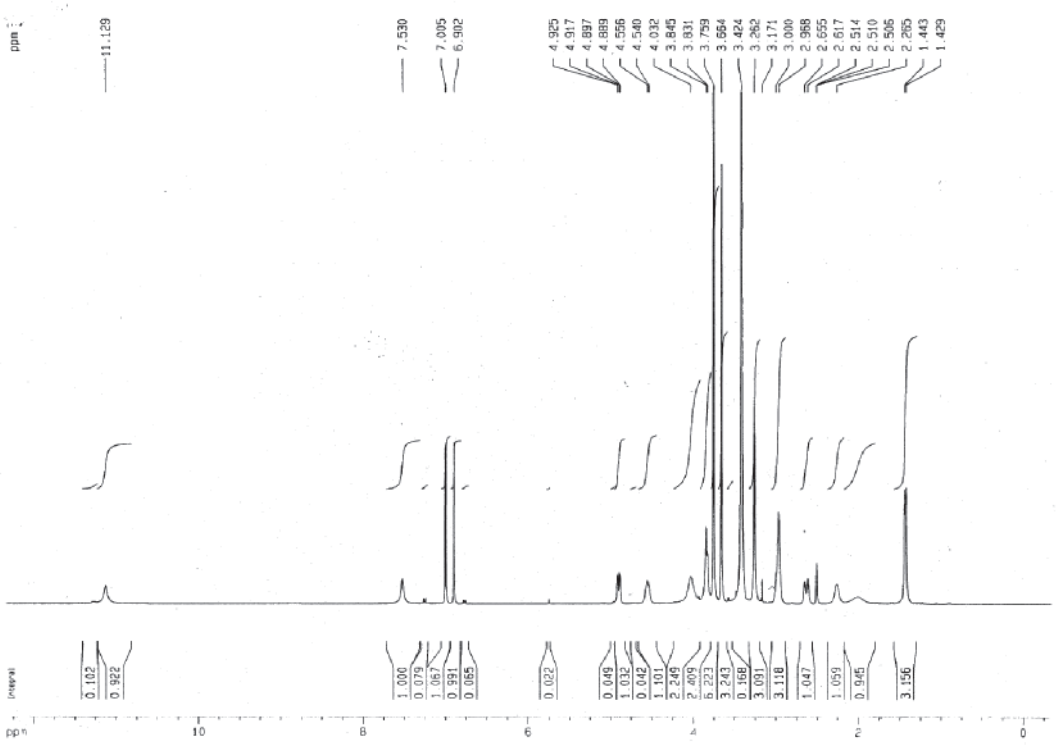

Figure S1. ^{1}H NMR spectrum of Braznitidumine (**I**) in DMSO-d_6, 400 MHz.

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This name is an homage to Professor Raimundo Braz-Filho. This article was submitted to the special issue dedicated to Professor Raimundo Braz-Filho on the occasion of his 70th birthday.

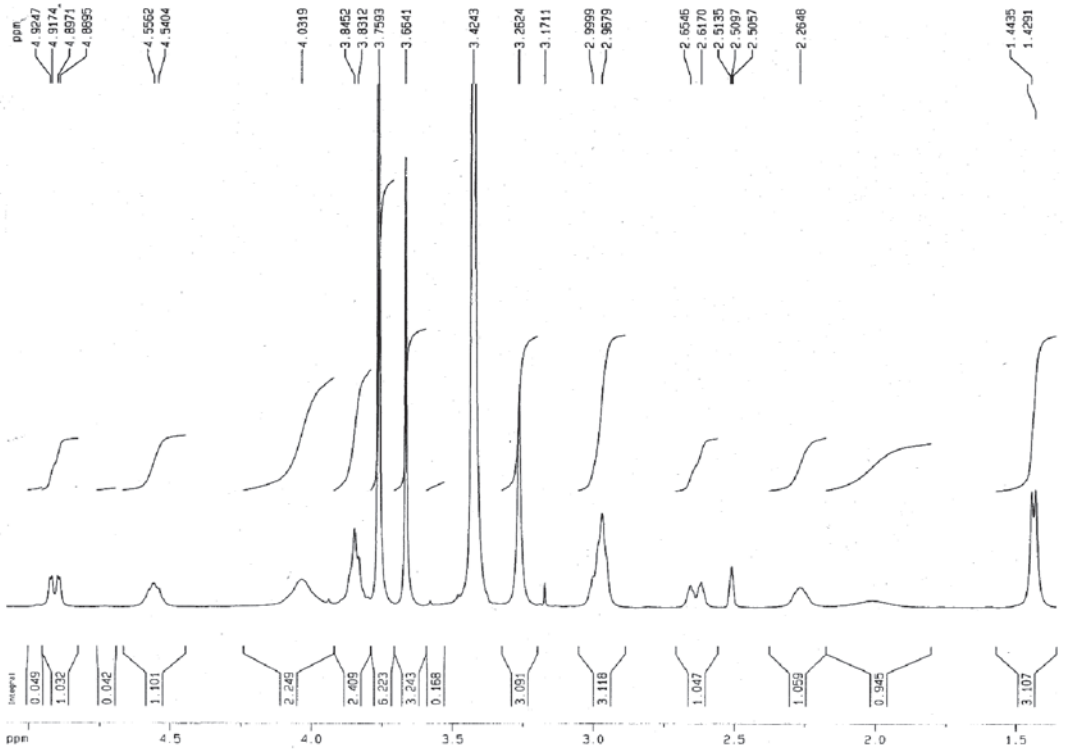

Figure S2. Partial ^{1}H NMR spectrum of Braznitidumine (**I**) in DMSO-d_6, 400 MHz.

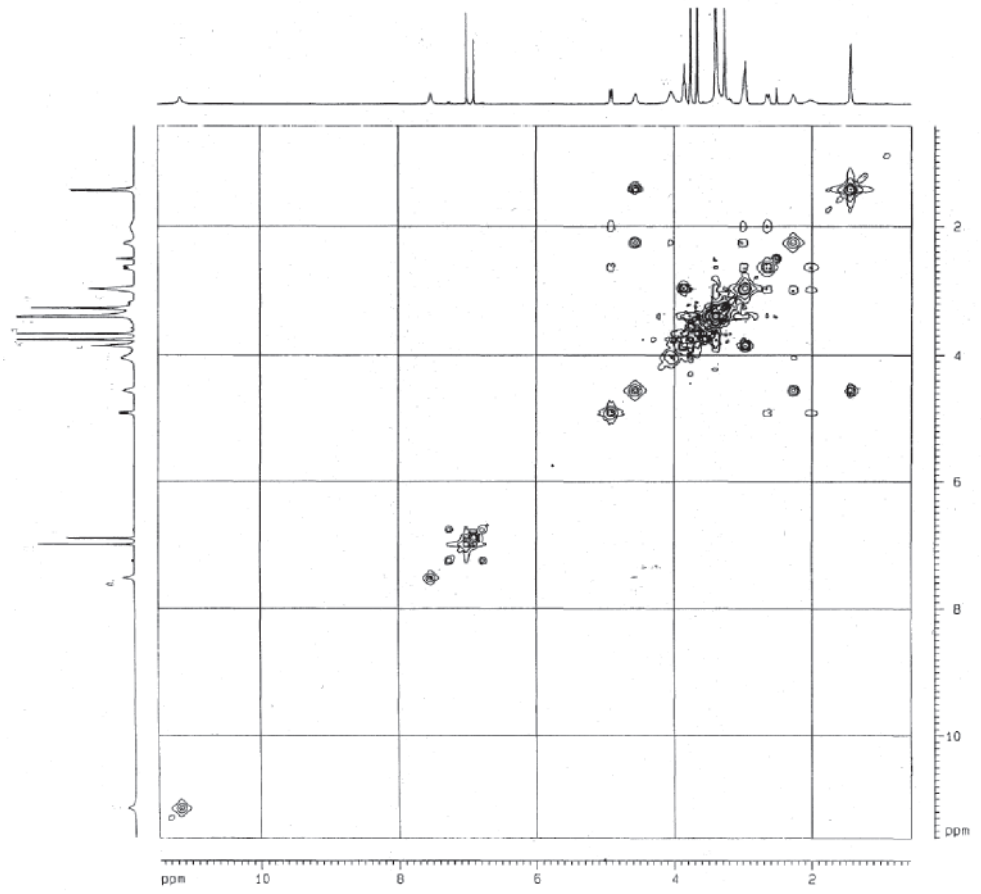

Figure S3. ^{1}H ^{1}H COSY contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz.

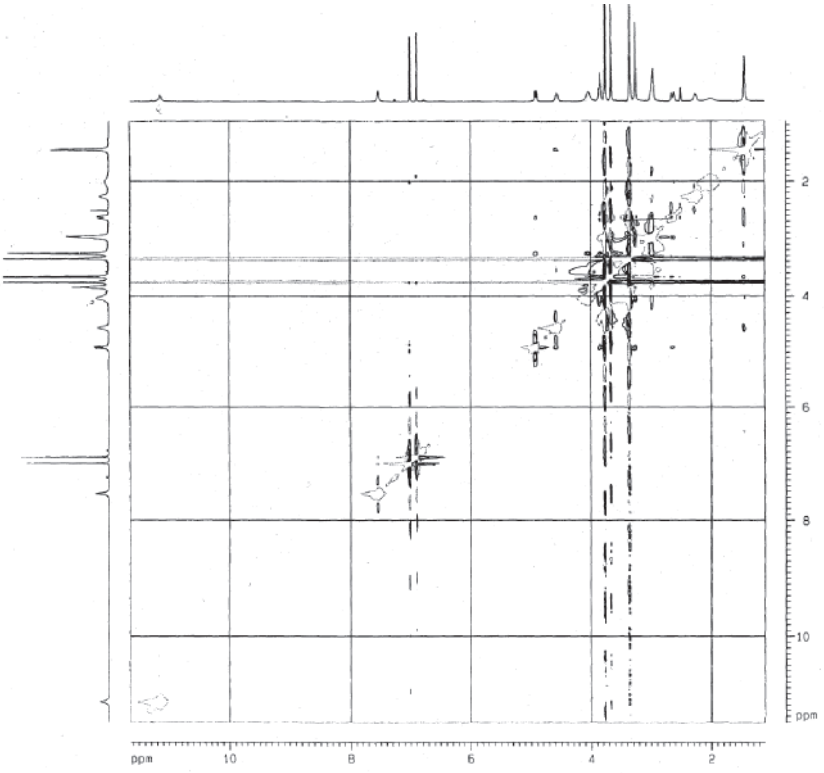

Figure S4. ^{1}H ^{1}H NOESY contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz; mixing time = 350 ms.

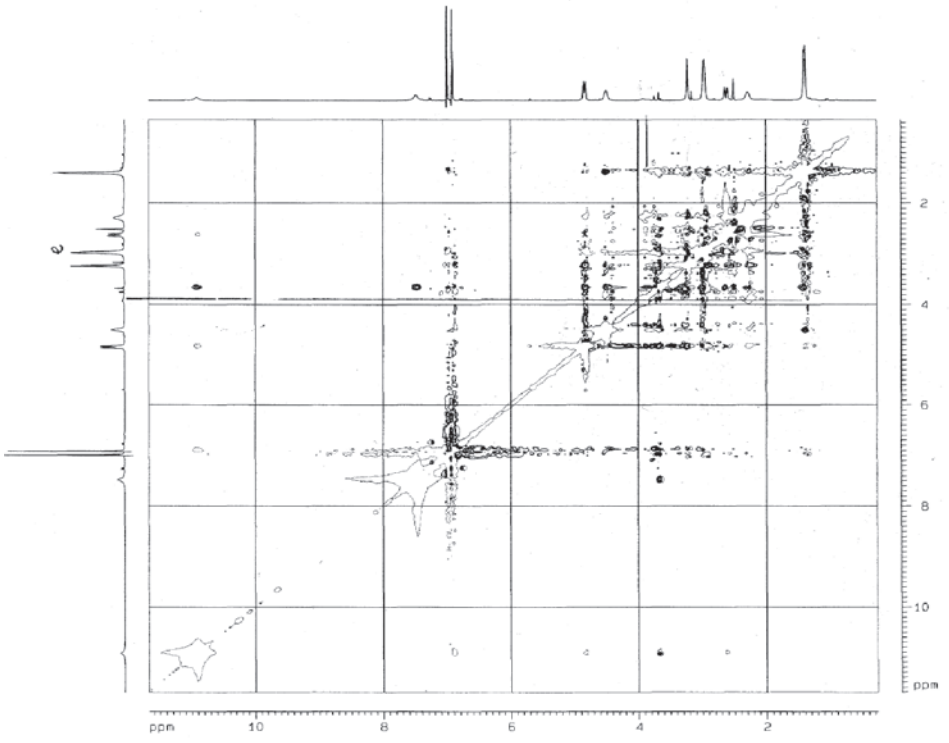

Figure S5. ^{1}H ^{1}H NOESY contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz; mixing time = 700 ms.

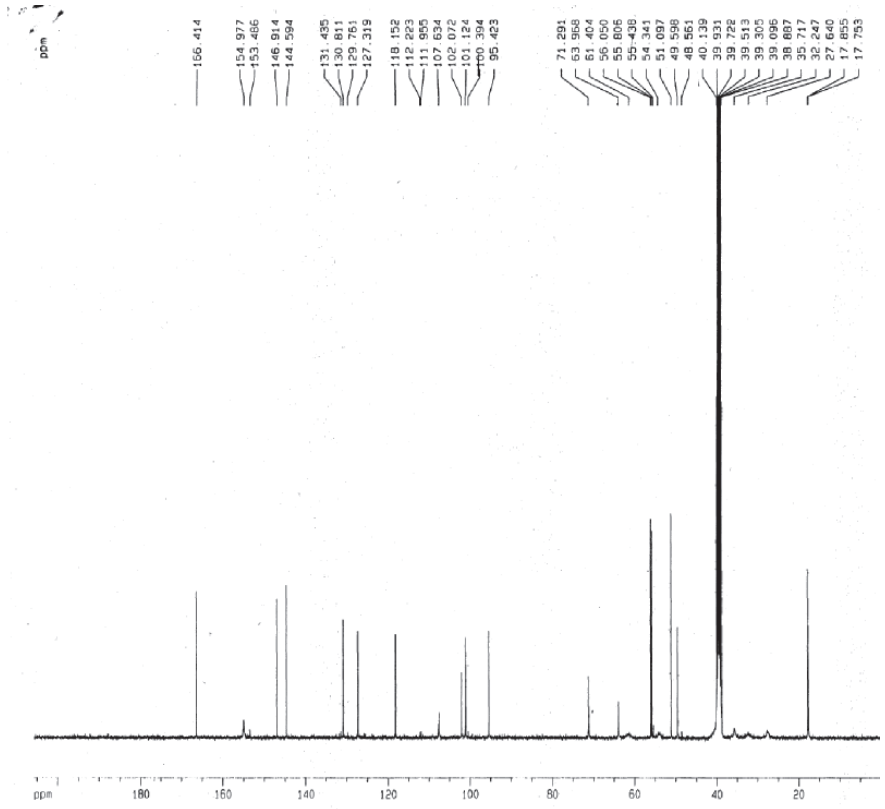

Figure S6. ^{13}C NMR spectrum of Braznitidumine (**I**) in DMSO-d_6, 100 MHz.

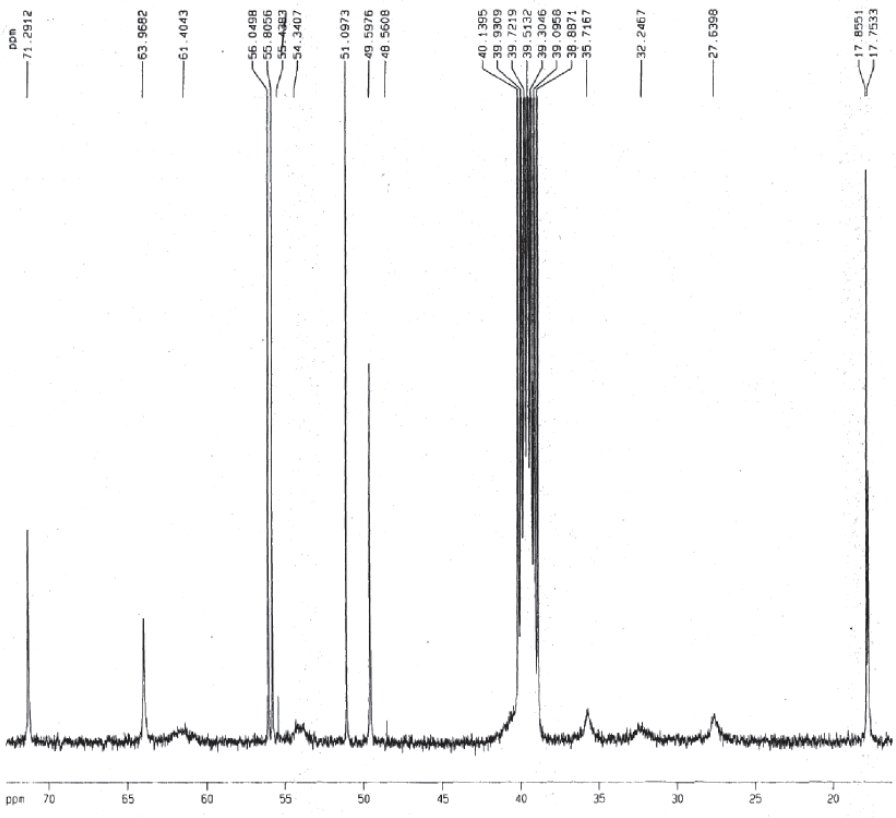

Figure S7. Partial ^{13}C NMR spectrum of Braznitidumine (**I**) in DMSO-d_6, 100 MHz.

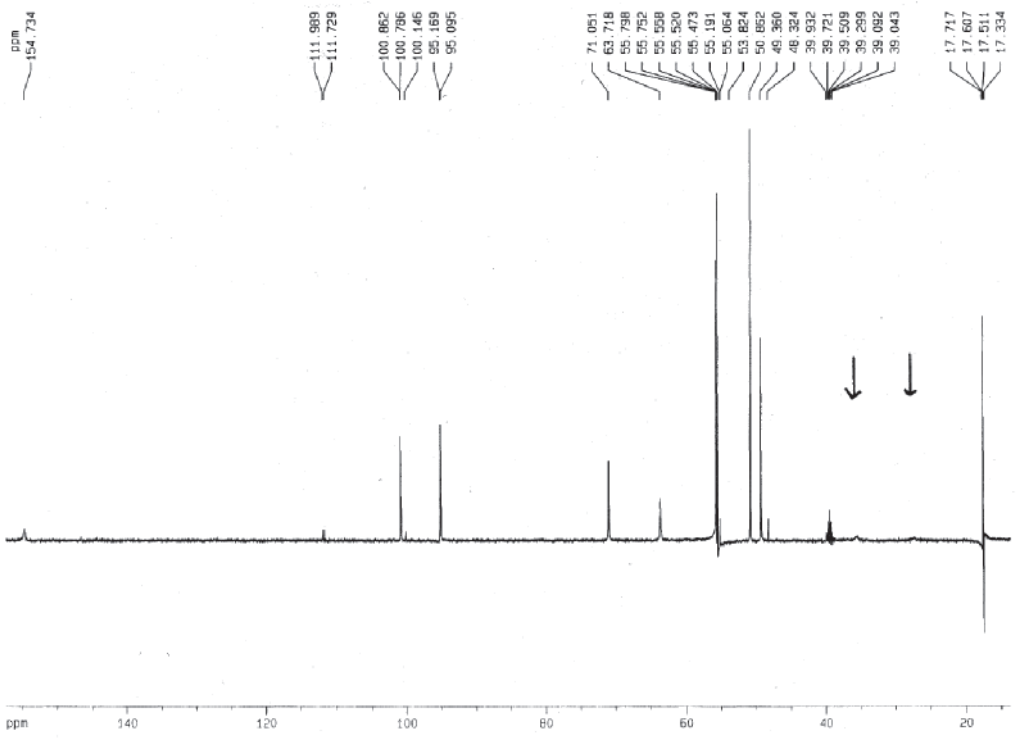

Figure S8. ^{13}C NMR DEPT-135 spectrum of Braznitidumine (**I**) in DMSO-d_6, 100 MHz.

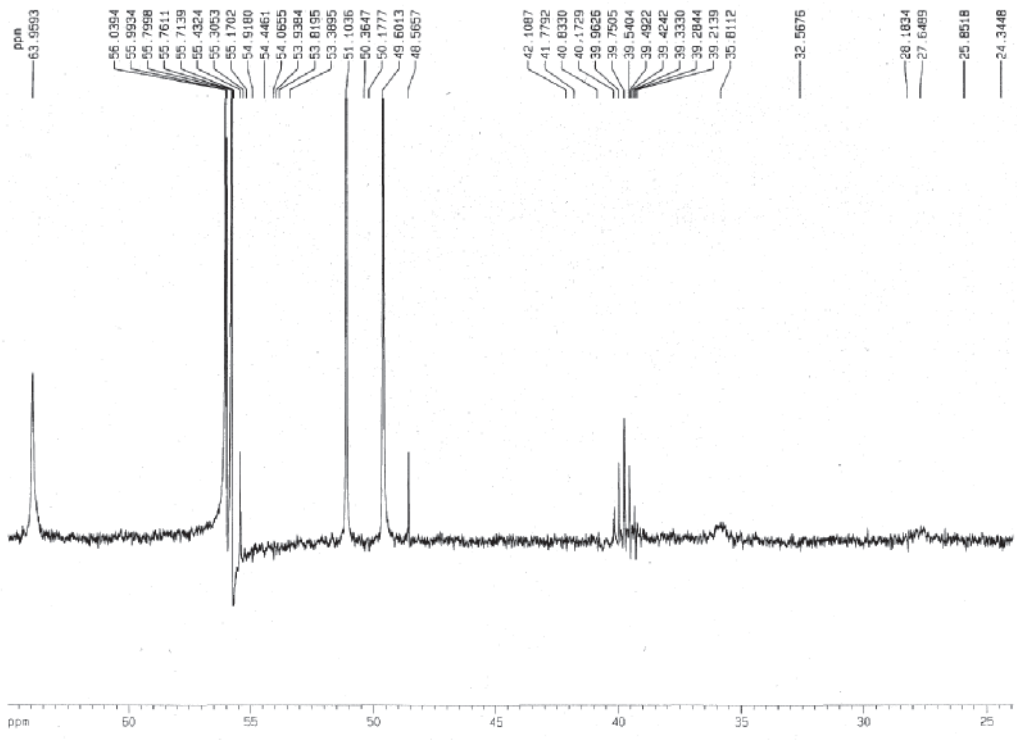

Figure S9. ^{13}C NMR DEPT-135 partial spectrum of Braznitidumine (**I**) in DMSO-d_6, 100 MHz.

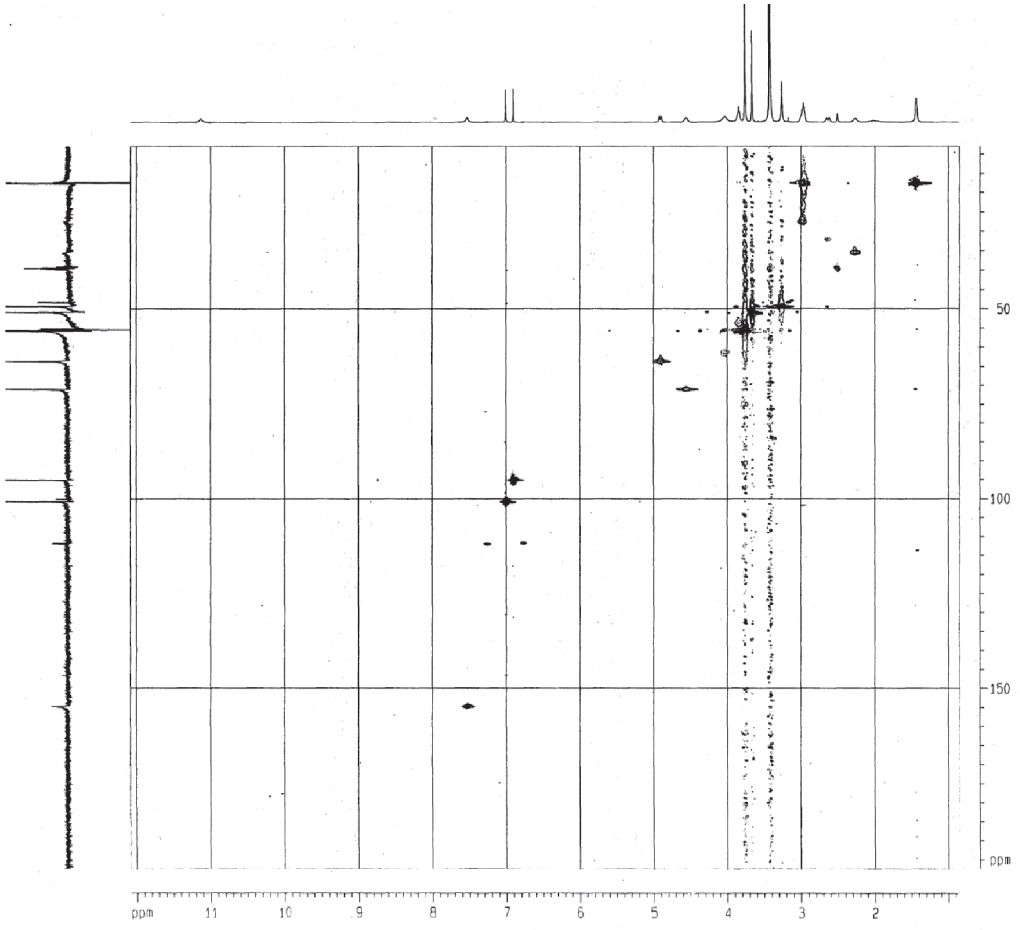

Figure S10. ^{1}H ^{13}C HSQC contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz x 100 MHz.

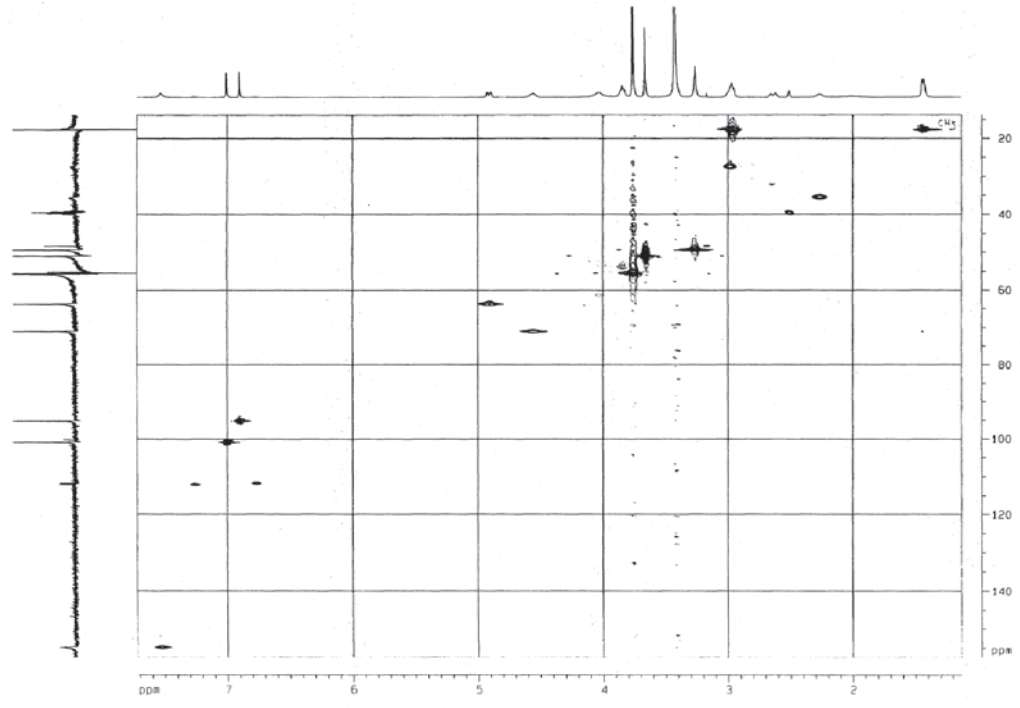

Figure S11. ^{1}H ^{13}C HSQC partial contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz x 100 MHz.

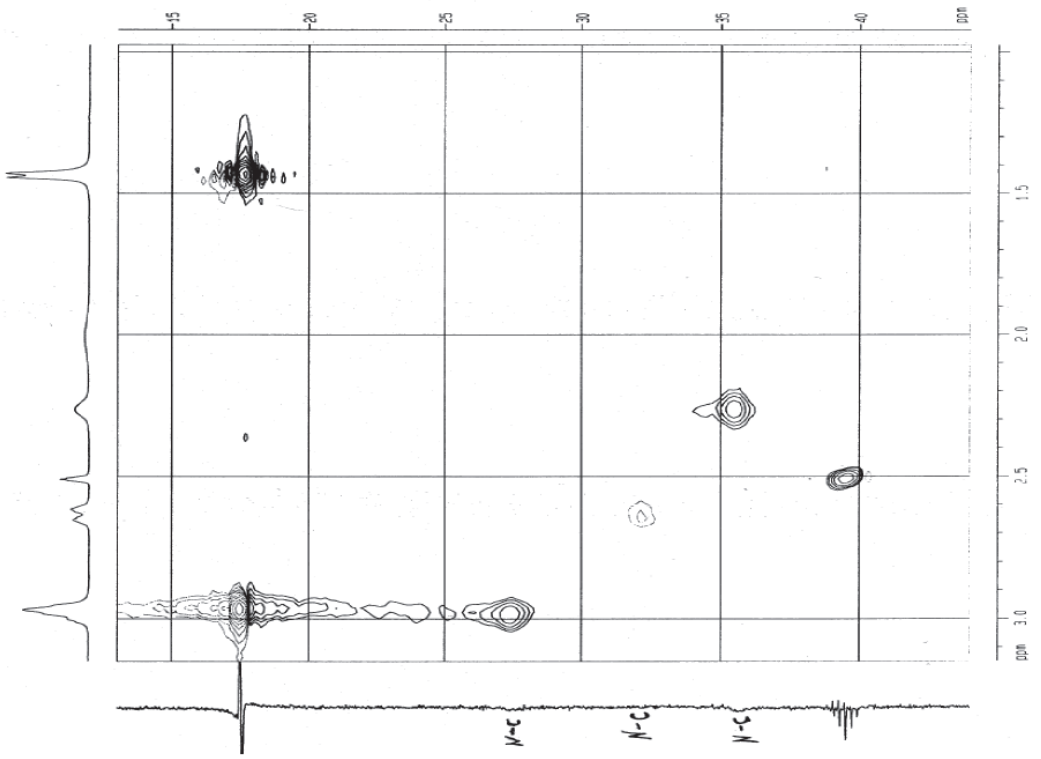

Figure S12. ^{1}H ^{13}C HSQC partial contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz x 100 MHz.

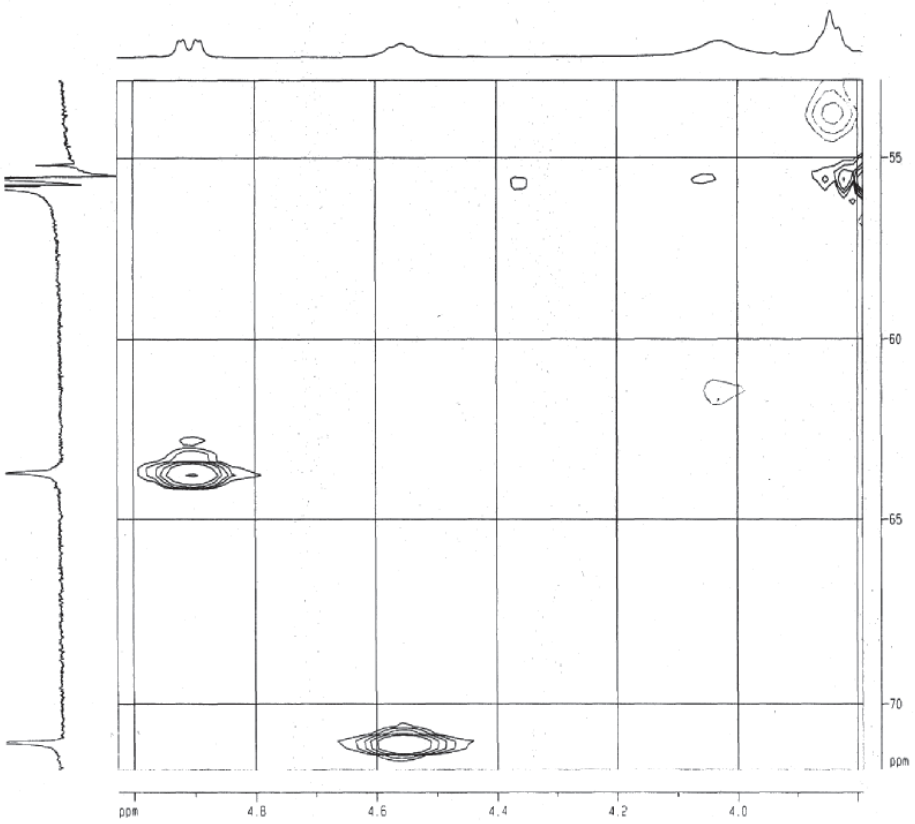

Figure S13. ^{1}H ^{13}C HSQC partial contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz x 100 MHz.

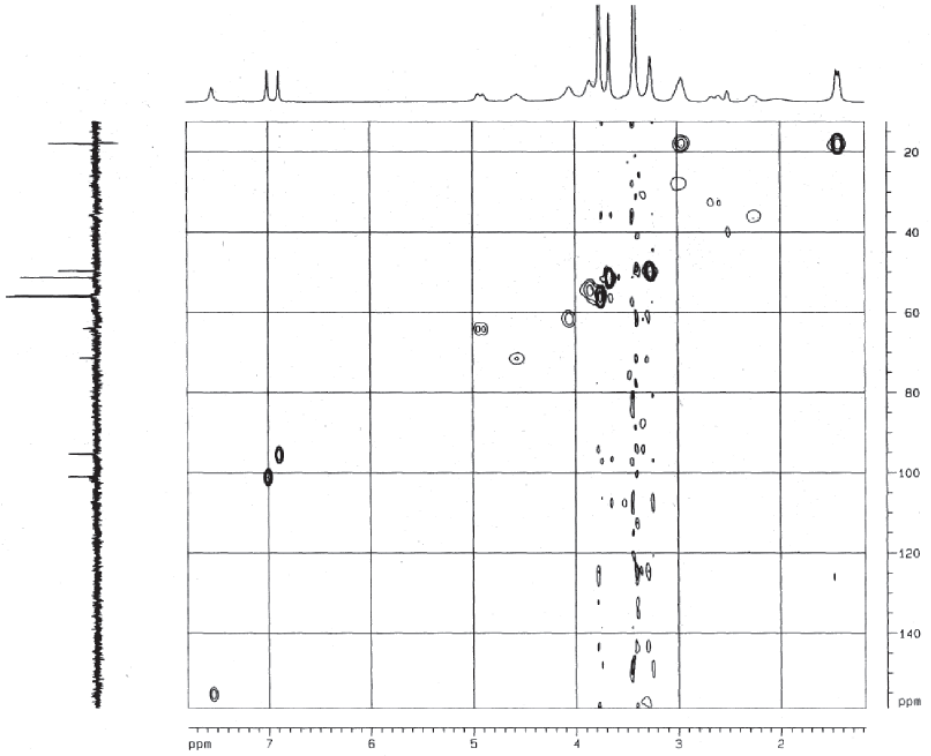

Figure S14. ^{1}H ^{13}C HMQC contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz x 100 MHz.

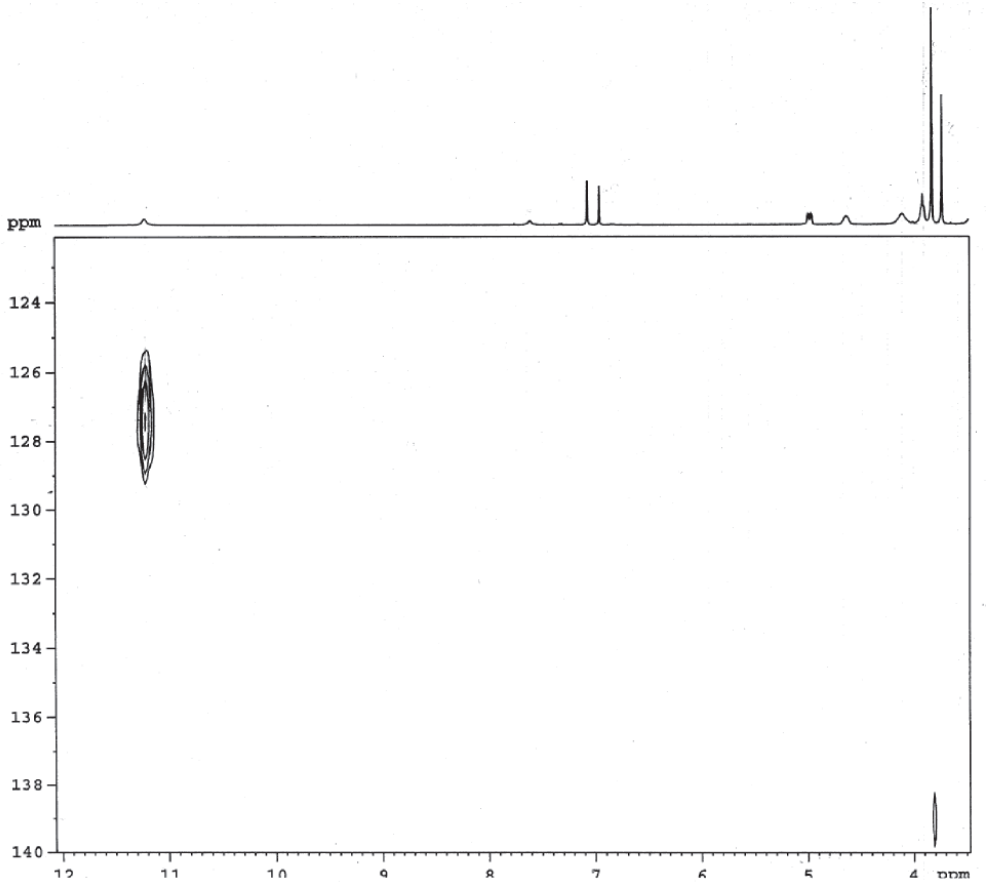

Figure S15. ^{1}H ^{15}N HSQC partial contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz x 40.55 MHz.

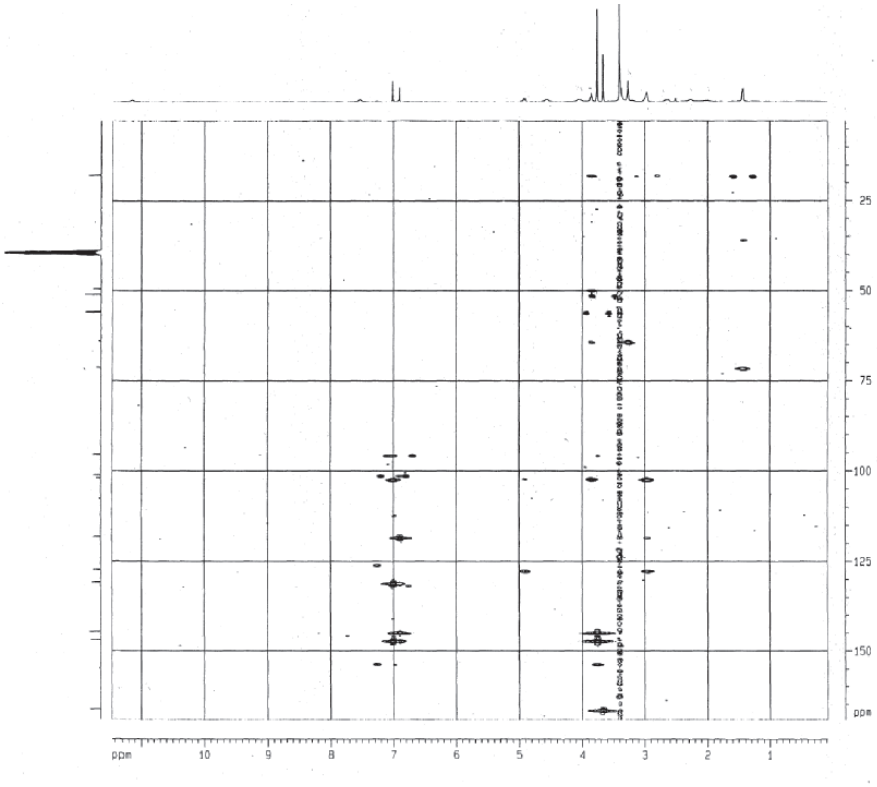

Figure S16. ^{1}H ^{13}C HMBC contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz x 100 MHz; delay 65 ms.

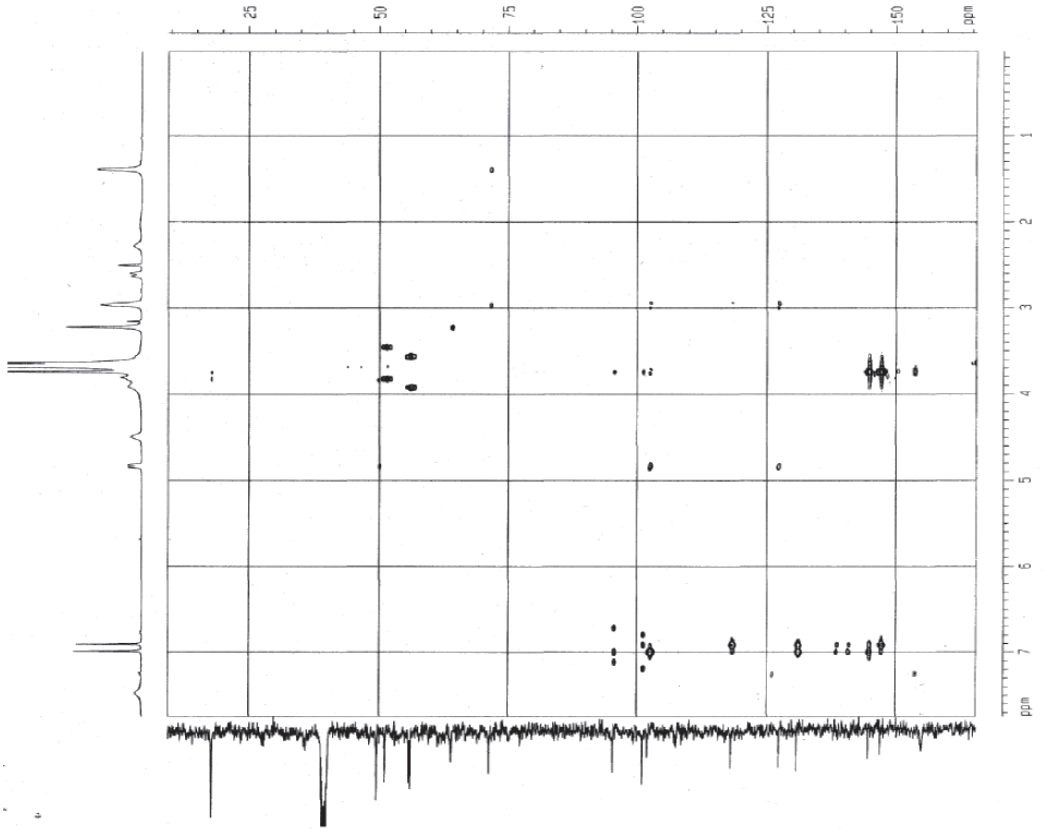

Figure S17. ^{1}H ^{13}C HMBC contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz x 40.55 MHz; delay 125 ms.

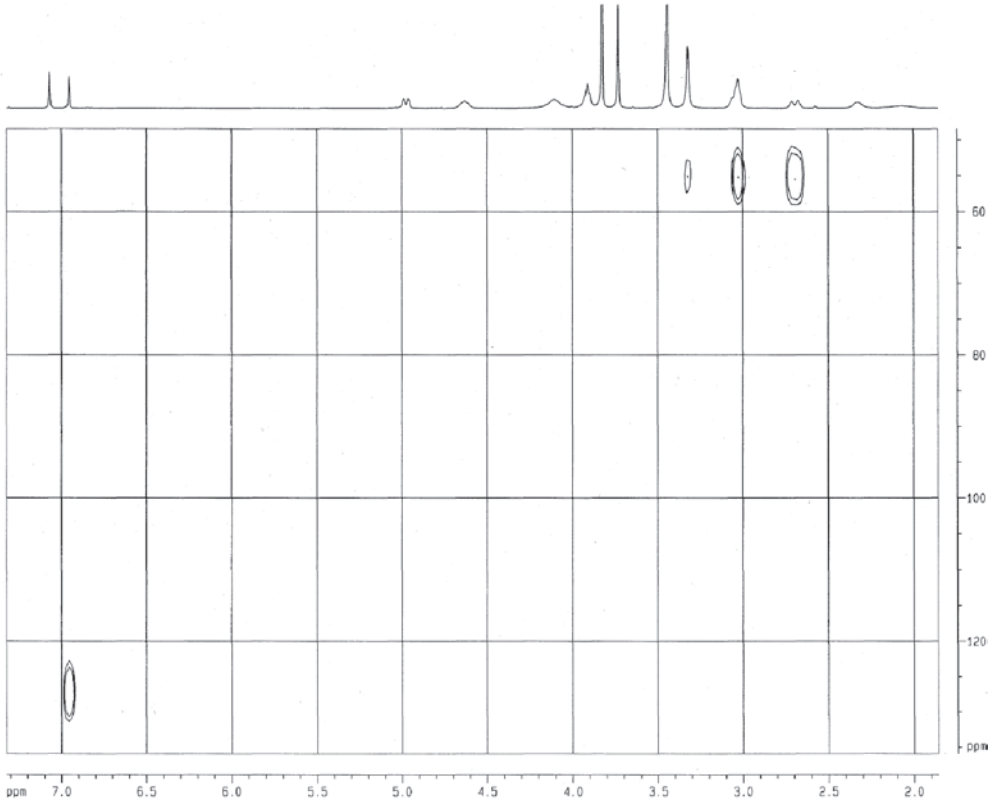

Figure S18. ^{1}H ^{15}N HMBC contour map of Braznitidumine (I) in DMSO- d_6, 400 MHz x 100 MHz; delay 130 ms.