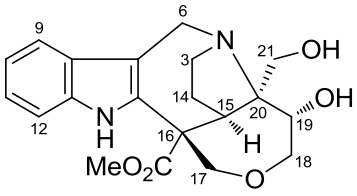
Chapter Two

Results and Discussions

2.1 Alkaloids from *Alstonia angustiloba* Miq.

Investigation of the alkaloidal content of the Malayan *Alstonia angustiloba* Miq. has provided a total of twenty alkaloids of which three are new. The new alkaloids obtained are angustilobine C (**1**), andransinine (**2**), and angustiphylline (**3**). The other seventeen known alkaloids obtained are 19,20-*E*-vallesamine (**4**), 17-*O*-acetylvallesamine (**5**), yunnanensine (**6**), angustilobine A (**7**), angustilobine B (**8**), *nor*-6,7-*seco*angustilobine B (**9**), *nor*-6,7-*seco*-19,20α-epoxyangustilobine B (**10**), undulifoline (**11**), condylocarpine (**12**), 20*S*-tubotaiwine (**13**), *N*(4)-demethylechitamine (**14**), 17-*O*-acetyl-*N*(4)-demethylechitamine (**15**), alstolucine B (**16**), vincamine (**17**), 16*R*,19*E*-isositsirikine (**18**), venoterpine (**19**), and cantleyine (**20**). Of these twenty alkaloids, thirteen are from the leaf extract while twelve are from the stem-bark extract. Five of the alkaloids are common to both the leaves and stem-bark extracts. The alkaloidal composition of the leaf and stem-bark extracts of *A. angustiloba* Miq. is summarized in Table 2.1.



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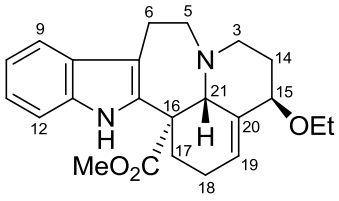

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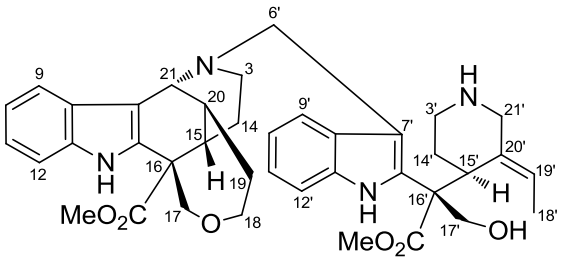

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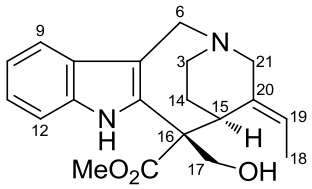

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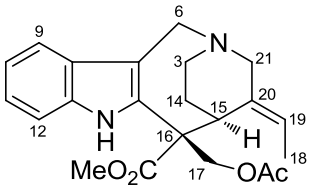

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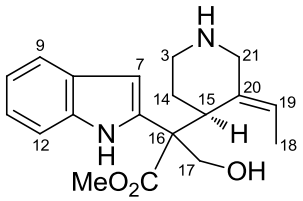

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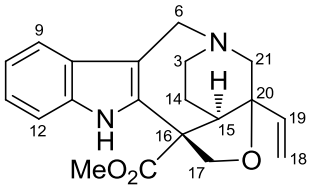

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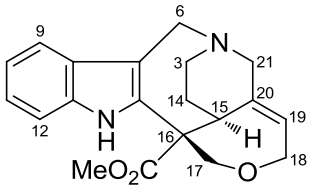

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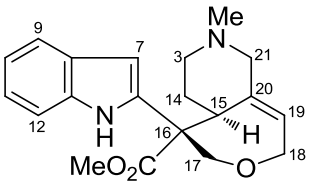

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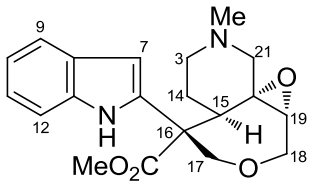

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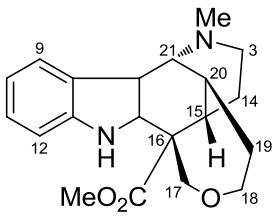

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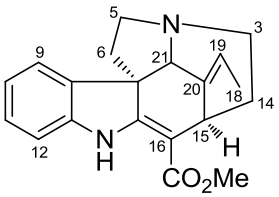

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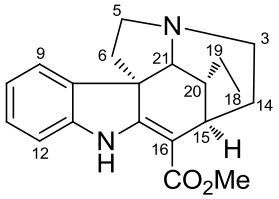

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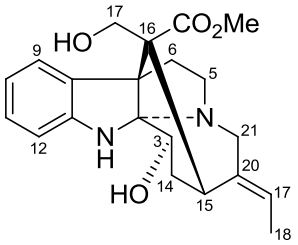

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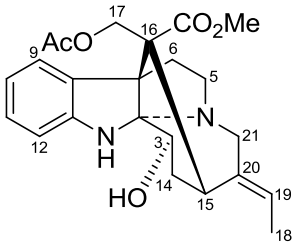

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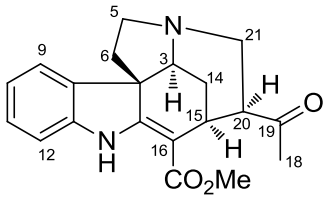

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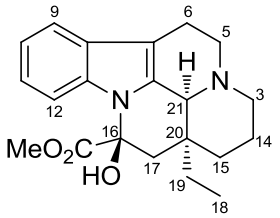

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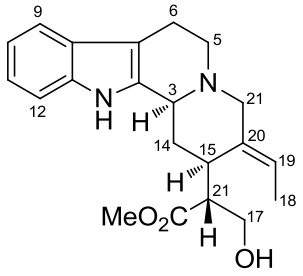

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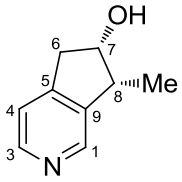

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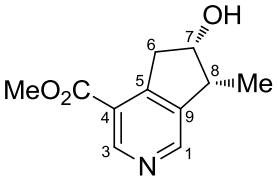

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Table 2.1. Alkaloidal Composition of *Alstonia angustiloba* Miq.

Plant Part	**Alkaloid**	**Yield (g kg^{-1})**
Leaves	Angustilobine C (**1**) [New]	0.0002
(21.0 kg)	Andransinine (**2**) [New]	0.0005
	19,20-*E*-Vallesamine (**4**)	0.0248
	17-*O*-Acetylvallesamine (**5**)	0.0052
	Angustilobine A (**7**)	0.0005
	Angustilobine B (**8**)	0.0008
	Nor-6,7-*Seco*angustilobine B (**9**)	0.0071
	Nor-6,7-*Seco*-19,20α-epoxyangustilobine B (**10**)	0.0007
	Condylocarpine (**12**)	0.0007
	20*S*-Tubotaiwine (**13**)	0.0007
	Alstolucine B (**16**)	0.0004
	Vincamine (**17**)	0.0002
	16*R*,19*E*-Isositsirikine (**18**)	0.0003
Stem-bark	Angustiphylline (**3**) [New]	0.0001
(20.0 kg)	19,20-*E*-Vallesamine (**4**)	0.0076
	Yunnanensine (**6**)	0.0010
	Angustilobine A (**7**)	0.0002
	Angustilobine B (**8**)	0.0005
	Nor-6,7-*Seco*angustilobine B (**9**)	0.0015
	Undulifoline (**11**)	0.0004
	20*S*-Tubotaiwine (**13**)	0.0004
	N(4)-Demethylechitamine (**14**)	0.0180
	17-*O*-Acetyl-*N*(4)-demethylechitamine (**15**)	0.0008
	Venoterpine (**19**)	0.0018
	Cantleyine (**20**)	0.0020

2.1.1 Angustilobine C (1)

Angustilobine C (**1**) was obtained as a light yellowish oil, with $[\alpha]^{25}_{D}$ –3 ($CHCl_3$, *c* 0.13). The UV spectrum showed absorption maxima at 222 and 283 nm, characteristic of an indole chromophore. The IR spectrum (thin film) showed a broadened band at 3410 cm^{-1} due to OH/NH functions and a band at 1732 cm^{-1} due to an ester function. The ESIMS of **1** showed a pseudomolecular ion peak at *m*/*z* 373, and HRESIMS measurements yielded the molecular formula $C_{20}H_{24}N_2O_5$ (DBE 10). The ^{13}C NMR data (Table 2.2) accounted for all of the 20 carbon resonances, comprising one methyl, six methylene, seven methine, and six quaternary carbons. The presence of ester functionality was supported by the observed quaternary carbon signal at δ 175.2 and the corresponding methyl signal at δ 53.3. Three downfield signals at δ 76.4, 72.1, and 62.0 are observed due to three oxymethylenes (C-17, C-18, and C-21, respectively), while another at δ 70.9 is assigned to an oxymethine (C-19). The methylene carbon signal at δ 50.4 is due to an aminomethylene (C-6). The ^{1}H NMR spectrum (Table 2.2) showed the presence of an unsubstituted aromatic moiety from the presence of signals due to the four aromatic hydrogens (H-9, δ 7.45, d, *J* = 8 Hz; H-10, 7.10, t, *J* = 8 Hz; H-11, 7.21, t, *J* = 8 Hz; H-12, 7.34, d, *J* = 8 Hz), an indolic NH as a broad singlet at δ 8.99, and a methoxy group associated with a methyl ester function as a singlet at δ 3.81. Three pairs of AB doublets were observed at δ 4.36 and 4.62 (*J* = 17 Hz), 3.77 and 4.03 (*J* = 13 Hz), 3.54 and 3.91 (*J* = 11 Hz). The first pair corresponds to the C-6 aminomethylene, which is consistent with the corresponding δ_C resonance observed at δ 50.4, as well as with the observed three-bond correlations from H-3 to C-6, and from H-6 to C-2, C-3, in the HMBC spectrum of **1** (Figure 2.1). The oxymethylene at d 3.77 and 4.03 (*J* = 13 Hz) is bridged by an oxygen atom to another methylene, which was seen as a multiplet at δ 3.79 (δ_C 72.1). This was clearly shown by the reciprocal three-bond correlations from

H-17 to C-18 and from H-18 to C-17. The remaining oxymethylene seen at δ 3.54 and 3.91 (J = 11 Hz) must be due to the methylene (C-21) associated with a hydroxymethyl group from the observed three-bond correlations from H-15 and H-19 to C-21, and H-21 to C-19, in the HMBC spectrum. These HMBCs also allowed assignment of the lone oxymethine to C-19. These pairs of isolated methylenes are strongly suggestive of an alkaloid possessing a skeleton similar to those of the angustilobine B subgroup. For instance the 17 Hz coupling of the C-6 hydrogens (Table 2.2) is characteristic of the aminomethylenes in eight-membered azocane moieties present in the 5-*nor* indole alkaloid vallesamine, and the related angustilobine B compounds,[25,31,78,85] while the 13 Hz coupling of the two C-17 hydrogens is characteristic of an oxepane moiety, such as that present in angustilobine B alkaloids.[25,28,29,31,78]

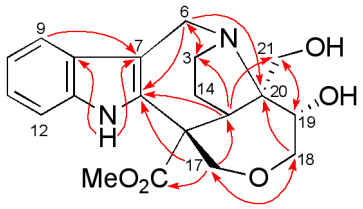


Figure 2.1. Selected HMBCs of Angustilobine C (**1**).

The COSY spectrum showed the presence of the following partial structures, an NCH_2CH_2CH and an OCH_2CHO, in addition to the four contiguous aromatic hydrogens, and the various isolated methylenes (including the hydroxymethyl moiety) already discussed. Putting these fragments together with the help of the HMBC data led to structure **1**, which is distinguished from the known angustilobine B type alkaloids by contraction of the piperidine to a pyrrolidine ring, with the concomitant extrusion of C-21 to forge the hydroxymethyl side chain, constituting part of a diol functionality as shown in **1**. The proposed structure is consistent with the full HMBC data (Figure 2.1).

The relative configurations at the various stereogenic centers were determined from the NOESY spectrum (Figure 2.2). The observed NOE between the indolic NH and the aromatic resonance at δ 7.34 allowed the assignment of the latter signal to H-12 and the signal at δ 7.45 to H-9 (Figure 2.2). This was also in agreement with the H-9 (δ 7.45) to C-7 correlation in HMBC. The observed NOE between H-9 and the H-6 signal at δ 4.36, allowed this signal to be H-6α and the signal at δ 4.62 to be H-6β. The observed NOE between H-6β and H-19 indicated the presence of a α-oriented OH at C-19, while the NOE between NH and H-17β indicated α-orientation of the methyl ester function at C-16. These NOEs also indicate that the pyrrolidine and the oxepane rings must be on opposite faces with respect to the common C-15-C-20 bond, which is consistent with the observed NOEs for H-6α/H-3 and H-14/CO_2Me. These NOEs therefore allowed the relative configurations at C-15, C-16, C-19, C-20, to be assigned as *R*, *S*, *S*, and *S*, respectively (Figure 2.2), which are consistent with the relative configurations previously determined for several angustilobine type alkaloids.[28,78,90]

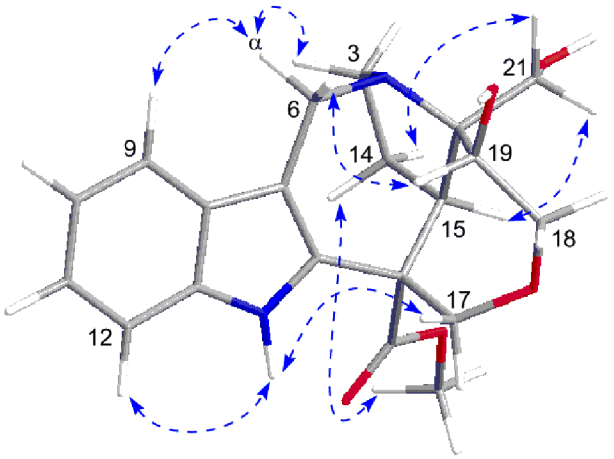
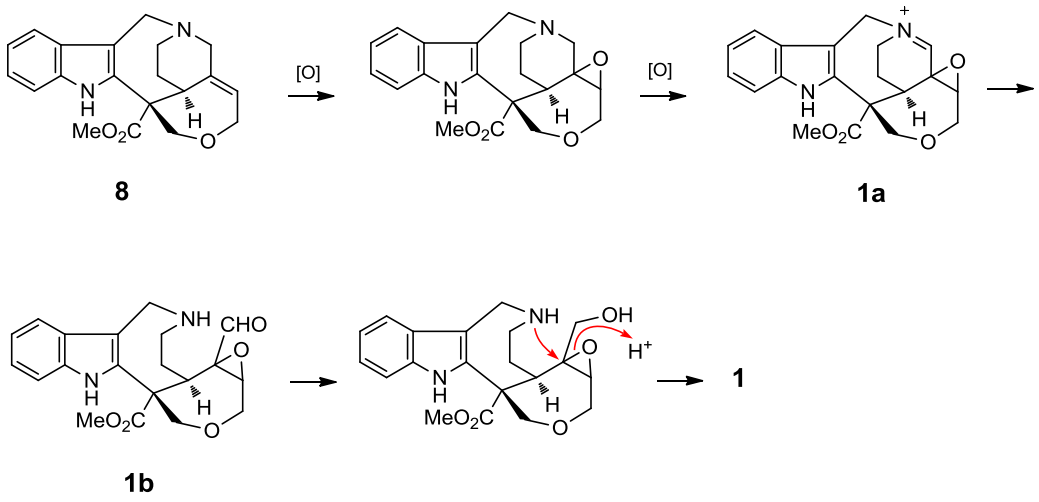


Figure 2.2. Selected NOEs of Angustilobine C (**1**).

A possible pathway to **1** is from an angustilobine precursor such as angustilobine B (**8**), which on successive oxidation gives the iminium ion, **1a**, incorporating an epoxide function. Hydrolytic cleavage of **1a** gives the amino-aldehyde, **1b**, which on subsequent reduction to the alcohol, followed by epoxide ring-opening by the tertiary amine, furnishes the diol **1** (Scheme 2.1).



Scheme 2.1. Possible biogenetic pathway to angustilobine C (**1**).

Table 2.2. ^{1}H, ^{13}C and HMBC NMR Data of Angustilobine C (**1**).[a,b]

Position	δ_H	δ_C	**HMBC** ^{2}J	^{3}J
2	–	132.0	–	–
3a	3.01 m	52.4	–	C-6
3b	3.28 ddd (13, 10, 8)			
6α	4.36 d (17)	50.4	C-7	C-2, C-3,
6β	4.62 d (17)			C-20
7	–	113.0	–	–
8	–	127.2	–	–
9	7.45 d (8)	118.4	–	C-7, C-11, C-13
10	7.10 t (8)	119.7	–	C-8, C-12
11	7.21 t (8)	122.9	–	C-9, C-13
12	7.34 d (8)	111.2	–	C-8, C-10
13	–	136.5	–	–
14a	1.73 m	31.2	–	C-16
14b	2.18 m		–	–
15	2.96 d (7)	45.4	C-14, C-16	C-2, C-3, C-21
16	–	58.9	–	–
17α	4.03 d (13)	76.4	–	C-2, C-15, C-18, $\underline{CO_2}Me$
17β	3.77 d (13)			
18a	3.79 m	72.1	–	C-17, C-20
18b	3.79 m			
19	4.47 ddd (9, 5, 1)	70.9	C-18	C-21
20	–	72.1	–	–
21a	3.54 br d (11)	62.0	–	C-19
21b	3.91 d (11)			
$CO_2\underline{Me}$	3.81 s	53.3	–	$\underline{CO_2}Me$
$\underline{CO_2}Me$	–	175.2	–	–
NH	8.99 br s	–	C-13	C-7, C-8

[a]$CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC, HMBC, and NOESY.
[b]From H to C.

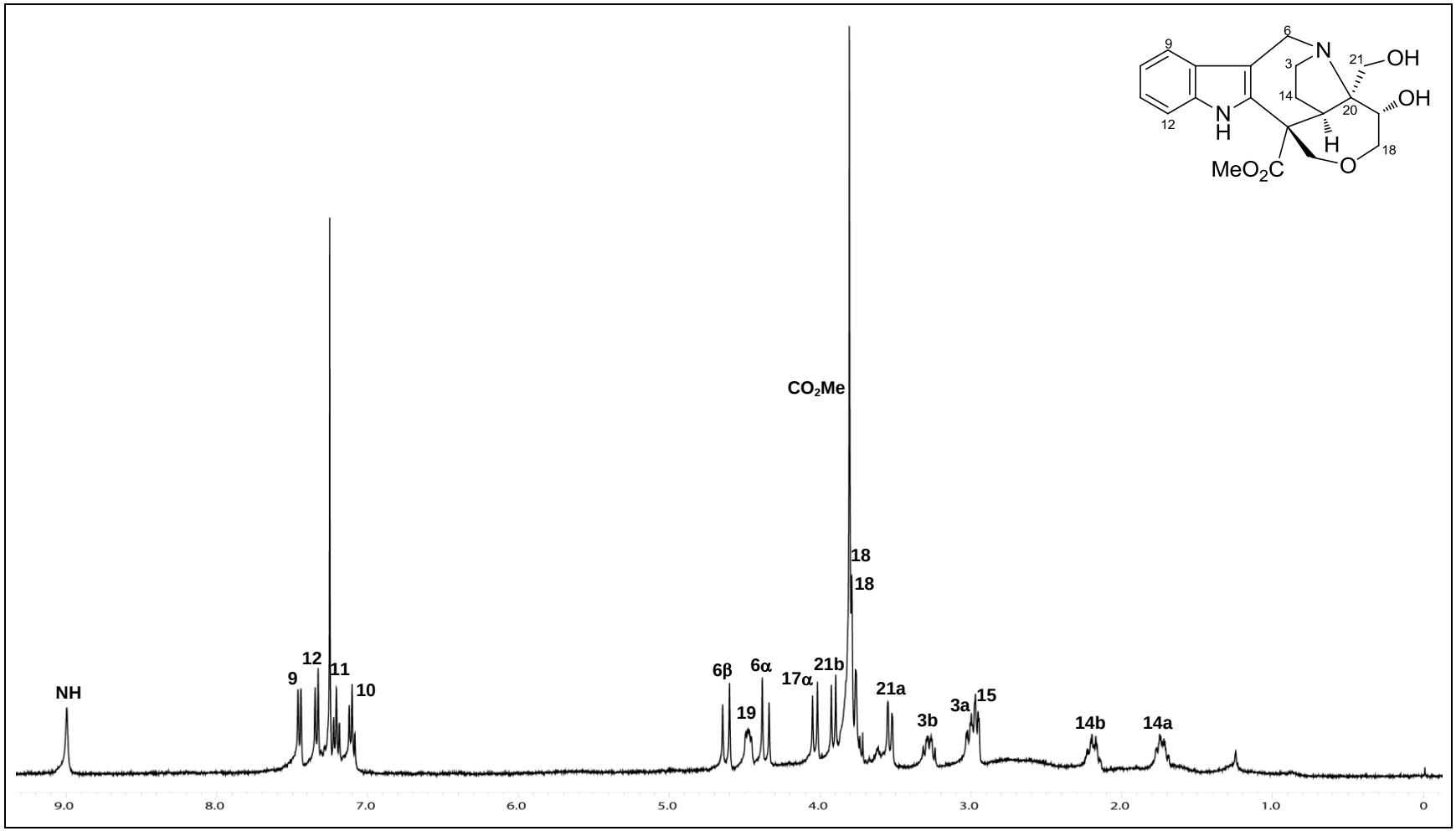
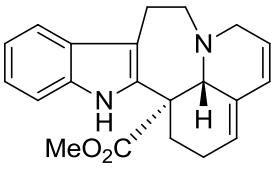


Figure 2.3. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Angustilobine C (**1**)

2.1.2 Andransinine (2)

Andransinine (**2**) was obtained from the leaf extract as a yellowish oil and subsequently colourless block crystals, mp 212–214˚C, with $[\alpha]^{25}_{D}$ −8 ($CHCl_3$, *c* 0.13). The UV spectrum was characteristic of an indole chromophore with absorption maxima at 223 and 284 nm, while the IR spectrum indicated the presence of NH (3387 cm^{-1}), and ester carbonyl (1732 cm^{-1}) functions. In addition, the presence of Wenkert-Bohlmann bands was noted at 2740 and 2885 cm^{-1}. The ESIMS of **2** showed a pseudomolecular ion peak at *m*/*z* 381 and HRESIMS measurements yielded the molecular formula $C_{23}H_{28}N_2O_3$ (DBE 11). The ^{13}C NMR data (Table 2.3) showed 23 carbon resonances, comprising two methyl, seven methylene, six methine, and eight quaternary carbons. An ester carbonyl resonance was observed at δ 171.8, while olefinic resonances due to a trisubstituted double bond were seen at δ 126.0 and 134.0, in addition to the characteristic peaks due to the indole chromophore. The ^1H NMR spectrum (Table 2.3) showed the presence of an unsubstituted indole moiety from the presence of four aromatic resonances (δ 7.50, d, *J* = 8 Hz, H-9; 7.11, t, *J* = 8 Hz, H-10; 7.17, t, *J* = 8 Hz, H-11; 7.33, d, *J* = 8 Hz, H-12), an indolic NH as a broad singlet at δ 8.17, a methoxy group associated with a methyl ester function as a singlet at δ 3.63, a vinylic hydrogen at δ 5.74, and an ethoxy group (δ 3.19, m, 1H, CH_3CHHO; 3.33, m, 1H, CH_3CHHO; 1.11, t, *J* = 7 Hz, CH_3CH_2O). In addition, an isolated aminomethine was observed as a singlet at δ 3.79 (δ_C 63.4). The COSY spectrum showed, in addition to the four aromatic hydrogens and the ethoxy group, NCH_2CH_2, NCH_2CH_2CHO, and CH_2CH_2CH= partial structures. The aminoethylene fragment corresponds to the C-5–C-6 unit from the observed three-bond correlations from H-6 to C-2, C-8 and H-5 to C-3, C-7, C-21 (Figure 2.4). These correlations also indicate branching of the aminomethine (corresponding to C-21) and the NCH_2CH_2CHO fragment (corresponding to C-3–C-

14–C-15 unit) from N-4, as well as substitution of the ethoxy side chain at C-15. The oxymethine C-15 is linked to the quaternary (olefinic) C-20 from the observed H-14 to C-20 three bond correlation. Insertion of the remaining $=CHCH_2CH_2$ fragment between C-20 and C-16 completes the assembly of the ring system of **2**. The remaining carbomethoxy group is attached to C-16 from the resonance of C-16 at δ 48.5, as well as from the observed correlations from H-21 and H-17 to the ester carbonyl. The resulting structure reveals an alkaloid belonging to the rare andranginine group [as exemplified by andranginine (**2a**)], the difference in the present alkaloid being replacement of the 14,15 double bond by an ethoxy substituent at C-15.



Andranginine (**2a**)

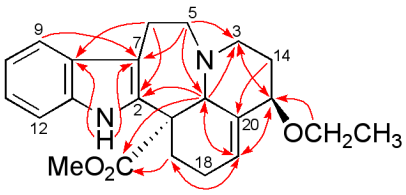


Figure 2.4. Selected HMBCs of Andransinine (**2**)

Andranginine was previously isolated as an optically inactive alkaloid from *Craspidospermum verticillatum*[109] and the relative configuration established by an X-ray analysis.[110] The observed NOE between H-21 and the hydrogens of the ethoxy group (H-22 and H-23) in andransinine (Figure 2.5) indicated an α-oriented H-15 and permitted the assignment of the relative configuration at C-15 as *R*. The observed H-21/H-3β, H-6β and H-15/H-19 NOEs (Figure 2.5) are also in accord with the relative configuration of andransinine as depicted in **2**, as is the observed Wenkert-Bolmann

bands in the IR spectrum, which is consistent with the *trans* disposition of H-21 and the N-4 lone pair.[111–114]

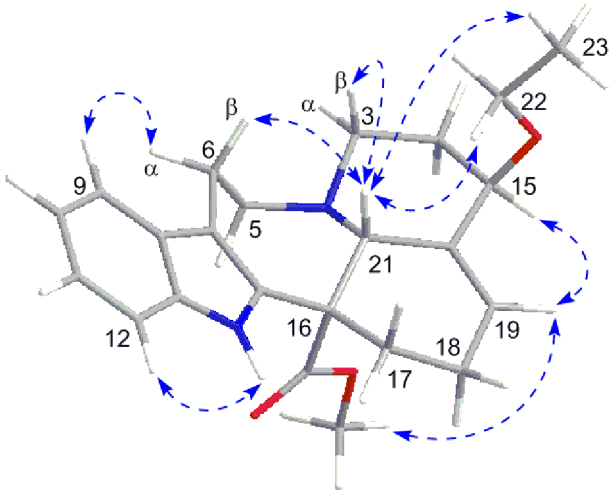


Figure 2.5. Selected NOEs of Andransinine (**2**)

Finally, to obtain support for the above deduction, as well as to secure unambiguous proof of the structure, X-ray diffraction analysis was carried out for **2** (Figure 2.6) which provided confirmation of the structure and relative configuration deduced from all the above observations.

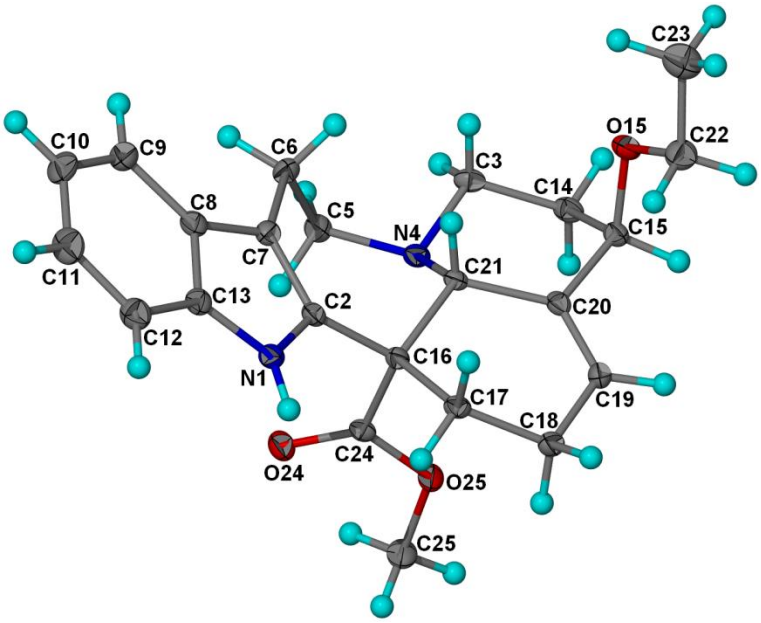


Figure 2.6. X-ray crystal structure of Andransinine (**2**). Thermal ellipsoids are shown at the 50% probability level.

Table 2.3 ^{1}H, ^{13}C and HMBC NMR Data of Andransinine (**2**).[a,b]

Position	δ_H	δ_C	**HMBC**	
			^{2}J	^{3}J
2	–	137.9	–	–
3α	2.80 m	50.0	–	–
3β	3.08 m			
5a	3.17 m	57.0	–	C-3, C-7, C-21
5b	3.31 m			
6α	2.76 m	18.6	C-5, C-7	C-2, C-8
6β	3.12 m			
7	–	114.8	–	–
8	–	127.6	–	–
9	7.50 d (8)	118.4	C-8	C-7, C-11, C-13
10	7.11 t (8)	121.9	–	C-8, C-12
11	7.17 t (8)	119.5	–	C-9, C-13
12	7.33 d (8)	110.8	–	C-8, C-10
13	–	134.8	–	–
14a	1.95 br dd (14, 3)	32.4	–	C-20
14b	2.07 m			
15	3.78 m	78.0	–	C-3, C-19, C-20
16	–	48.5	–	–
17a	2.07 m	32.4	–	–
17b	2.49 dd (13, 3)			
18α	2.05 m	22.2	–	–
18β	2.20 m			
19	5.74 d (5)	126.0	C-18	C-15, C-17, C-21
20	–	134.0	–	–
21	3.79 s	63.4	C-20	C-2, C-3, C-19, $\underline{CO_2}Me$
22	3.19 m	62.2	C-23	C-15
	3.33 m			
23	1.11 t (7)	15.4	–	–
$CO_2\underline{Me}$	3.63 s	52.4	–	$\underline{CO_2}Me$
$\underline{CO_2}Me$	–	171.8	–	–
NH	8.17 br s	–	C-2, C13	C-7, C-8

[a] $CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC, HMBC, and NOESY.

[b] From H to C.

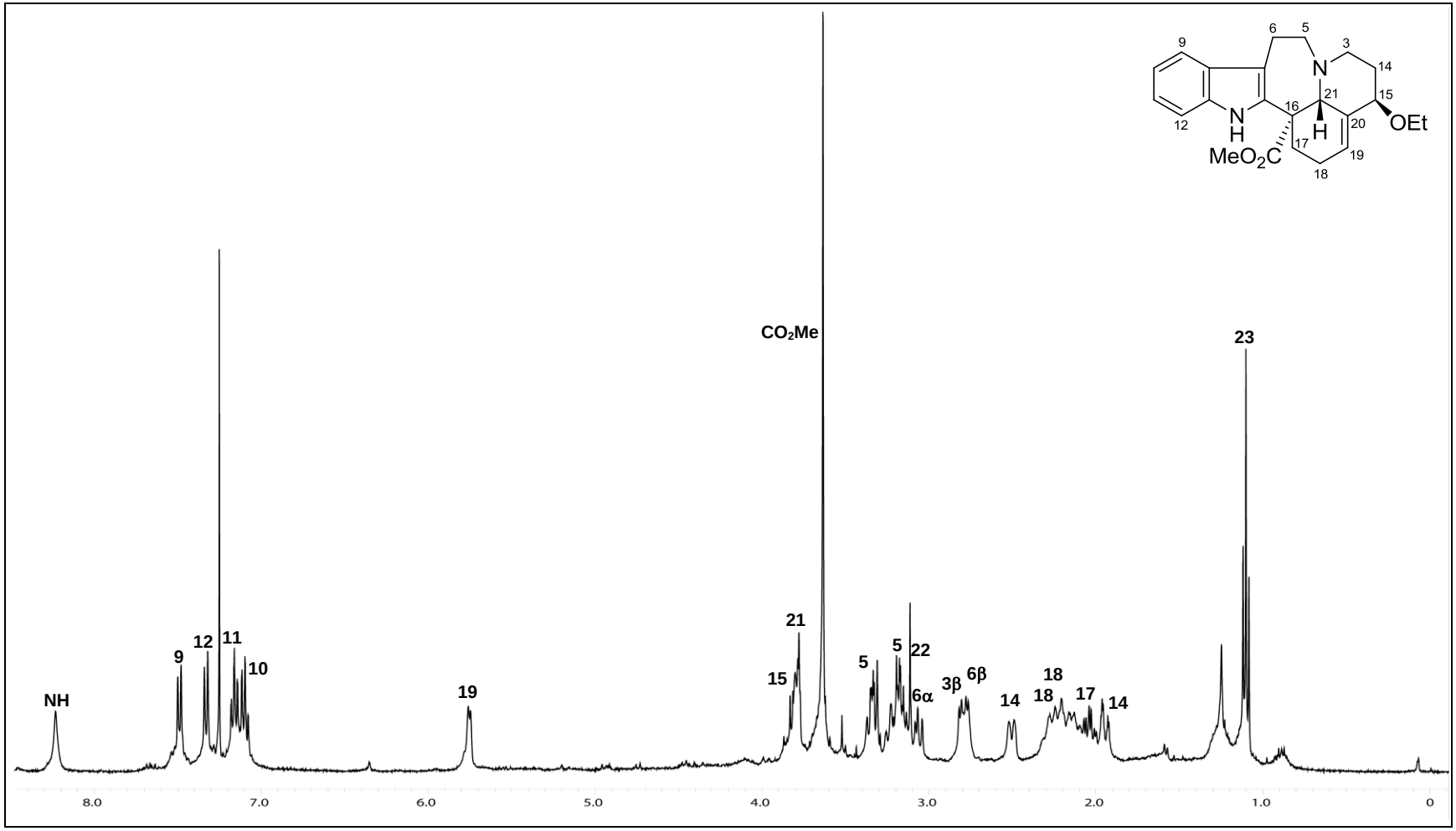


Figure 2.7 ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Andransinine (**2**)

2.1.3 Angustiphylline (3)

Angustiphylline (**3**) was obtained from the stem-bark extract as a light yellowish oil, $[\alpha]^{25}_{D}$ +16 ($CHCl_3$, *c* 0.58). The IR spectrum showed bands due to NH/OH (3287 cm^{-1}) and ester carbonyl (1732 cm^{-1}) functions, while the UV spectrum showed typical indole absorptions at 222 and 283 nm. The ESIMS of **3** showed a pseudomolecular ion peak of *m/z* 667 and HRESIMS measurements gave the molecular formula $C_{39}H_{46}N_4O_6$ (DBE 19). The ^{13}C NMR spectrum (Table 2.4) showed a total of 39 carbon resonances, comprising three methyl, 10 methylene, 13 methine and 13 quaternary carbons. The ^{1}H NMR spectrum (Figure 2.10) showed the presence of eight aromatic protons (δ 6.89–7.47) corresponding to two unsubstituted aromatic moieties, two indolic NH as broad singlets at δ 8.81 and 10.41, another broad singlet at δ 8.54 due to OH, two methyl ester groups (δ_H 3.72, δ_C 52.5, 172.6; δ_H 3.90, δ_C 53.1, 176.3), and a pair of signals at δ 1.82 and 5.79 due to an ethylidene side chain. In addition, four isolated methylene were indicated from the observation of four pairs of well-defined AB doublets at δ 2.67 and 3.03 (*J* = 13 Hz), 3.48 and 4.32 (*J* = 13 Hz), 3.85 and 4.18 (*J* = 12 Hz), 4.57 and 4.69 (*J* = 12 Hz). The former two correspond to two isolated aminomethylenes while the latter two to two oxymethylenes from the corresponding carbon resonances at δ 53.3, 51.9, 79.1, and 65.5, respectively. Examination of the NMR data, including the 2-D COSY and HMQC data revealed that one unit of the bisindole corresponds to the uleine type alkaloid, undulifoline (**11**),[97] from the presence of two characteristic fragments, *viz.*, the isolated oxymethylene at δ 3.85 and 4.18 (δ_C 79.1) and a $OCH_2CH_2CH(CH)CHCH_2CH_2N$ unit, corresponding to the O–C-17 and O–C-18–C-19–C-20–(C-21)–C-15–C-14–C-3–N fragments of undulifoline (**11**), respectively. These assignments are supported by the observed three-bond correlations

from H-18 to C-17, and from H-17 to C-18 in the HMBC spectrum (Figure 2.8), indicating that C-17 and C-18 are linked by an oxygen atom. The other unit constituting the bisindole, after discounting the uleine half, incorporates an unsubstituted indole moiety, an indolic NH, a methyl ester, a hydroxymethyl, an ethylidene side chain, a NCH_2CH_2CH, and two isolated methylene. Examination of the NMR data as well as assembly of these fragments with the help of the HMBC data (Figure 2.8) revealed an alkaloid of the vallesamine subclass (a 6,7-*seco*vallesamine).[25,106,108] The bisindole is therefore branched from C-6' of the *seco*vallesamine half to N-4 of the uleine half as shown in structure **3**. The proposed structure is in full accord with the full HMBC data (Figure 2.8).

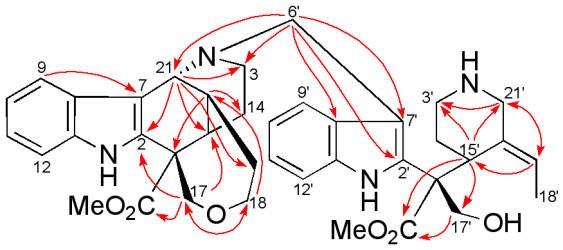


Figure 2.8. Selected HMBCs of Angustiphylline (**3**)

The relative configuration of the bisindole corresponds to that in the constituent monomeric units (undulifoline and vallesamine) which is in agreement with the NOESY data (Figure 2.9).

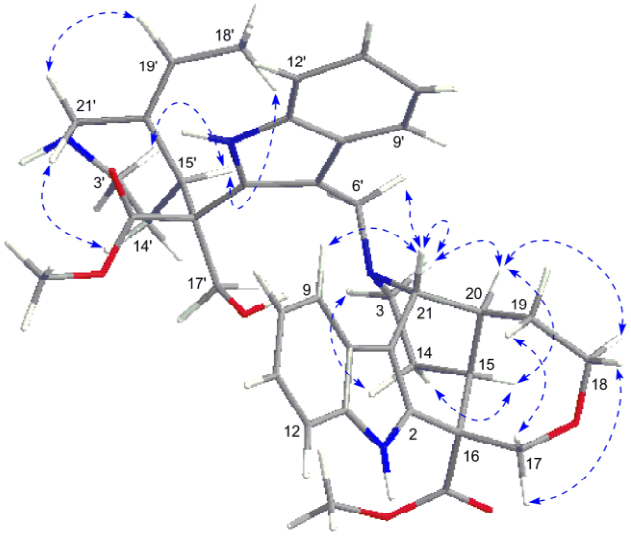
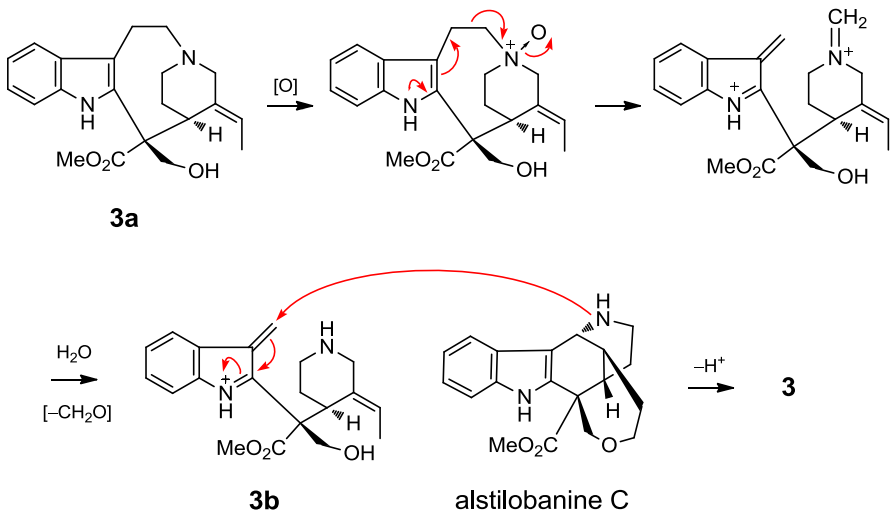


Figure 2.9. Selected NOEs of Angustiphylline (**3**)

A possible biogenetic pathway to **3** is from stemmadenine (**3a**), which on oxidation to the N-4 oxide, followed by Potier-Polonovski fragmentation and subsequent excision of C-5, leads to the ring-opened conjugated iminium ion, **3b**, which on intermolecular trapping by the demethylundulifoline (alstilobanine C) moiety,[29] furnishes the bisindole **3** (Scheme 2.2). Angustiphylline (**3**) represents the first member of the uleine-*seco*vallesamine group of bisindole alkaloids.



Scheme 2.2 Possible biogenetic pathway to angustiphylline (**3**)

Table 2.4. ^{1}H, ^{13}C and HMBC NMR Data of Angustiphylline (**3**).[a,b]

Position	δ_H	δ_C	HMBC ^2J	HMBC ^3J	Position	δ_H	δ_C	HMBC ^2J	HMBC ^3J
2	–	135.1	–	–	2′	–	132.7	–	–
3a	2.09 m	42.9	–	–	3′a	2.29 td (12, 2)	43.0	–	–
3b	2.42 dd (12, 3)		–	–	3′b	2.65 m			
6	–	–	–	–	6′a	3.48 d (13)	51.9	C-7′	C-2′, C-3, C-8′, C-21
	–	–			6′b	4.32 d (13)			
7	–	106.9	–	–	7′	–	109.3	–	–
8	–	128.3	–	–	8′	–	129.6	–	–
9	7.47 d (8)	118.2	C-8	C-7, C-11, C-13	9′	7.13 d (8)	118.3	–	C-7′, C-11′,
10	7.11 t (8)	119.9	–	C-8, C-12	10′	6.89 t (8)	119.4	C-9′	C-8′, C-12′
11	7.17 t (8)	122.2	–	C-9, C-13	11′	7.06 t (8)	121.7	–	C-9′, C-13′
12	7.36 d (8)	111.8	–	C-8, C-10	12′	7.32 d (8)	111.0	–	C-8′, C-10′
13	–	137.0	–	–	13′	–	134.5	–	–
14	1.47 br d (14)	30.4	–	–	14′a	1.70 m	30.2	–	–
	1.64 m				14′b	1.87 br d			
15	2.72 m	38.0	–	$\underline{CO_2}Me$	15′	3.42 br d (7)	40.4	C-20′	C-2′, C-3′, C-17′, C-19′, C-21′, $\underline{CO_2}Me'$
16	–	55.0	–	–	16′	–	61.0	–	–
17a	3.85 d (12)	79.1	–	C-2, C-15,	17′a	4.57 d (12)	65.5	–	$\underline{CO_2}Me'$
17b	4.18 d (12)		–	$\underline{CO_2}Me$	17′b	4.69 d (12)			
18a	3.47 t (13.5)	69.6	–	C-17, C-20	18′	1.82 d (7)	14.5	C-19′	C-20′
18b	3.71 m		–	–		–			
19a	1.37 m	33.0	–	–	19′	5.79 q (7)	125.2	C-18′	C-15′, C-21′
19b	2.08 m		–	–		–			
20	2.72 m	40.4	–	C-14, C-16	20′	–	137.2	–	–
21a	4.04 m	60.0	C-7, C-20	C-3, C-6′, C-8,	21′α	2.67 d (13)	53.3	C-20′	C-19′
21b	–			C-15, C-19	21′β	3.03 d (13)		–	–
$CO_2\underline{Me}$	3.72 s	52.5	–	$\underline{CO_2}Me$	$CO_2\underline{Me}'$	3.90 s	53.1	–	$\underline{CO_2}Me'$
$\underline{CO_2}Me$	–	172.6	–	–	$\underline{CO_2}Me'$	–	176.3	–	–
NH	8.81 br s	–	C-13	C-7, C-8	NH′	10.41 br s	–	C-13′	C-7′, C-8′
					17′-OH	8.54 br s	–	–	–

[a]$CDCl_3$, 400 MHz (^1H), 100 MHz (^{13}C); assignments based on COSY, HMQC, HMBC, and NOESY.
[b]From H to C.

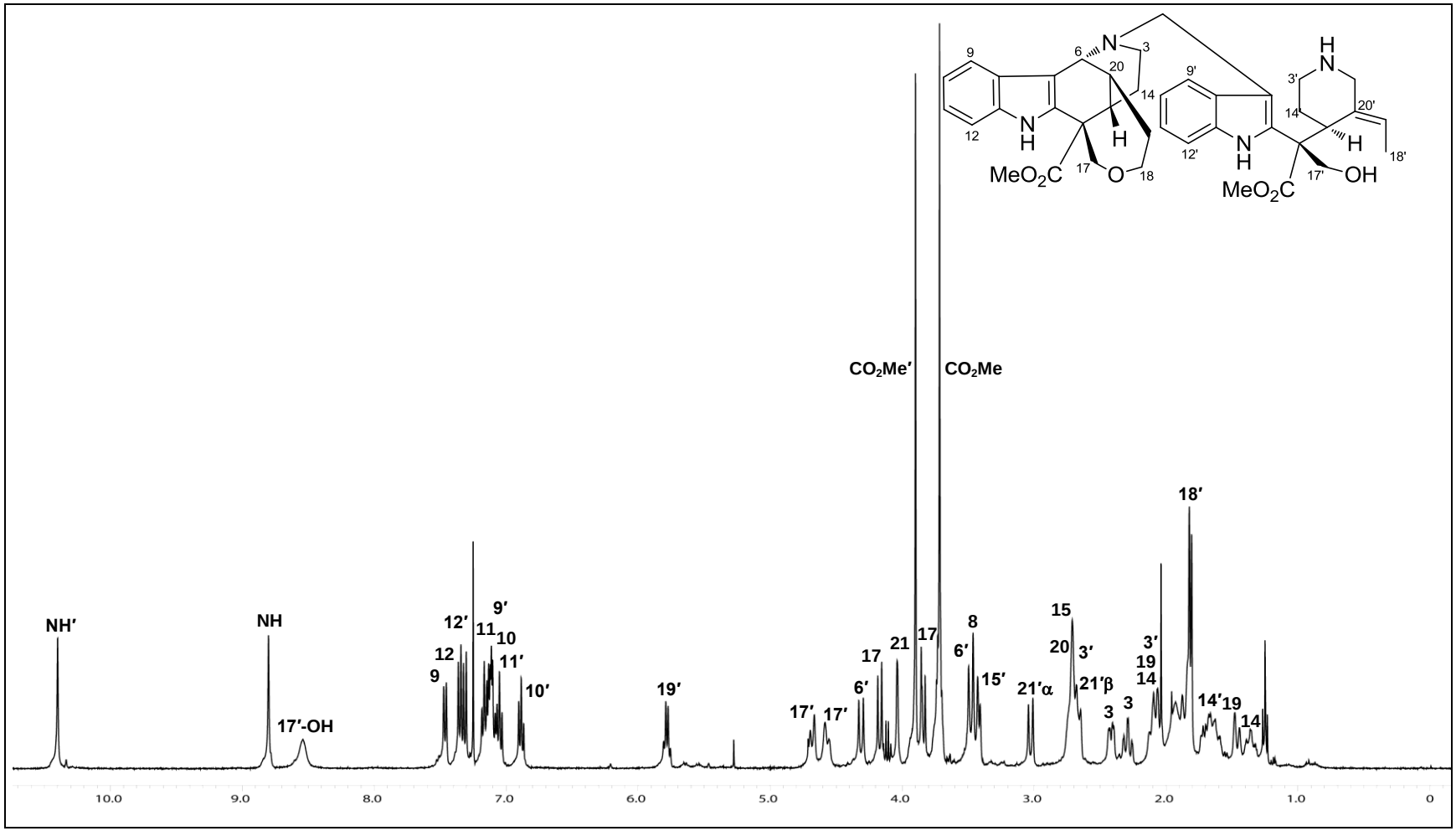


Figure 2.10. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Angustiphylline (**3**)

2.1.4. Known Alkaloids

In addition to the alkaloids already mentioned, a further seventeen known alkaloids were also obtained from the leaf and stem-bark extracts of *Alstonia angustiloba* Miq.. The characterization data of these known alkaloids are presented in the Table 2.5.

Table 2.5. Compound data of known alkaloids from *Alstonia angustiloba* Miq.

Alkaloids	**Physical appearance**	**$[\alpha]^{25}_{D}$**	**UV /nm (EtOH)**	**IR /cm^{-1}**	**NMR data**
19,20-*E*-Vallesamine (**4**)	Light yellowish oil	+14 ($CHCl_3$, *c* 2.66)	226, 276, 284, 292	3348, 1726	Table 2.6, 2.7
17-*O*-Acetylvallesamine (**5**)	Light yellowish oil	+371 ($CHCl_3$, *c* 0.16)	223, 276, 285, 292	3390, 1733	Table 2.6, 2.7
Yunnanensine (**6**)	Light yellowish oil	+31 ($CHCl_3$, *c* 3.16)	222, 280, 283, 295	3388, 1720	Table 2.6, 2.7
Angustilobine A (**7**)	Light yellowish oil	+115 (MeOH, *c* 0.02)	219, 282	3350, 1726	Table 2.8
Angustilobine B (**8**)	Light yellowish oil	–30 ($CHCl_3$, *c* 0.44)	223, 285	3400, 1730	Table 2.8
Nor-6,7-*seco*angustilobine B (**9**)	Light yellowish oil	+166 ($CHCl_3$, *c* 3.76)	223, 283	3380, 1725	Table 2.9
Nor-6,7-*seco*-19,20α-epoxyangustilobine B (**10**)	Light yellowish oil	+55 ($CHCl_3$, *c* 0.08)	222, 290	3360, 1740	Table 2.9
Undulifoline (**11**)	Light yellowish oil	–33 ($CHCl_3$, *c* 0.16)	220, 288	3350, 1725	Table 2.10
Condylocarpine (**12**)	Light yellowish oil	+501 ($CHCl_3$, *c* 0.6)	227, 296, 329	3363, 1673	Table 2.11
20*S*-Tubotaiwine (**13**)	Light yellowish oil	+653 ($CHCl_3$, *c* 0.1)	210, 231, 295	3360, 1672	Table 2.11
N(4)-Demethyl-echitamine (**14**)	White amorphous	+6 ($CHCl_3$, *c* 1.0)	215, 243, 302	3350, 2975	Table 2.12
17-*O*-Acetyl-*N*(4)-demethyl-echitamine (**15**)	Light yellowish oil	–17 ($CHCl_3$, *c* 1.23)	210, 240, 300	3350, 2977	Table 2.12

Table 2.5 continued

Alstolucine B (**16**)	Light yellowish oil	–308 ($CHCl_3$, *c* 0.29)	232, 295, 326	3361, 1704, 1678	Table 2.13
Vincamine (**17**)	Light yellowish oil	+27 ($CHCl_3$, *c* 0.14)	226, 279	1730, 742	Table 2.14
16*R*,19*E*-Isositsirikine (**18**)	Light yellowish oil	+5 ($CHCl_3$, *c* 0.23)	227, 282, 290	3379, 2830, 2785, 1726, 1630	Table 2.15
Venoterpine (**19**)	Light yellowish oil	–6 ($CHCl_3$, *c* 0.58)	262	3160, 1600	Table 2.16
Cantleyine (**20**)	Light yellowish oil	–24 ($CHCl_3$, *c* 1.02)	260	3160, 1700, 1630	Table 2.16

Table 2.6. ^{1}H NMR Data of 19,20-*E*-Vallesamine (**4**), 17-*O*-Acetylvallesamine (**5**), and Yunnanensine (**6**).[a]

Position	**4**	**5**	**6**
3	3.02 m	2.82 br dd (14, 7)	2.58 m
	3.02 m	2.95 td (14, 6)	2.70 m
6	4.20 d (17)	4.16 d (17)	–
	4.93 d (17)	4.77 d (17)	–
7	–	–	6.42 s
9	7.61 br d (8)	7.48 d (8)	7.51 d (8)
10	7.22 br t (8)	7.09 t (8)	7.07 t (8)
11	7.32 br t (8)	7.21 t (8)	7.15 t (8)
12	7.48 br d (8)	7.31 d (8)	7.38 d (8)
14	2.07 tt (12, 3)	1.98 ddd (14, 12, 6)	1.48 m
	2.44 qd (12, 3)	2.33 tdd (14, 7, 3)	1.85 br d
15	3.82 dd (12, 3)	3.85 dd (12, 3)	3.42 br d (8)
17	3.96 d (10)	4.32 d (11)	4.21 d (11)
	4.38 d (10)	4.47 d (11)	4.39 d (11)
18	1.89 br d (7)	1.77 dd (7, 2)	1.61 d (7)
19	5.68 br q (7)	5.63 br q (7)	5.53 q (7)
21	3.70 d (16)	3.61 br dd (16, 2)	3.00 br s
	3.77 br d (16)	3.70 d (16)	3.00 br s
CO_2Me	3.90 s	3.80 s	3.77 s
OCOMe	–	2.09 s	–
NH	9.50 br s	8.62 br s	9.92 br s

[a]$CDCl_3$, 400 MHz; assignments based on COSY and HMQC

Table 2.7. ^{13}C NMR Data of 19,20-*E*-Vallesamine (**4**), *O*-acetylvallesamine (**5**), and Yunnanensine (**6**).[a]

Position	**4**	**5**	**6**
2	133.8	128.2	136.3
3	47.4	47.3	52.1
6	50.7	52.6	–
7	108.6	112.0	102.1
8	128.0	127.9	127.6
9	118.0	118.5	120.3
10	118.7	119.2	119.9
11	121.3	122.8	121.9
12	110.5	110.4	111.4
13	135.1	135.3	136.1
14	24.0	25.7	28.5
15	36.2	34.8	39.3
16	58.7	55.8	57.4
17	70.3	70.4	65.9
18	14.0	13.9	13.9
19	123.6	124.5	126.2
20	132.9	134	134.2
21	52.6	54.9	52.1
CO_2Me	53.7	53.0	52.7
CO_2Me	175.1	173.9	174.5
OCOMe	–	21.0	–
OCOMe	–	169.6	–

[a]$CDCl_3$, 100 MHz; assignments based on HMQC and HMBC.

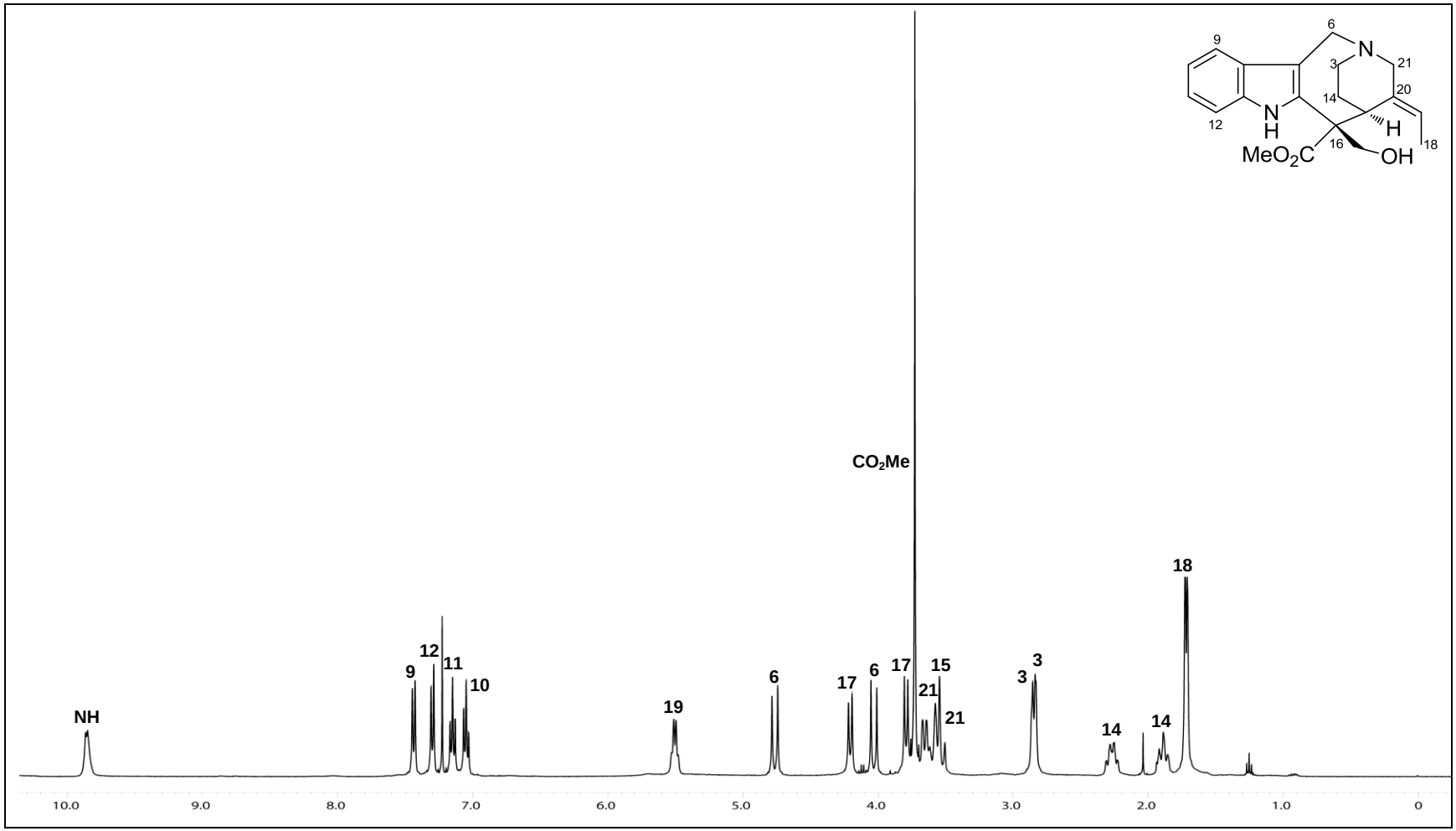


Figure 2.11. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of 19,20-*E*-Vallesamine (**4**)

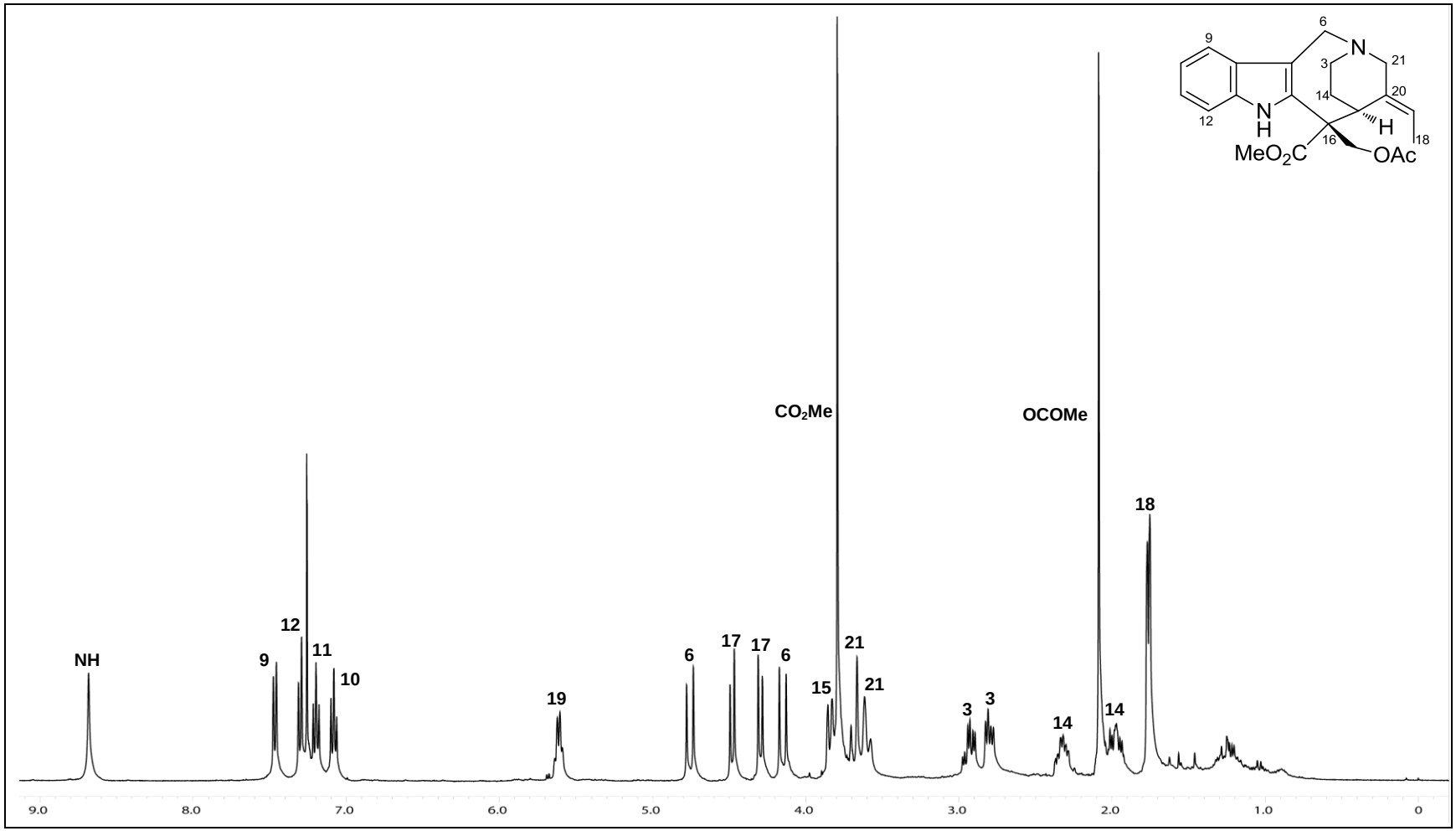


Figure 2.12. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of 17-*O*-Acetylvallesamine (**5**)

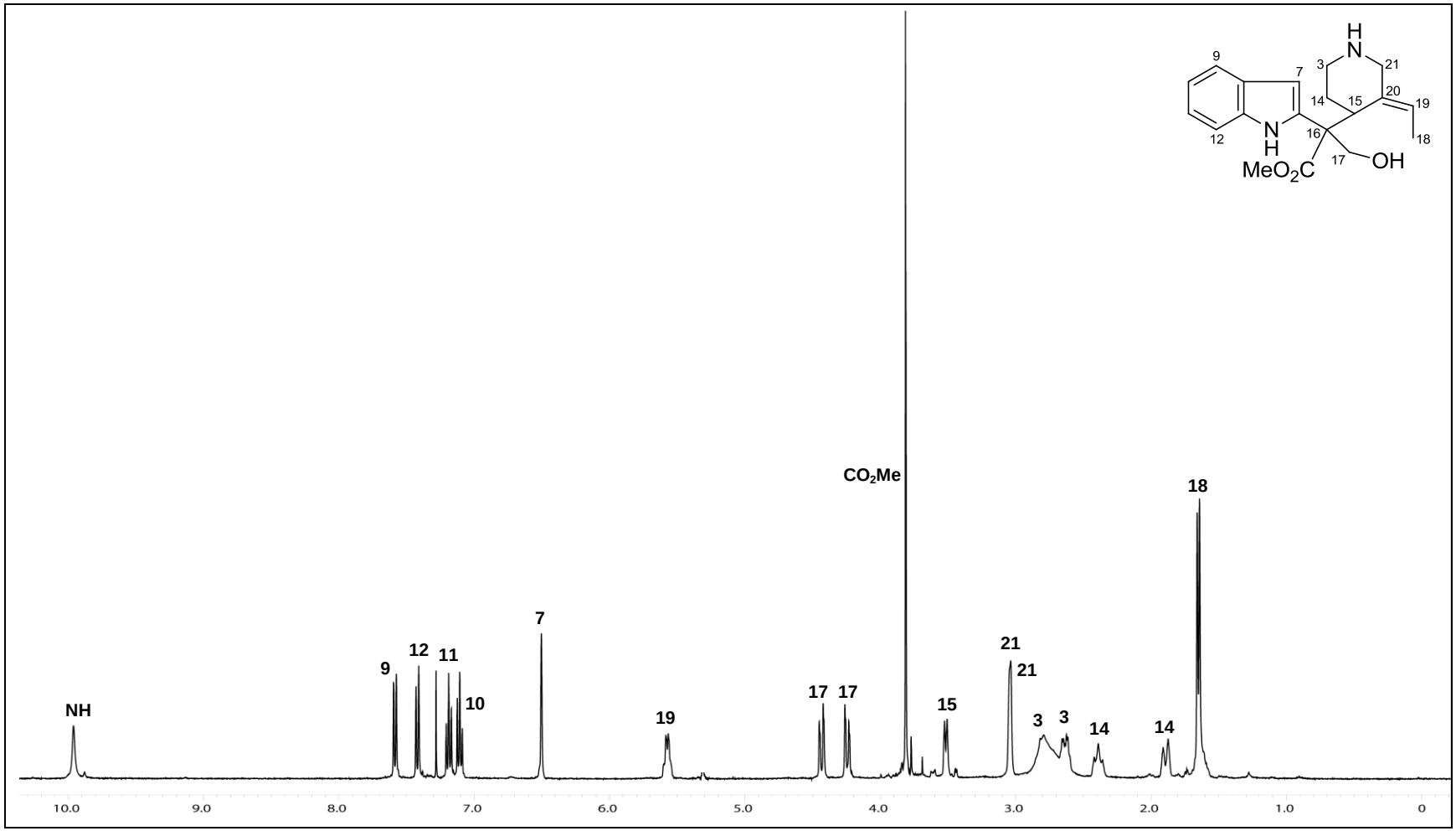


Figure 2.13. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Yunnanensine (**6**)

Table 2.8. ^{1}H and ^{13}C NMR Data of Angustilobine A (**7**) and Angustilobine B (**8**).[a]

Position	**7**		**8**	
	δ_H	δ_C	δ_H	δ_C
2	–	132.9	–	131.4
3	3.05 m	42.1	2.92 m	43.9
	2.85 m		3.18 dd (13,10)	
6	4.73 d (16)	50.8	3.97 d (17)	51.1
	4.33 d (16)		4.73 d (17)	
7	–	111.5	–	106.3
8	–	129.4	–	128.9
9	7.51 d (8)	118.3	7.48 br d (8)	118.2
10	7.19 t (8)	122.4	7.08 td (8, 1)	119.3
11	7.11 t (8)	119.7	7.16 td (8, 1)	122.2
12	7.32 d (8)	110.8	7.29 br d (8)	110.6
13	–	134.7	–	135.3
14	2.03 m	17.6	1.67 dd (15, 8)	21.6
	1.75 m		1.97 dtd (15, 10, 7)	
15	3.50 m	49.3	n.d.	36.5
16	–	60.0	–	58.3
17	4.14 d (8)	76.8	n.d.	77.5
	3.98 d (8)		4.35 d (13)	
18	5.39 dd (7, 1)	112.2	4.19 dd (16, 5)	71.2
	5.13 dd (11, 1)		4.48 br d (16)	
19	5.92 dd (17, 11)	140.2	5.39 br s	121.8
20	–	81.7		132.1
21	3.17 d (15)	57.7	3.28 d (16)	55.7
	3.02 d (15)		3.72 br d (16)	
$CO_2\underline{Me}$	3.91 s	53.1	3.86 s	53.0
$\underline{CO_2}Me$	–	173.7	–	175.0
NH	8.35 br s	–	8.66 br s	–

[a]$CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC and HMBC.

Table 2.9. ^{1}H and ^{13}C NMR Data of *Nor*-6,7-*seco*angustilobine B (**9**) and *Nor*-6,7-*seco*-19,20α-epoxyangustilobine B (**10**).[a]

Position	**9**		**10**	
	δ_H	δ_C	δ_H	δ_C
2	–	135.6	–	134.0
3	2.10 td (12, 3)	56.4	1.95 td (13, 3)	56.2
	2.79 br d (12)		2.86 br d (13)	
7	6.28 br s	100.3	6.20 dd (2, 1)	100.5
8	–	127.6	–	127.8
9	7.56 br d (8)	120.3	7.54 br d (8)	120.4
10	7.10 td (8, 1)	119.9	7.10 td (8, 1)	120.1
11	7.18 td (8, 1)	121.9	7.19 td (8, 1)	122.4
12	7.33 dd (8, 1)	110.8	7.34 dd (8, 1)	110.9
13	–	135.8	–	135.7
14	1.05 dq (12, 3)	28.8	1.17 dq (13, 3)	26.6
	1.51 qd (12, 3)		1.61 qd (13, 4)	
15	3.23 br d (12)	46.3	3.17 br d (13)	46.0
16	–	56.4	–	53.2
17	4.11 d (11)	70.6	3.74 d (13)	70.3
	4.77 d (11)		4.76 dd (13, 2)	
18	4.23 br d (17)	69.0	3.96 d (15)	67.1
	4.35 dd (17, 3)		4.38 dd (15, 3)	
19	5.57 t (3)	123.3	2.97 d (3)	62.9
20	–	137.5	–	n.d.
21	2.81 d (11)	66.9	2.34 dd (11, 1)	66.0
	3.17 d (11)		2.59 d (11)	
$CO_2\underline{Me}$	3.73 s	52.5	3.79 s	53.1
$\underline{CO_2}Me$	–	173.5	–	173.5
N(4)-Me	2.28 s	45.3	2.28 s	45.7
NH	8.29 br s	–	8.34 br s	–

[a]$CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC and HMBC.

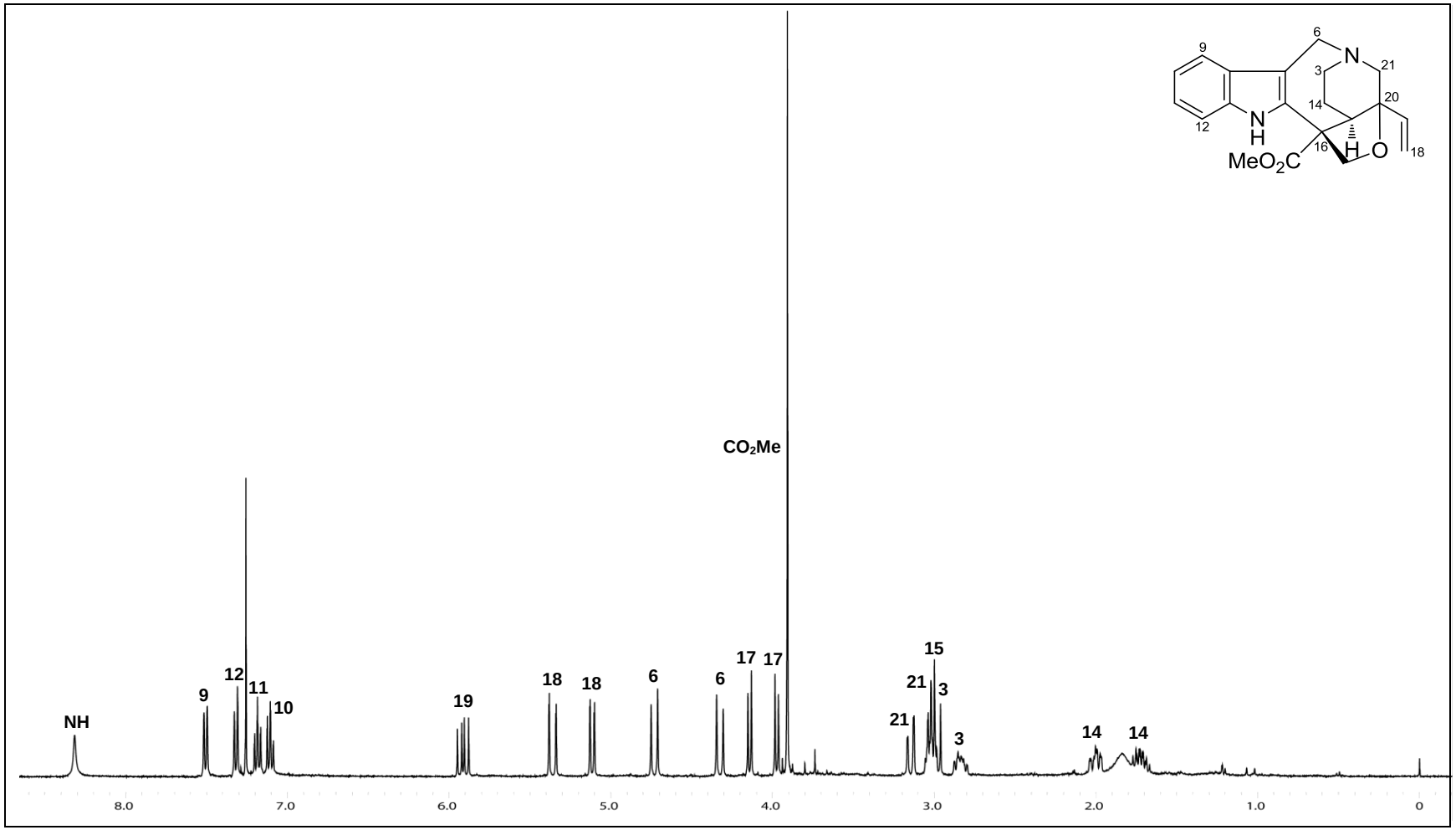


Figure 2.14. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Angustilobine A (**7**)

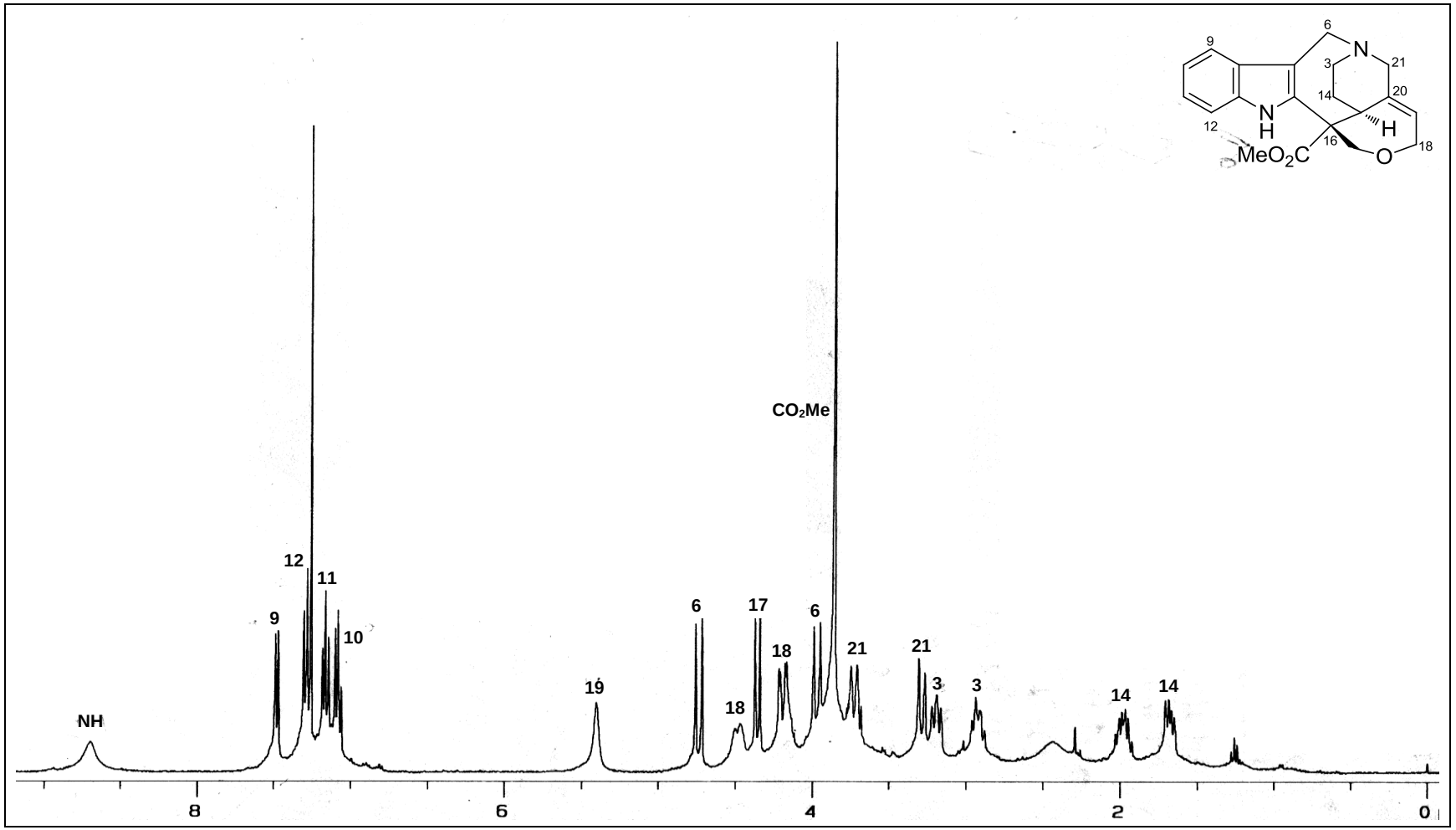


Figure 2.15. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Angustilobine B (**8**)

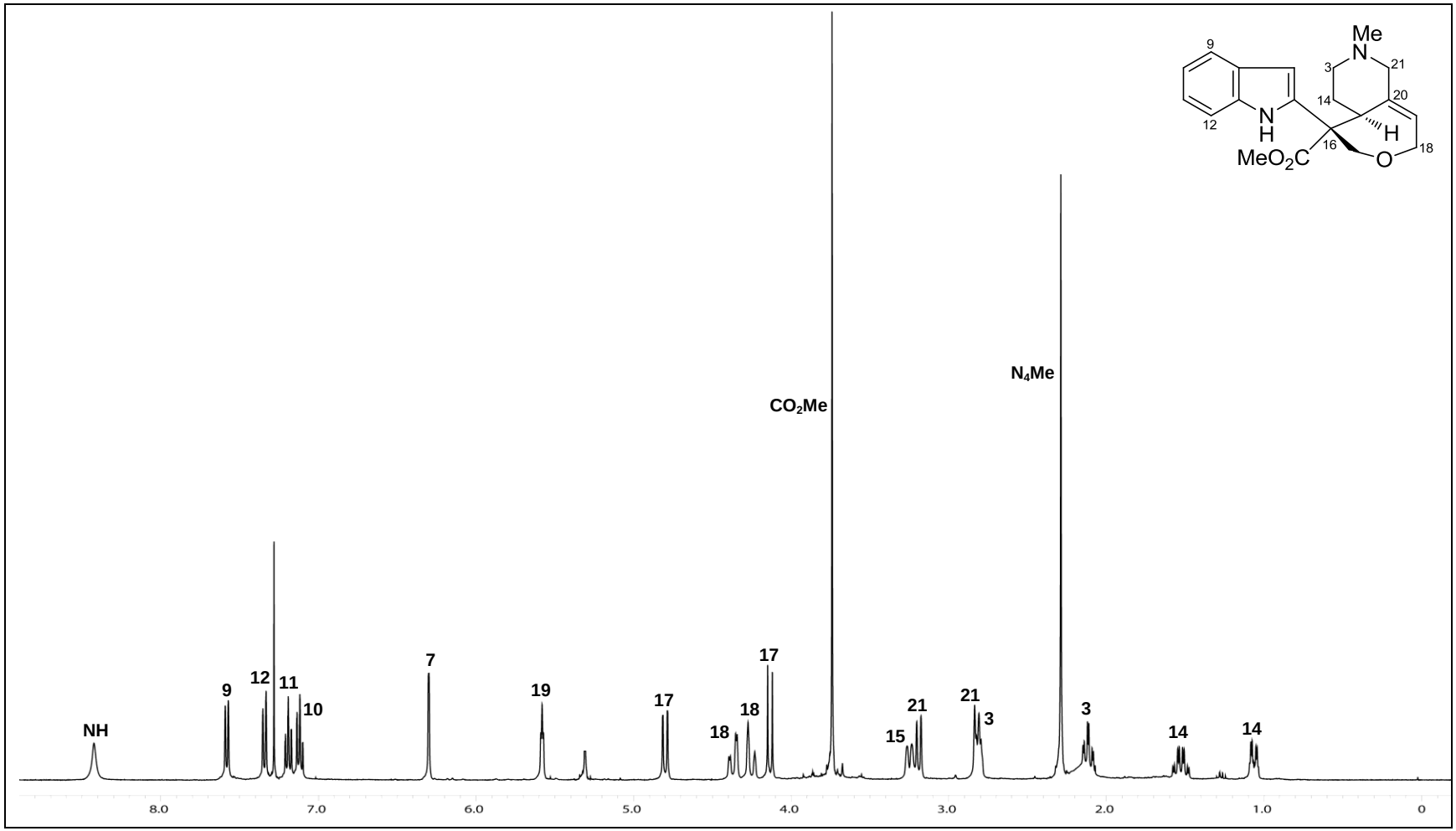


Figure 2.16. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of *Nor*-6,7-*seco*angustilobine B (**9**)

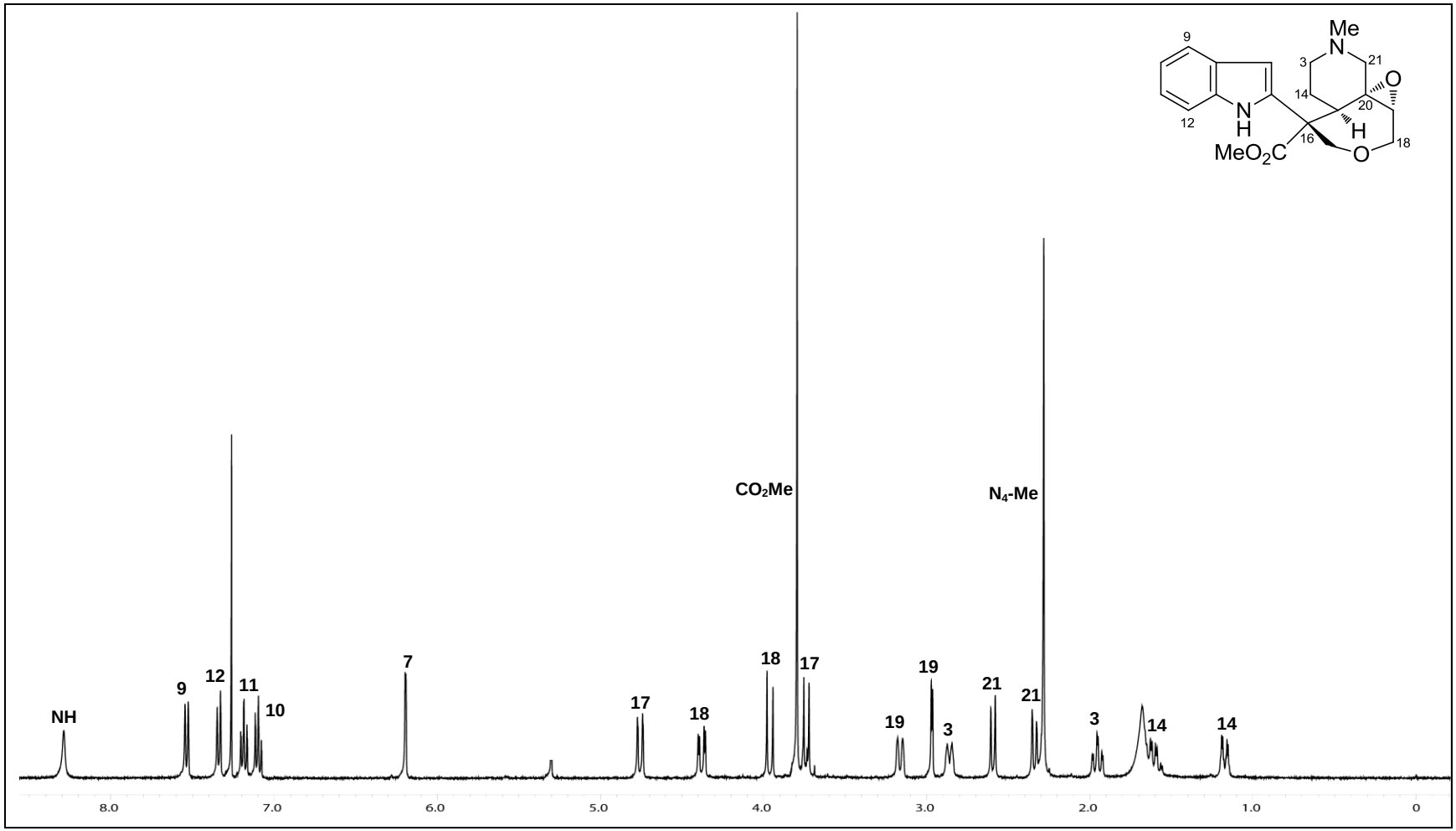


Figure 2.17. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of *Nor*-6,7-*seco*-19,20α-epoxyangustilobine B (**10**).

Table 2.10. ^{1}H and ^{13}C NMR Data of Undulifoline (**11**).[a]

Position	δ_H	δ_C
2	–	135.1
3	2.14 td (12, 3)	46.2
	2.49 dd (12, 4)	
7	–	106.6
8	–	128.8
9	7.51 d (8)	118.8
10	7.08 t (8)	119.8
11	7.13 t (8)	122.1
12	7.31 d (8)	111.5
13	–	136.9
14	1.61 br d (14)	30.5
	2.01 m	
15	2.78 m	37.8
16	–	55.5
17	3.88 d (12)	79.0
	4.22 d (12)	
18	3.46 br t (12)	69.6
	3.69 td (12, 3)	
19	1.28 m	33.1
	1.98 m	
20	2.73 m	40.1
21	3.95 br s	58.9
$CO_2\underline{Me}$	3.79 s	52.5
$\underline{CO_2}Me$	–	172.7
N(4)-Me	2.32	–
NH	8.76 br s	–

[a]$CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC and HMBC.

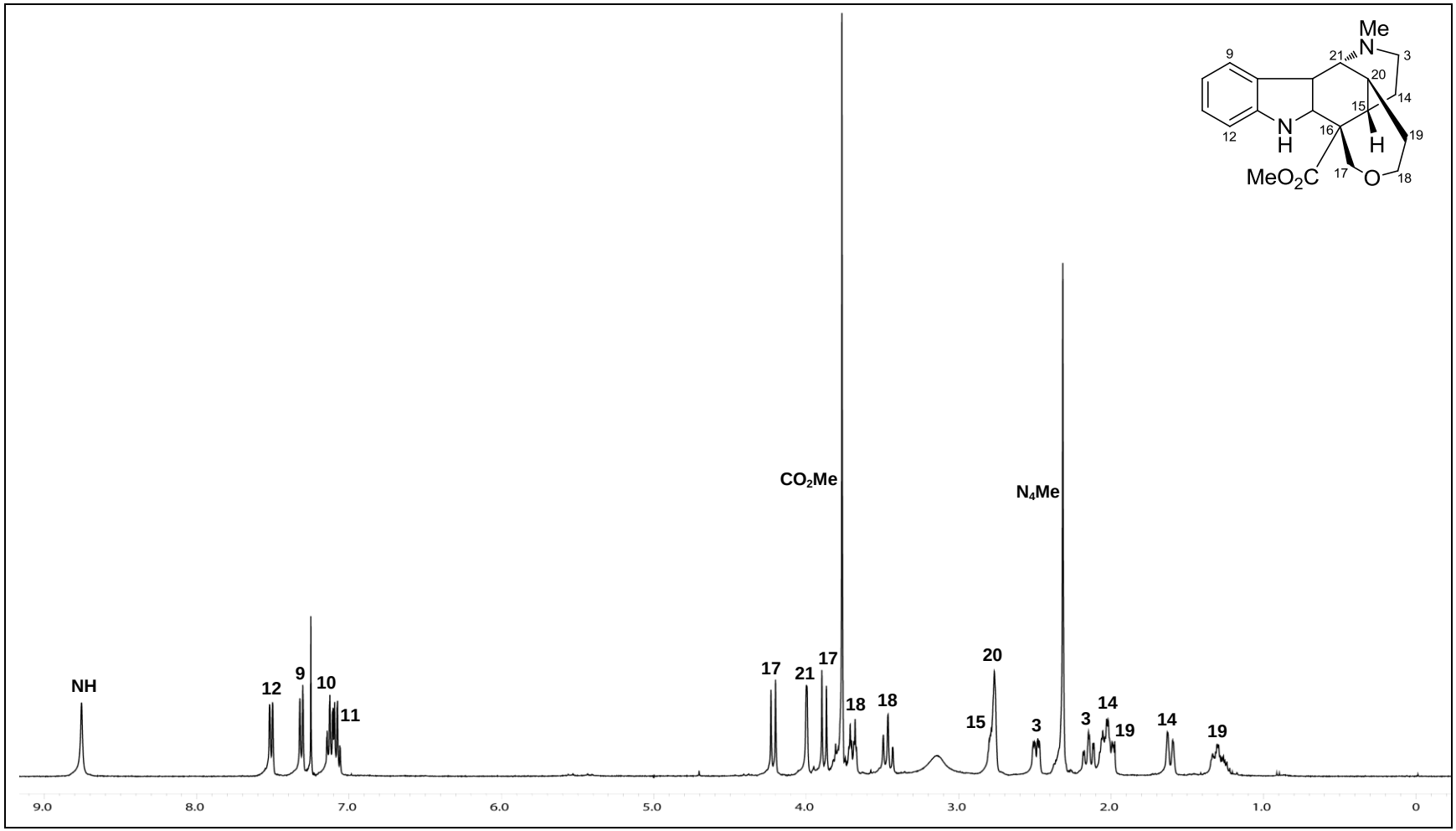


Figure 2.18. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Undulifoline (**11**).

Table 2.11. ^{1}H and ^{13}C NMR Data of Condylocarpine (**12**) and 20*S*-Tubotaiwine (**13**).[a]

Position	**11**		**12**	
	δ_H	δ_C	δ_H	δ_C
2	–	169.2	–	168.7
3	3.03 ddd (13, 7, 5)	45.9	2.50 dt (11, 5)	43.8
	2.66 ddd (13, 7, 5)	–	2.95 dt (11, 5)	–
5	2.97 ddd (12, 7, 3)	52.9	3.83 dd (10, 7)	53.8
	3.09 ddd (12, 10, 7)	–	2.89 m	–
6	1.97 ddd (13, 7, 3)	45.0	1.78 m	45.1
	2.77 ddd (13, 10, 7)	–	3.04 m	–
7	–	59.8	–	55.0
8	–	135.2	–	131.0
9	7.17 d (7)	120.1	7.14 d (7)	120.9
10	6.89 td (7, 1)	121.0	6.88 t (7)	119.4
11	7.11 td (7, 1)	127.6	7.10 t (7)	127.0
12	6.78 d (7)	109.6	6.80 d (7)	110.0
13	–	144.4	–	143.5
14	1.88 m	28.2	1.78 m	28.3
	1.88 m	–	1.79 m	–
15	3.91 ddd (7, 3, 2)	28.9	3.04 br s	30.8
16	–	101.4	–	95.4
18	1.59 d (7)	13.0	0.69 t (7)	11.4
19	5.32 q (7)	117.4	0.82 m	23.8
		–	0.82 m	–
20	–	137.2	1.95 tt (7, 3)	41.1
21	4.13 br d (1.7)	68.7	3.79 br d (3)	65.4
NH	8.67 br s	–	8.85 br s	–
CO_2Me	3.79 s	51.2	3.78 s	51.0
CO_2Me	–	168.0	–	170.5

[a]$CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC and HMBC.

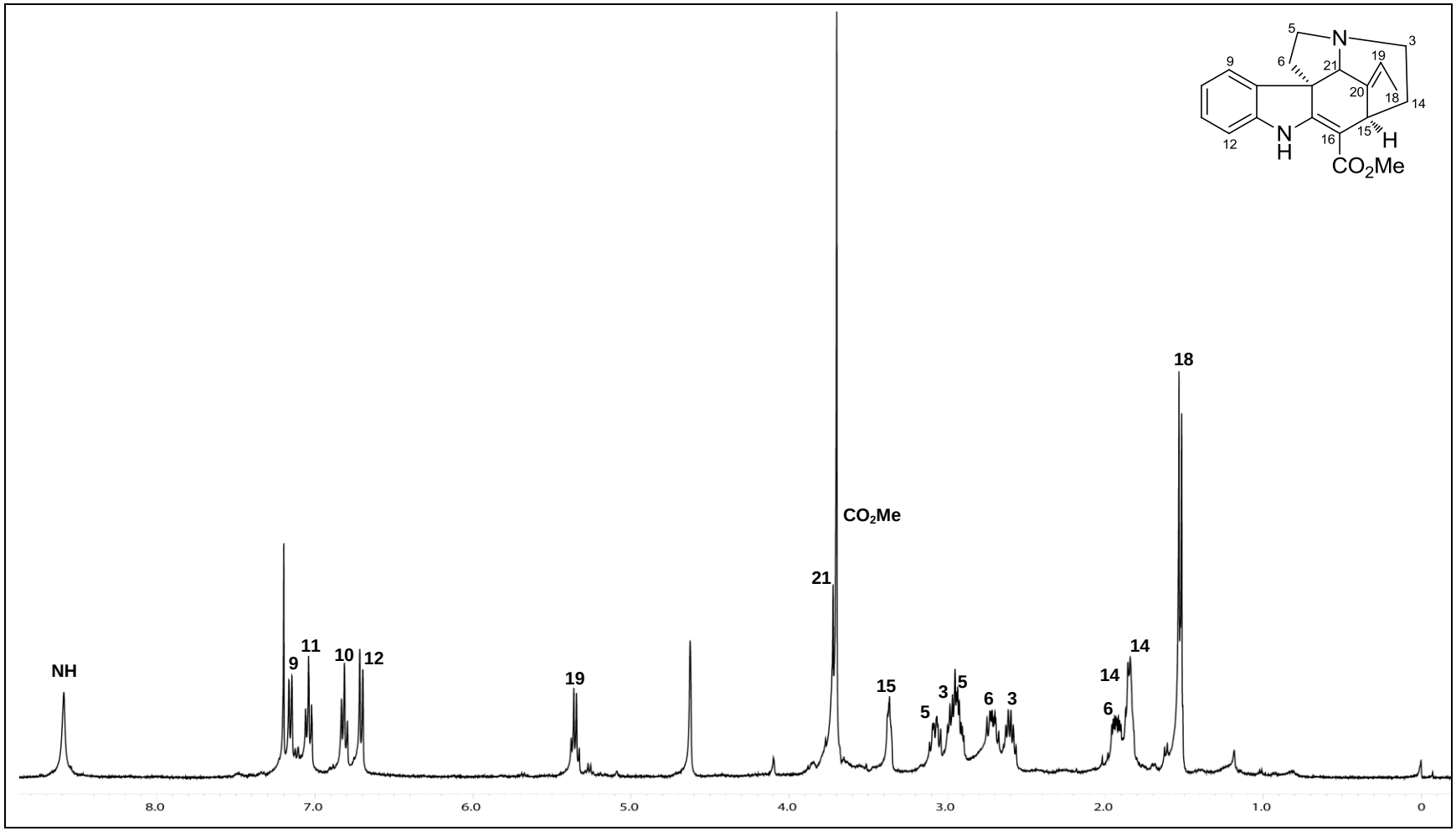


Figure 2.19. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Condylocarpine (**12**)

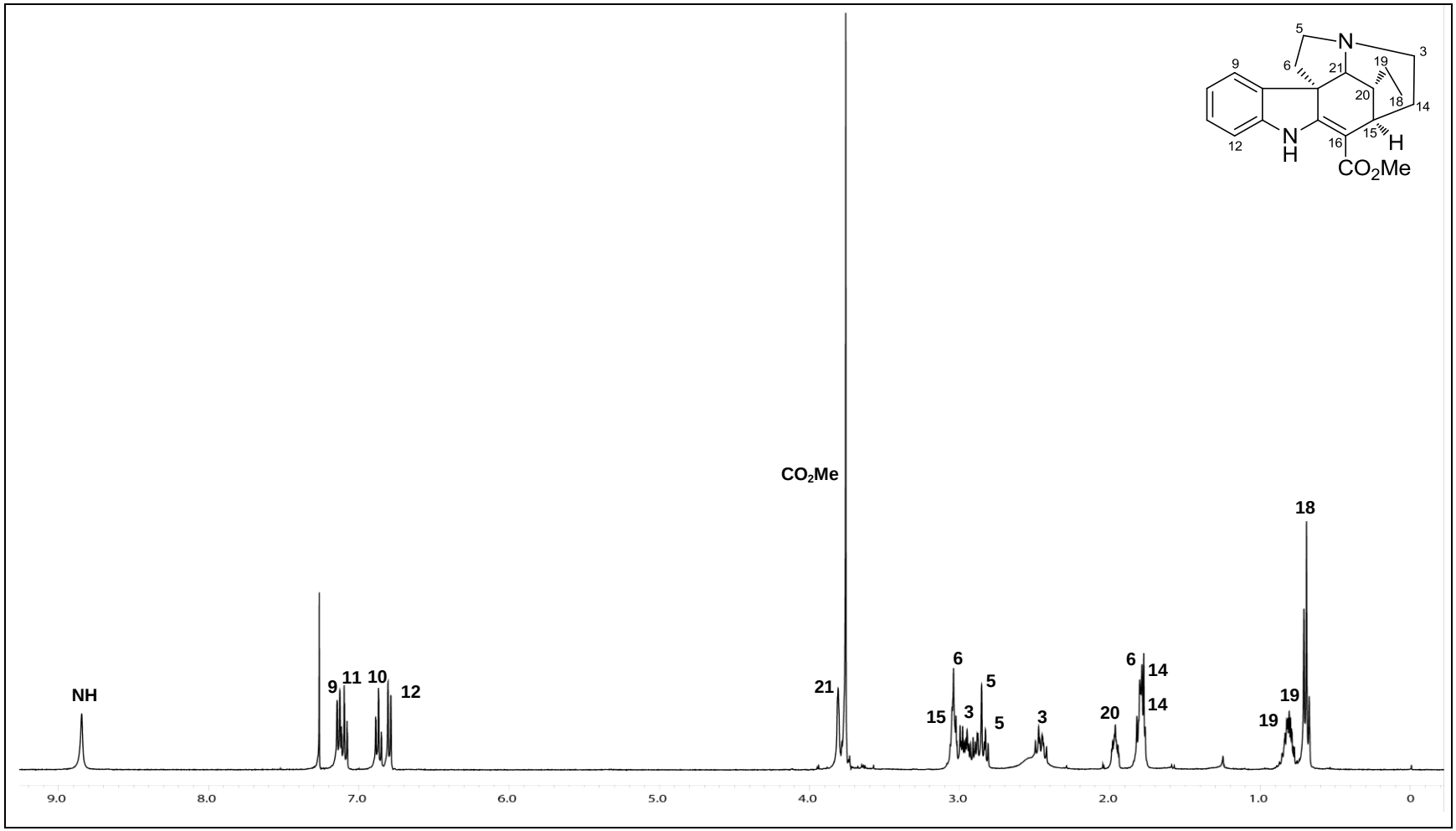


Figure 2.20. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of 20*S*-Tubotaiwine (**13**)

Table 2.12. ^{1}H and ^{13}C NMR Data of *N*(4)-Demethylechitamine (**14**) and 17-*O*-Acetyl-*N*(4)-demethylechitamine (**15**).[a]

Position	**14**		**15**	
	δ_H	δ_C	δ_H	δ_C
2	–	96.0	–	96.2
3	4.33 dd (11, 5)	68.7	4.28 dd (11, 6)	68.4
5	2.82 dd (12, 8)	53.9	2.75 dd (12, 8)	54.0
	3.46 m		3.40 dt (11, 7)	
6	2.17 dd (14, 8)	46.8	2.07 dd (14, 8)	46.5
	2.39 m		2.18 br dt (15, 8)	
7	–	60.8	–	60.9
8	–	131.4	–	130.8
9	7.52 dd (8, 1)	126.7	7.69 dd (8, 1)	127.2
10	6.68 td (8, 1)	118.5	6.68 td (8, 1)	119.0
11	6.99 td (8, 1)	128.3	7.00 td (8, 1)	128.8
12	6.43 br d (8)	110.0	6.45 br d (8)	110.2
13	–	148.7	–	148.7
14	1.65 dd (15, 5)	32.2	1.64 dd (15, 5)	32.4
	2.63 ddd (15, 11, 5)		2.46 ddd (15, 10, 5)	
15	3.86 m	36.2	3.77 d (5)	36.2
16	–	56.0	–	54.2
17	3.40 d (12)	66.9	3.73 d (12)	67.2
	4.00 d (12)		4.79 d (12)	
18	1.73 dd (7, 2)	14.3	1.77 dd (7, 2)	14.9
19	5.44 br q (7)	123.2	5.41 br q (7)	124.2
20	–	139.0	–	138.2
21	3.07 d (16)	57.2	3.01 d (16)	57.1
	4.36 br d (16)		4.21 br d (16)	
CO_2Me	3.84 s	51.8	3.79 s	52.1
CO_2Me	–	174.8	–	173.4
OCOMe	–	–	2.06 s	21.0
OCOMe	–	–	–	170.4

[a]$CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC and HMBC.

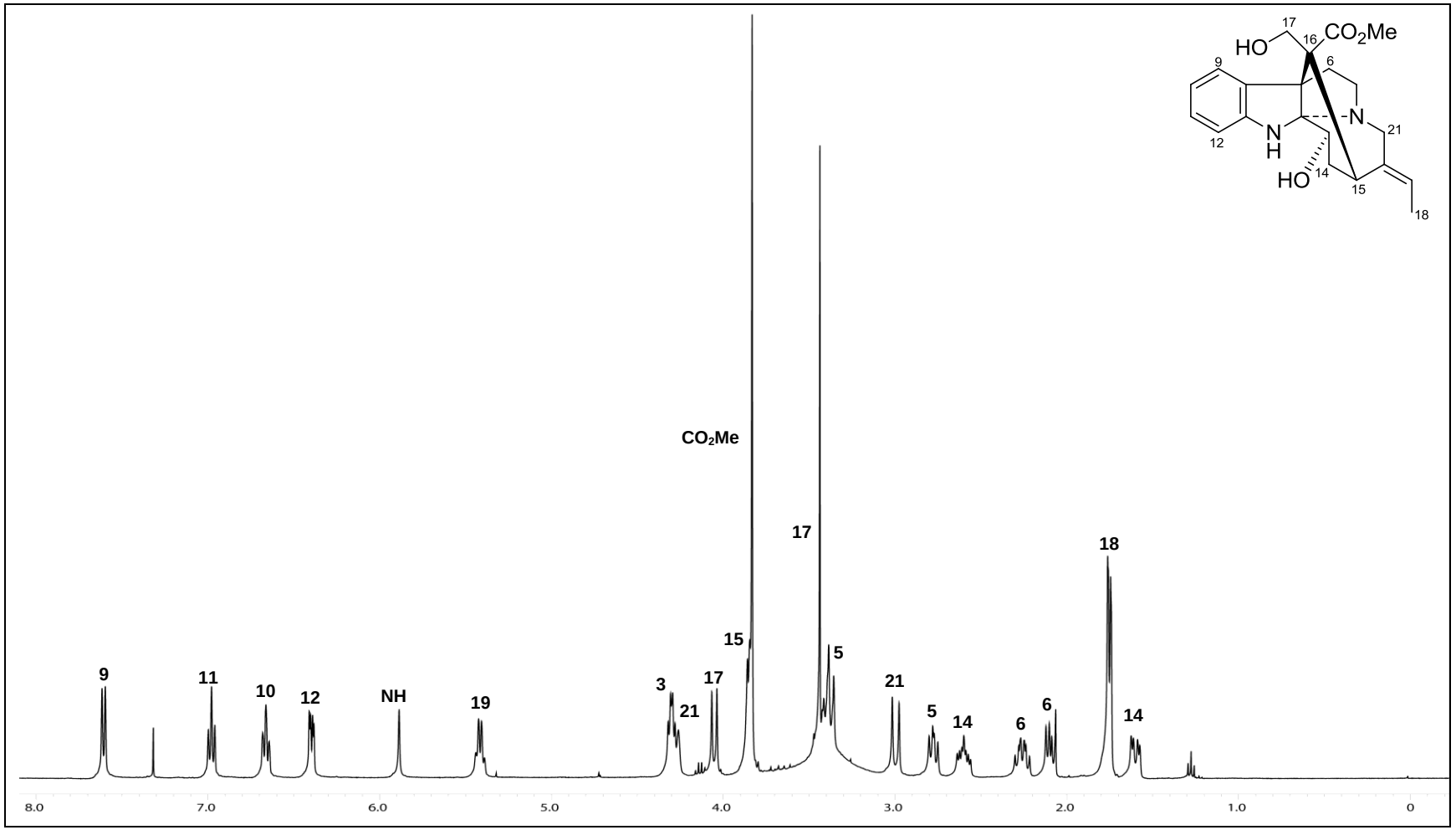


Figure 2.21. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of *N*(4)-Demethylechitamine (**14**)

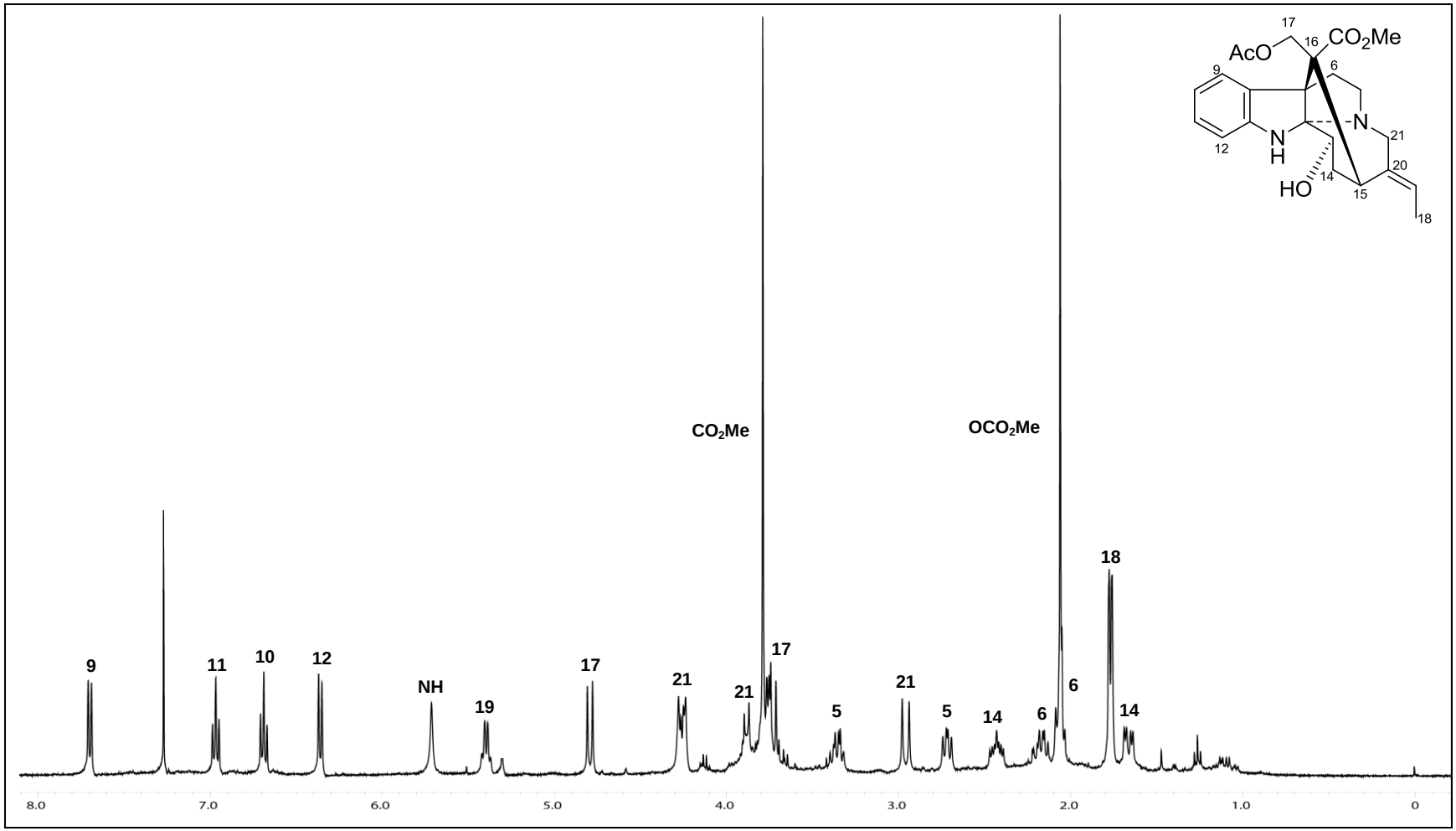


Figure 2.22. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of 17-*O*-Acetyl-*N*(4)-demethylchitamine (**15**)

Table 2.13. ^{1}H and ^{13}C NMR Data of Alstolucine B (**16**).[a]

Position	δ_H	δ_C
2	–	172.2
3	3.87 br t (3)	60.6
5	2.87 m	54.0
	3.05 m	
6	1.83 m	43.3
	3.04 m	
7	–	56.7
8	–	135.4
9	7.15 br d (8)	119.6
10	6.90 td (8, 1)	121.1
11	7.11 td (8, 1)	127.6
12	6.80 br d (8)	109.7
13	–	144.2
14	1.47 dt (13, 3)	31.7
	2.12 dt (13, 3)	
15	3.47 m	30.8
16	–	96.5
18	2.30 s	29.2
19	–	208.5
20	2.87 m	50.0
21	2.64 t (12)	45.6
	2.83 dd (12, 4)	
$CO_2\underline{Me}$	3.68 s	50.9
$\underline{CO_2}Me$	–	167.2
N-H	8.93 br s	–

[a]$CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC and HMBC.

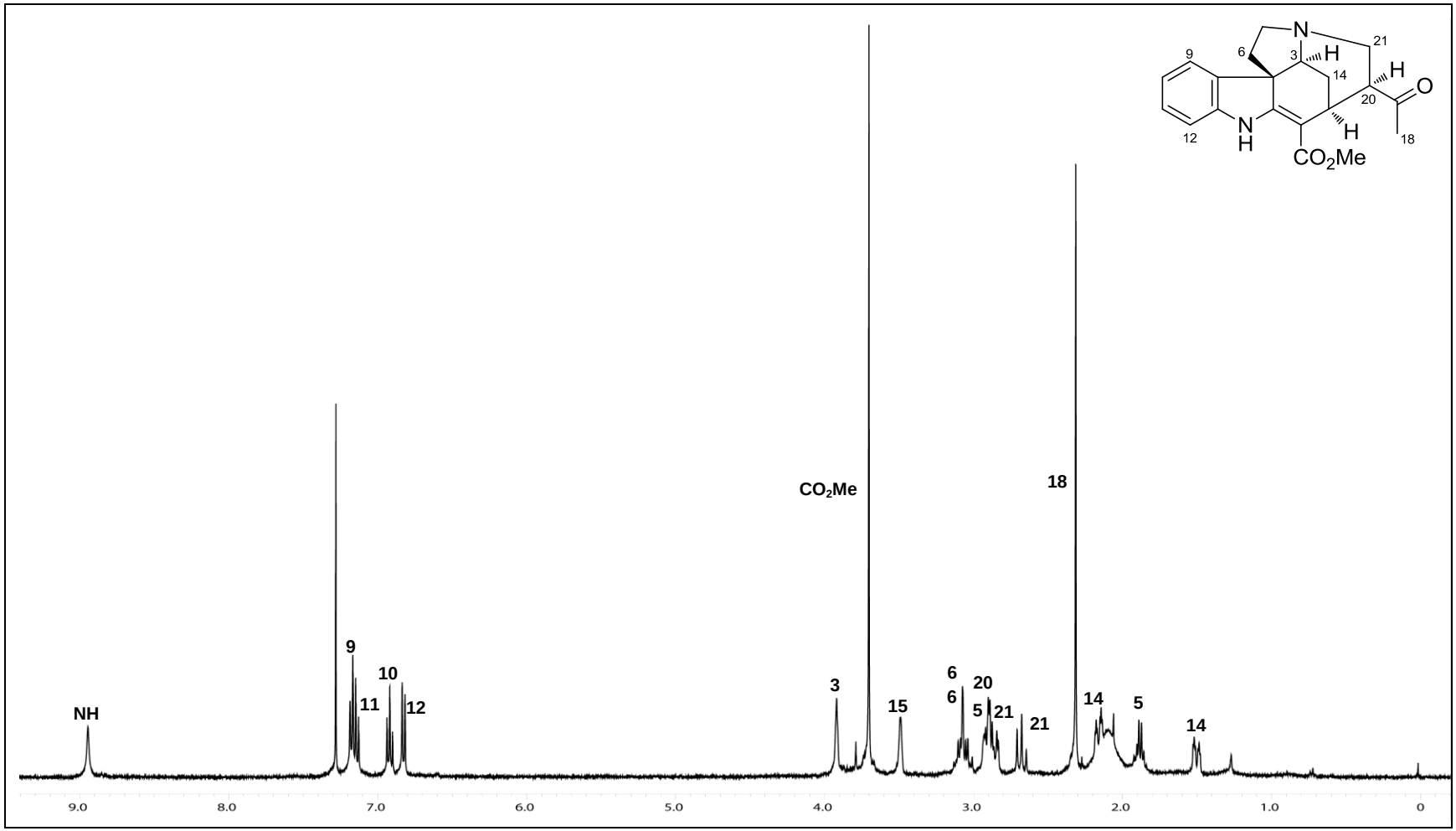


Figure 2.23. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Alstolucine B (**16**)

Table 2.14. ^{1}H and ^{13}C NMR Data of Vincamine (**17**).[a]

Position	**17**	
	δ_H	δ_C
2	–	127.8
3	2.73 t (11)	44.6
	3.02 m	
5	3.49 m	51.3
	3.61 m	
6	2.90 br d (11)	16.5
	3.02 m	
7	–	105.4
8	–	127.9
9	7.48 d (8)	118.9
10	7.17 m	121.2
11	7.15 m	123.2
12	7.09 d (8)	110.8
13	–	134.8
14	1.60 m	19.1
	2.02 br d (13)	
15	1.53 m	23.8
	1.75 t (14)	
16	–	81.7
17	2.23 br d (4)	43.8
	2.23 br d (4)	
18	0.94 t (8)	7.6
19	1.55 m	28.9
	2.50 q (7)	
20	–	35.7
21	4.26 br s	59.7
$CO_2\underline{Me}$	3.82 s	54.7
$\underline{CO_2}Me$	–	173.8

[a]$CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC and HMBC.

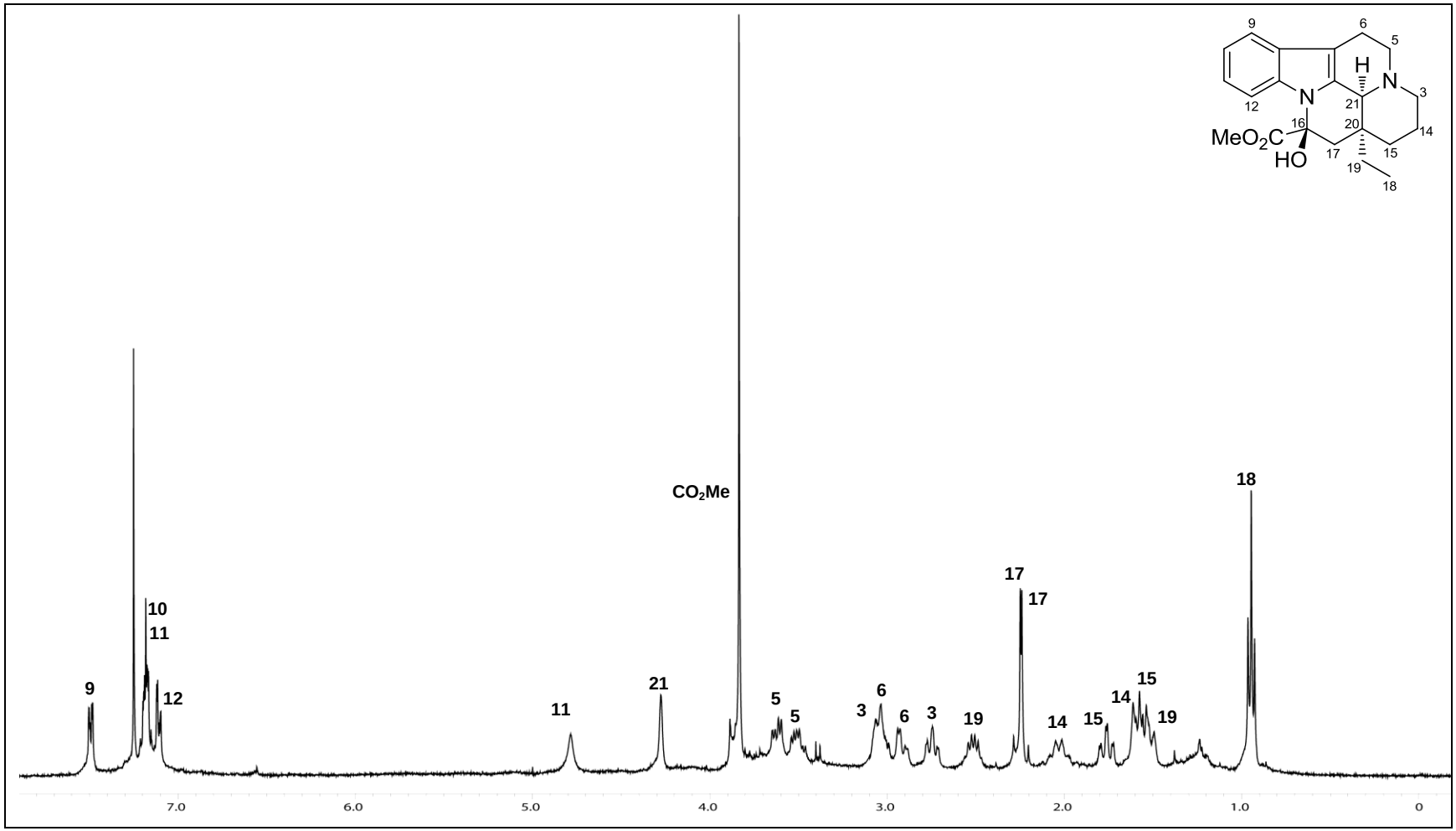


Figure 2.24. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Vincamine (**17**)

Table 2.15. ^{1}H and ^{13}C NMR Data of 16*R*,19*E*-Isositsirikine (**18**).[a]

Position	**18**	
	δ_H	δ_C
2	–	133.8
3	4.33 br s (11, 5)	52.8
5	3.15 m	51.3
	3.27 ddd (13, 6, 2)	
6	2.67 dd (16, 6)	17.7
	2.99 m	
7	–	107.7
8	–	127.6
9	7.47 br d (8)	118.0
10	7.10 td (8, 1)	119.5
11	7.16 td (8, 1)	121.6
12	7.39 br d (8)	111.3
13	–	136.2
14	2.24 m	30.2
	2.24 m	
15	3.15 m	32.6
16	2.52 ddd (11, 8, 5)	49.6
17	3.54 m	62.1
	3.54 m	
18	1.66 dd (7,2)	13.3
19	5.65 br q (7)	123.7
20	–	133.7
21	2.98 d (13)	52.5
	3.54 m	
CO_2Me	3.81 s	52.2
CO_2Me	–	175.4
N-H	8.81 s	–

[a]$CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC and HMBC.

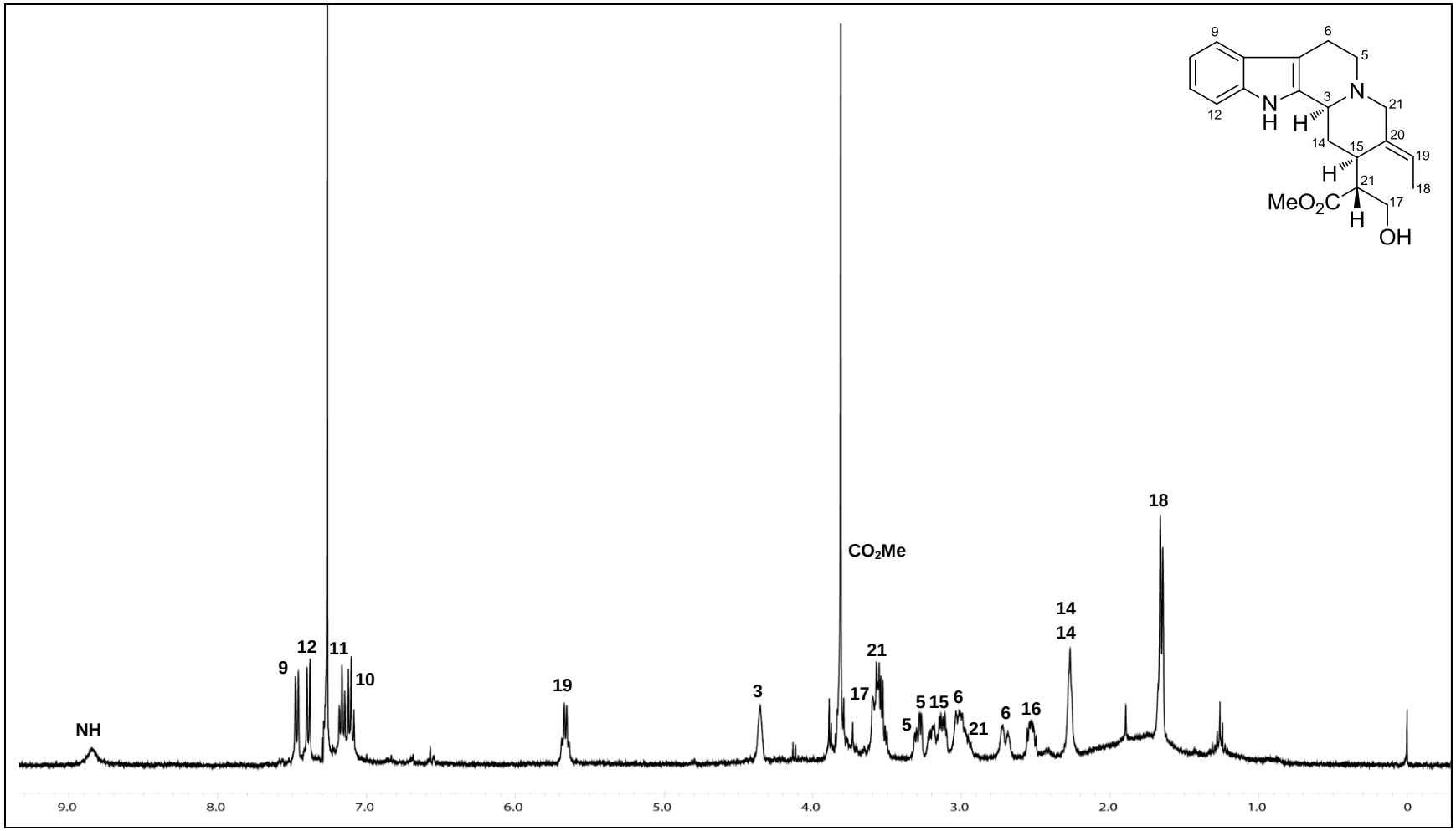


Figure 2.25. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of 16*R*,19*E*-Isositsirikine (**18**)

Table 2.16. ^{1}H and ^{13}C NMR Data of Venoterpine (**19**) and Cantleyine (**20**).[a]

Position	**19**		**20**	
	δ_H	δ_C	δ_H	δ_C
1	8.37 s	147.6	8.51 s	149.1
3	8.35 d (5)	145.1	8.99 d	147.8
4	7.18 d (5)	120.4	–	123.0
5	–	150.4	–	153.4
6	2.93 dd (17, 2)	40.9	3.37 dd (18, 5)	42.2
	3.12 dd (17, 5)		3.46 dd (18, 2)	
7	4.58 td (5, 2)	75.2	4.63 td (5, 2)	74.8
8	3.24 qd (7, 5)	42.7	3.26 qd (7, 5)	42. 5
9	–	141.9	–	–
7-OH	2.32 br s	–	2.07 br s	–
8-Me	1.39 d (7)	11.9	1.43 d (7)	11.8
$CO_2\underline{Me}$	–	–	3.94 s	52.1
$\underline{CO_2}Me$	–	–	–	166.0

[a]$CDCl_3$, 400 MHz (^{1}H), 100 MHz (^{13}C); assignments based on COSY, HMQC and HMBC.

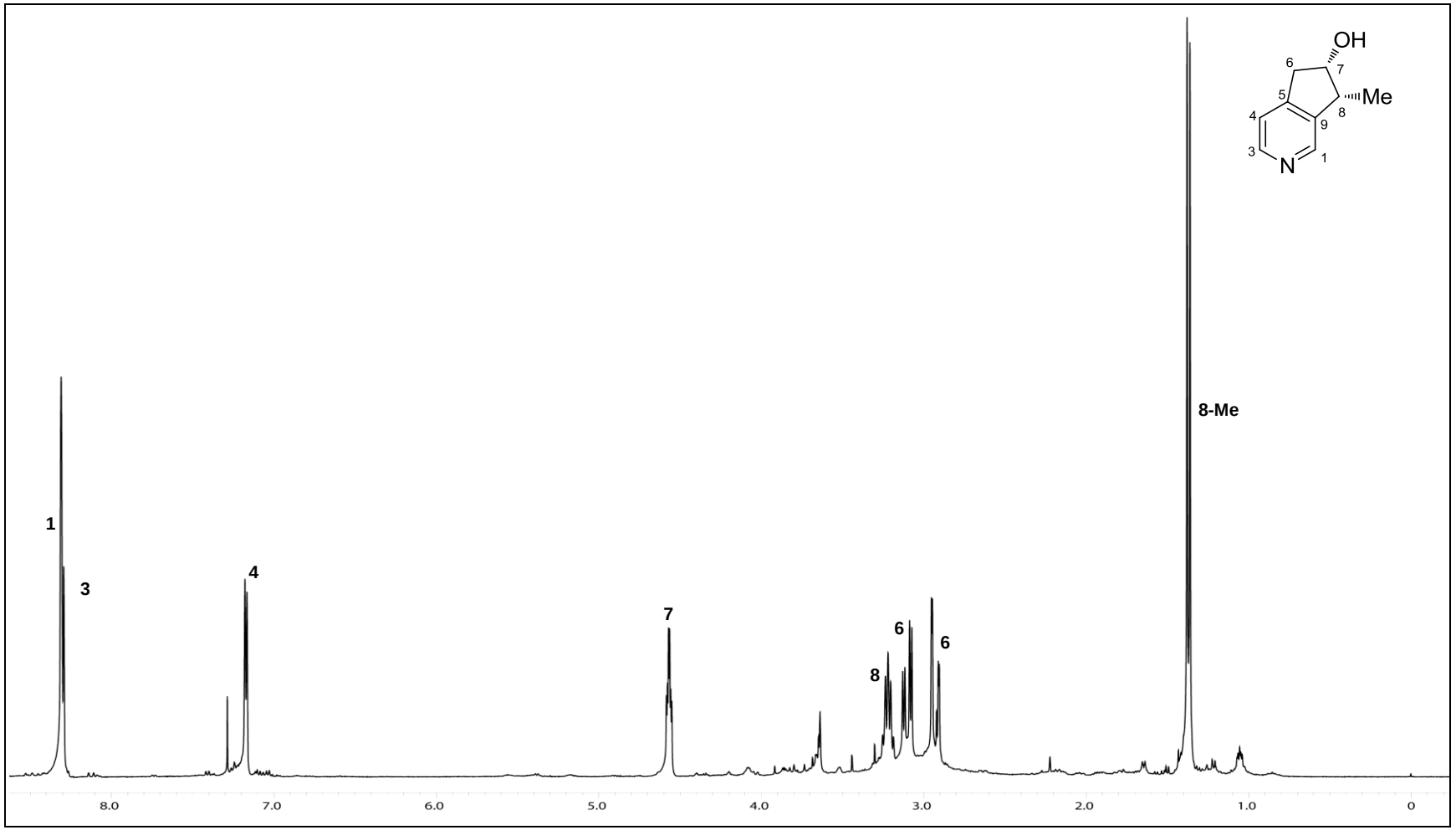


Figure 2.26. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Venoterpine (**19**)

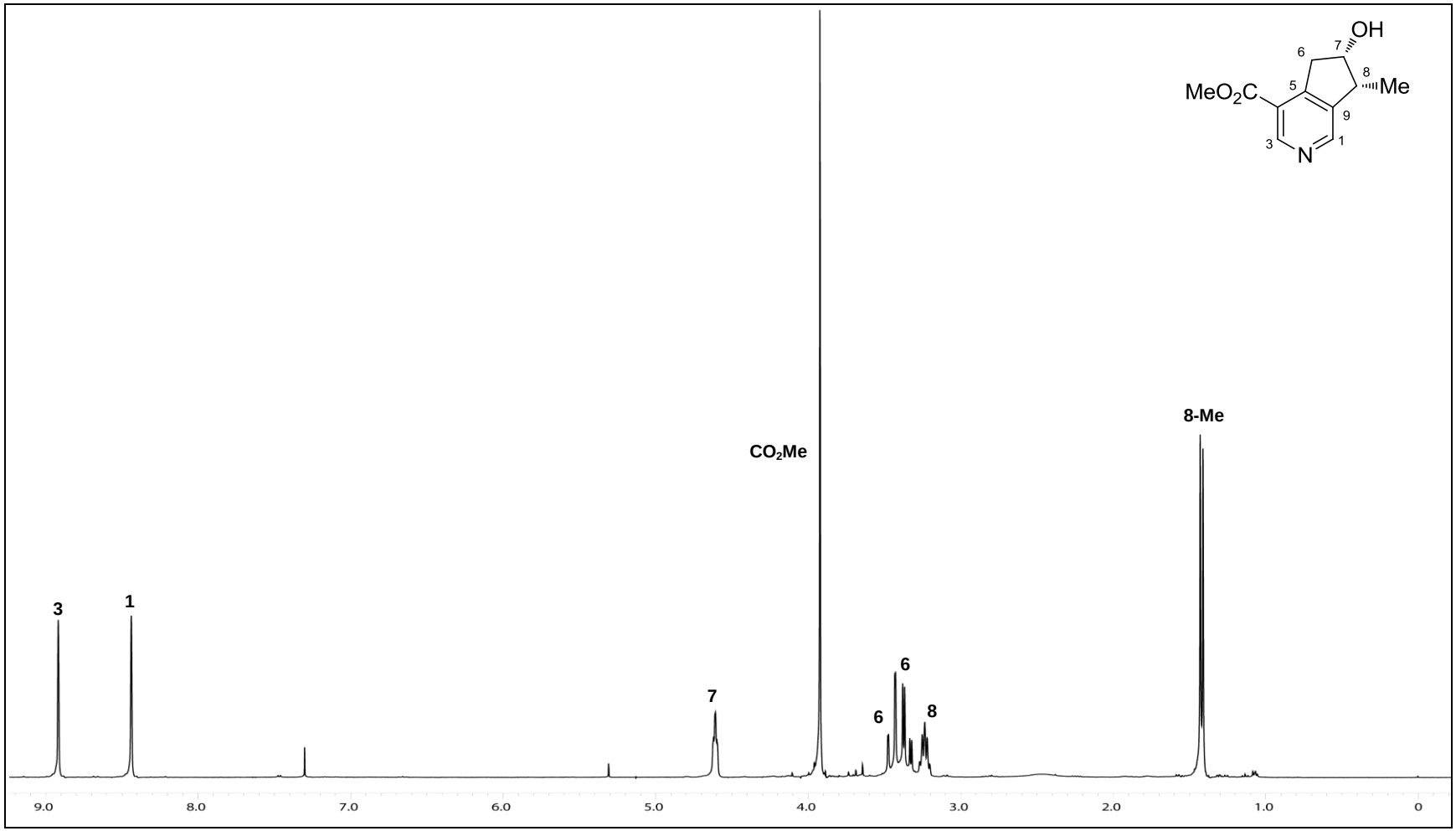


Figure 2.27. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz) of Cantleyine (**20**)

2.2 Biological Activity

2.2.1 Cytotoxicity and Reversal of Multidrug Resistance (MDR)

Alkaloids have been known to possess various pharmacological effects. In addition to the systematic chemical investigations, pure compounds isolated from the present study were screened for their cytotoxic effects and also for their potential in reversing multidrug resistance (MDR) in vincristine-resistant KB cells. KB refers to the human oral epidermoid carcinoma cell lines. This part of work was carried out by Dr. K. Komiyama and his associates at the Kitasato Institute, Tokyo, Japan. The compounds were tested at an initial concentration of 25 μg/mL and IC_{50} values were then determined for the more active compounds and the results are summarized in Table 2.17.

Angustilobine C (**1**), 17-*O*-acetylvallesamine (**5**), angustilobine A (**7**), and condylocarpine (**12**) showed moderate cytotoxicity towards both vincristine-sensitive and vincristine-resistant KB cells, while andransinine (**2**), and alstolucine B (**16**) showed appreciable activity in reversal of multidrug resistance.

Table 2.17. Cytotoxic Effects of Alkaloids From *A. angustiloba* Miq. against KB cells.

Compound	IC_{50}, μg/mL		
	KB/S	**KB/VJ300 VCR (–)**	**KB/VJ300 VCR (+)**
Angustilobine C (**1**)	10.34	11.85	10.74
Andransinine (**2**)	>25	>25	1.61
19,20-*E*-Vallesamine (**4**)	>25	>25	18.99
17-*O*-Acetylvallesamine (**5**)	3.5	3.4	1.5
Angustilobine A (**7**)	5.23	9.69	7.43
Nor-6,7-*Seco*angustilobine B (**9**)	>25	>25	>25
Nor-6,7-*Seco*-19,20α-epoxyangustilobine B (**10**)	>25	>25	>25
Undulifoline (**11**)	>25	>25	>25
Condylocarpine (**12**)	5.53	9.60	1.39

Table 2.17 continued

20*S*-Tubotaiwine (**13**)	21	>25	5.1
Alstolucine B (**16**)	>25	>25	0.64

KB/S – vincristine-sensitive human oral epidermoid carcinoma cell line.
KB/VJ300 – vincristine-resistant human oral epidermoid carcinoma cell line.
VCR (+) – with added vincristine, 0.1 μg/mL (0.12 mM) which did not affect the growth of the KB/VJ300 cells.
VCR (–) – without added vincristine.