A REINVESTIGATION OF THE STEREOCHEMISTRY OF TUBOTAIWINE USING NMR SPECTROSCOPY[1]

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ABSTRACT.—The stereochemistry of tubotaiwine has been reinvestigated by nOe-meas-
urements, ^{13}C-H coupling constants, and protonation shifts. It was proved that C-20 of
tubotaiwine has the S configuration. The reported isolations of tubotaiwine and dihydrocon-
dylocarpine were evaluated. Most of these appeared to concern tubotaiwine, identical to our
sample. No indication for the existence of 20R-19,20-dihydrocondylocarpine was found.

Tubotaiwine, synonymous with dihydrocondylocarpine, was isolated for the first
time from *Pleiocarpa tubicina* Stapf. Since then, it has been found in a large number of
other species, and in recent years it has also been isolated from several cell-cultures.

The isolations, reported in the literature, are listed in Table 1 (1-42, 62, 64). As
can be seen, tubotaiwine occurs in all four alkaloid-containing tribes of the
Apocynaceae (46). Apart from the Apocynaceae, it was only found in two *Strychnos*
species, belonging to the closely related Loganiaceae family. As indicated in Table 1, in
the literature two structures are given for tubotaiwine, **1** and **2**, differing in the
stereochemistry of C-20. This, however, does not reflect the existence of 20-*epi*-
tubotaiwine, because almost certainly in all cases the same compound was meant. 20-
epi-Tubotaiwine should be clearly distinguishable from tubotaiwine (47). Catalytic hy-
drogenation of condylocarpine [**9**] yields only one of the two possible isomers (1).

Only one study, by Schumann and Schmid in 1963 (1), concerned the
stereochemistry of C-20. Structure **1** as proposed by them is almost entirely based on
chemical evidence. A few melting points, optical rotations, albeit in different solvents,
and uv and ir spectra were recorded as well. This is one of the weak points of the struc-
tural proof for tubotaiwine. None of the initial, intermediate, or end products was di-
rectly characterized by more modern methods of analysis such as ^{1}H nmr, ^{13}C nmr, ms,
and cd. Even if one assumes all products to have been correctly identified, a close study
of the reasoning which led to the proposed structure **1** reveals a weak point in the evi-
dence. For convenience, the most important experiments carried out by Schumann and
Schmid are briefly summarized and discussed as follows: (1) When tubotaiwine was
heated with 3 N HCl in vacuo at 115-120° for 1.5 h, 93% crude condyfoline [**3**] was re-
covered. No data are given about the final purity or the identity of the other 7%. (2)
When condyfoline [**3**] was submitted to the same treatment, no isomerization could be

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TABLE 1.　Reported Isolations of Tubotaiwine

Species[a]	Family[m]	Tribe[n]	Configuration C-20		References
			reported	actual[o]	
Aspidosperma limae	A	P	S	n.d.	1,2
Pleiocarpa tubicina	A	C	S	n.d.	1,3
Vallesia dichotoma	A	R	S	(S)	4
Amsonia tabernaemontana	A	P		S	5
Tabernaemontana stapfiana[b]	A	T	R	n.d.	6
Tabernaemontana mauritiana[c]	A	T		S	7
Tabernaemontana eusepala[d]	A	T		S	8
Alstonia quaternata	A	P	R	S	9
Tabernaemontana minutiflora[e]	A	T		S	10
Alstonia scholaris	A	P	R/S	n.d./S	11,12,62
Vallesia antillana	A	R		n.d.	13
Melodinus aeneus	A	C	S	n.d.	14
Strychnos angolensis	L	S	R	S	15
Stemmadenia glabra	A	T	R	n.d.	16
Catharanthus ovalis	A	P	R	S	17
Tabernaemontana mocquerysii[f]	A	T		S	18
Strempeliopsis strempelioides	A	P		n.d.	19,33
Tabernaemontana amblyocarpa	A	T		n.d	20
Tabernaemontana beyneana[g]	A	T		(S)	21
Tabernaemontana attenuata[h]	A	T	R	S	22
Tabernaemontana psychotrifolia[i]	A	T	R	S	23
Strychnos dolichothyrsa	L	S	R	S	24
Hunteria zeylanica	A	C		S	25
Pterotaberna inconspicua	A	T		S	26
Tabernaemontana eglandulosa	A	T	R	S	27
Alstonia sphaerocapitata	A	P		S	28
Tabernaemontana pachysiphon	A	R	R	S	29
Tabernaemontana humblotii[j]	A	T		S	30
Tabernaemontana siphilitica[k]	A	T	R	S	31,32
Kopsia hainanensis	A	R		n.d.	34
Tabernaemontana africana[l]	A	T		S	35
Tabernaemontana elegans	A	T		S	36
Tabernaemontana dichotoma	A	T		S	37
Tabernaemontana ventricosa	A	T		S	38
Tabernaemontana divaricata	A	T	S	S	62[q]
Alstonia angustiloba	A	P		S	64
Alstonia pneumatophora	A	P		S	64

Cell cultures	Sort[p]					
Stemmadenia tomentosa	S	A	T	R	S	39
Tabernaemontana divaricata	S	A	T		S	40
Tabernanthe iboga	S	A	T		S	40
Catharanthus roseus	C	A	P		S	41
Tabernaemontana elegans	C	A	T		S	42

[a]The current botanical name of the species is given, according to revisions by Leeuwenberg (43-45). The name under which the article was published, is given below.

[b]Conopharyngia johnstonii, [c]Pandaca mauritiana, [d]Pandaca eusepala, [e]Pandaca minutiflora, [f]Pandaca boiteaui, [g]Ervatamia beyneana, [h]Anartia cf meyeri, [i]Peschiera echinata, [j]Pandaca ochrascens, [k]Bonafousia tetrastachya, [l]Tabernaemontana chippii.

[m]A=Apocynaceae; L=Loganiaceae.

[n]C=Carisseae; P=Plumerieae; T=Tabernaemontaneae; R=Rauvolfieae; S=Strychneae.

[o]S=Certainly 20S, determined by direct comparison with our sample, which was identical to previous isolations of tubotaiwine in our laboratories. Originally, these had been identified with the aid of an authentic sample from Prof. P. Potier (Gif-sur-Yvette). Our sample has also been compared directly with samples from Prof. L. Le Men-Olivier and Dr. G. Massiot (Reims) and from Dr. J. Stöckigt (München). (S)=most probably 20S, on the basis of reported data (especially ¹H nmr). n.d.=not determinable.

[p]S=suspension culture; C=callus culture.

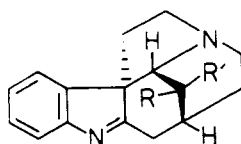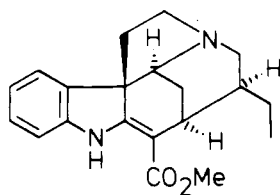[q]Unpublished results, T.A. van Beek.
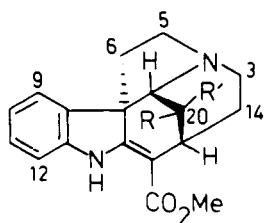
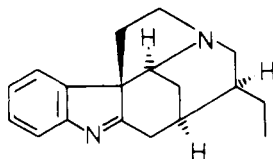1   R=C$_2$H$_5$, R'=H   tubotaiwine (20 S)
2   R=H, R'=C$_2$H$_5$ (20 R)
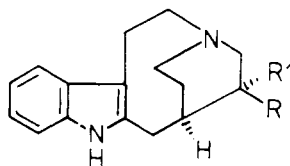
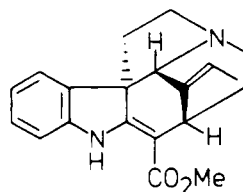6   R=C$_2$H$_5$, R'=H
7   R=H, R'=C$_2$H$_5$

3   R=C$_2$H$_5$, R'=H   condyfoline
4   R=H, R'=C$_2$H$_5$ 20-*epi*-condyfoline

8   19,20-dihydroakuammicine

5   tubifoline
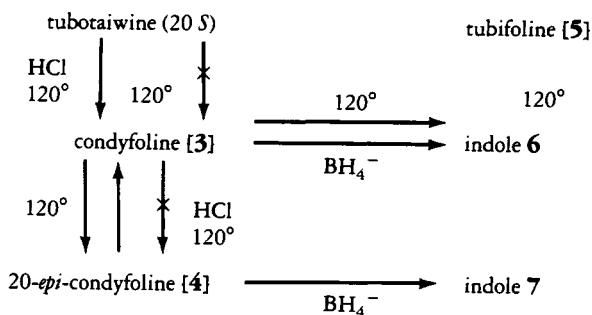
9   condylocarpine

observed. (3) Condyfoline [3] heated in vacuo without HCl at 117-120° for 3 h was partly converted to 20-*epi*-condyfoline [4] and tubifoline [5]. (4) 20-*epi*-Condyfoline [4] submitted to this treatment was partly converted to condyfoline [3] and tubifoline [5].

The C-20 stereochemistry of 3 and 4 was determined by NaBH$_4$ reduction to the corresponding indoles 6 and 7. Indole 6 was also obtained by NaBH$_4$ reduction of tubifoline [5]. In a separate study (48) tubifoline was shown to have the same C-20 stereochemistry as 19,20-dihydro-akuammicine (20 R). The C-20 stereochemistry of 6 was, thus, correlated with the known stereochemistry of 19,20-dihydroakuammicine. These facts, which are summarized in Scheme 1, led Schumann and Schmid to propose structure 1 for tubotaiwine.

Although this reasoning is not necessarily incorrect, we feel that at the same time it also proves little, as the data can also be interpreted in another way. This alternative explanation is depicted in Scheme 2. The fact that 3 is not converted to 4 in HCl at 120° can be explained by a non-equilibrium situation (no reaction) under these conditions, but it can be equally well explained by the fact that 3 is more stable than 4 under these conditions (equilibrium). An interesting experiment which might have distinguished between these two possibilities is the heating of 4 in HCl. If only 20-*epi*-condyfoline [4] would have been recovered, this would have proved the correctness of the reasoning of

tubotaiwine (20 S)   tubifoline [5]

HCl
120°   │ │   ✗ │   120°   120°
        ▼ ▼   ▼   ─────────────────────▶
        condyfoline [3] ═══════════════════▶ indole 6
                              BH₄⁻

120° │ ▲ │ ✗ │ HCl
      ▼ │ ▼   ▼ 120°

20-*epi*-condyfoline [4]   ─────────────────────▶ indole 7
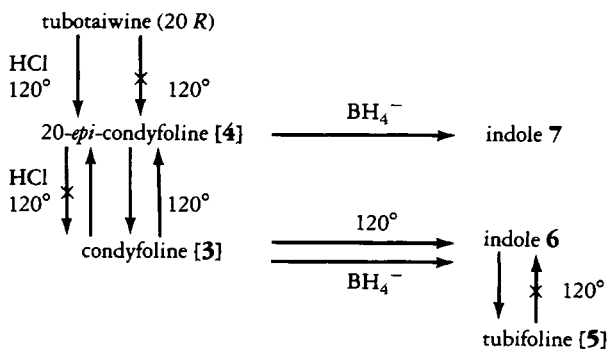   BH₄⁻

SCHEME 1.

Schumann and Schmid, and structure **1** would be the correct structure for tubotaiwine, assuming that all products were correctly identified, of course.

If, however, condyfoline [**3**] had been found as the major product, both explanations would still be possible. Regrettably, such an experiment has not been reported, which makes a definite interpretation of these chemical data impossible in our opinion.

Obviously, Schmid also began to have some doubts about his own experiments, for a few years later, without an explanation, he gave the opposite stereochemistry for tubotaiwine in another publication (6), and subsequently structure **2** has almost exclusively been given for tubotaiwine—to our knowledge without any underlying evidence. Recently, Husson in reviewing *Strychnos* and closely related alkaloids also mentioned that according to him the stereochemistry of tubotaiwine had never been satisfactorily solved (49).

So there has been a lot of confusion and a thorough investigation of the stereochemistry of tubotaiwine was needed to remove all uncertainties.

Two publications on this subject appeared when this publication was first submitted. Atta-ur-Rahman (62) reported on the stereochemistry of 19,20-dihydrocondylocarpine isolated from *Ervatamia coronaria* [=*Tabernaemontana divaricata* (43)] and *Alstonia scholaris*. The compound was reported not to be identical with tubotaiwine, however, the stereochemistry of C-20 was concluded to be *S*, i.e., the same as originally reported for tubotaiwine (1). The proof, however, is doubtful, e.g., nOes between H-20 and both H-3α and H-3β are impossible according to a model. Lounasmaa (63) reported a 20 *S* configuration for his sample of tubotaiwine. The evidence was mainly based on a cross peak of H-20 with H-14β in the 2D-NOESY spectrum. A cross peak of H-18 with H-14, that was at least equally strong and could prove the opposite configuration, was not commented upon. In both publications several ¹H- and ¹³C-nmr assignments are erroneous.

tubotaiwine (20 R)

HCl
120°   │   ✗ │ 120°
        ▼   ▼   BH₄⁻
        20-*epi*-condyfoline [4]   ─────────────────────▶ indole 7

HCl   ✗ │ │   │ 120°
120°   ▼ ▼   ▼

        condyfoline [3]   ═══════════════════▶ indole 6
                                    BH₄⁻   │ ✗ ▲ 120°
                                                            ▼   │

                                                    tubifoline [5]

SCHEME 2.

RESULTS AND DISCUSSION

For the determination of the stereochemistry of C-20 the most logical approach is the detection of nOe's. However, first of all complete assignment of the ^{1}H-nmr spectra was necessary. This was achieved with 2D-COSY spectra and by analysis of coupling constants. Due to overlapping signals, not all coupling constants could be determined directly from the spectra. In order to obtain resolution of overlapping signals, initially several solvents were tried, but better results were obtained with CF_3COOH as a shift reagent (50), e.g., the two H-14 protons were separated for the first time (see below).

For the assignment of the aromatic signals, some 1D-nOe difference measurements were performed (Table 2). Irradiation of NH gave an enhancement of the most upfield

TABLE 2.   Results of Several 1 D-nOe Difference Measurements

Proton irradiated	nOe
NH	H-12
H-12	NH, H-11
H-21	H-9, H-5a, H-20, H-19, H-18
H-3b	H-3a, H-6a, H-14b(?)
H-15	H-14a/b, H-18, H-19, H-20
H-20	H-15, H-18, H-19, H-21
H-18	H-9, H-15, H-19, H-20, H-21, NH
H-19	H-9, NH, H-15, H-18, H-20, H-21

aromatic signal. This was, thus, assigned to H-12. Irradiation of H-12 gave an enhancement of the NH signal and of the most downfield aromatic triplet, which was assigned to H-11. Finally, irradiation of H-21 gave an enhancement of the other aromatic doublet, which was assigned to H-9. The ^{1}H-nmr data are given in Table 3.

Interpretation of the coupling constants showed the structure and stereochemistry of tubotaiwine, with the exception of the side-chain of C-20, to be identical to the one

TABLE 3. ^{1}H-nmr Spectra Tubotaiwine

Proton	δ (ppm)		J (Hz)	
	CDCl$_3$	C$_6$D$_6$		
NH	8.85	9.26	bs	
H-9	7.14	6.85	d	7.8 (10)
H-10	6.88	6.73	dd	7.8 (9), 7.8 (11)
H-11	7.10	6.88	dd	7.8 (10), 7.8 (12)
H-12	6.80	6.29	d	7.8 (11)
CO$_2$Me	3.77	3.52	s	
H-3a	2.97	2.83	ddd	12.4 (3b), 5.6 (14a), 3.0 (14b)
H-3b	2.46	2.26	ddd	12.4 (3a), 12.5 (14a), 5.6 (14b)
H-5a	3.04	2.81	ddd	11.9 (5b), 11.9 (6a), 8.0 (6b)
H-5b	2.85	2.44	ddd	11.9 (5a), 7.8 (6a), 1.5 (6b)
H-6a	2.88	2.70	ddd	14.2 (6b), 11.9 (5a), 7.8 (5b)
H-6b	1.79	1.56	ddd	14.2 (6a), 8.0 (5a), 1.5 (5b)
H-14a	1.79	1.80	dddd	14.8 (14b), 5.6 (3a), 12.5 (3b), 4.6 (15)
H-14b	1.79	1.80	dddd	14.8 (14a), 3.0 (3a), 5.6 (3b), 2.7 (15)
H-15	3.05	3.16	dddd	4.6 (14a), 2.7 (14b), 2.0 (20), 1.5 (21)
H-18	0.70	0.60	t	7.1 (19)
H-19	0.82	0.81	qd	7.1 (18), 7.0 (20)
H-20	1.97	1.95	tdd	7.0 (19), 3.2 (21), 2.0 (15)
H-21	3.81	3.74	dd	3.2 (20), 1.5 (15)

determined for the borine adduct of condylocarpine [9] by X-ray analysis (51). The stereochemistry of C-20 cannot be determined by interpretation of ^{1}H-^{1}H coupling constants, because H-15, C-20, and H-21 lie in one plane, bisecting the C-19, C-20, H-20 angle, so again 1D-nOe difference measurements were performed. Both H-18 and H-19 gave upon irradiation an enhancement of the signal assigned to H-9 and a slight enhancement of the NH signal (Figure 1). These nOes can only be explained when tubotaiwine has the 20 S configuration as depicted in Figure 2.
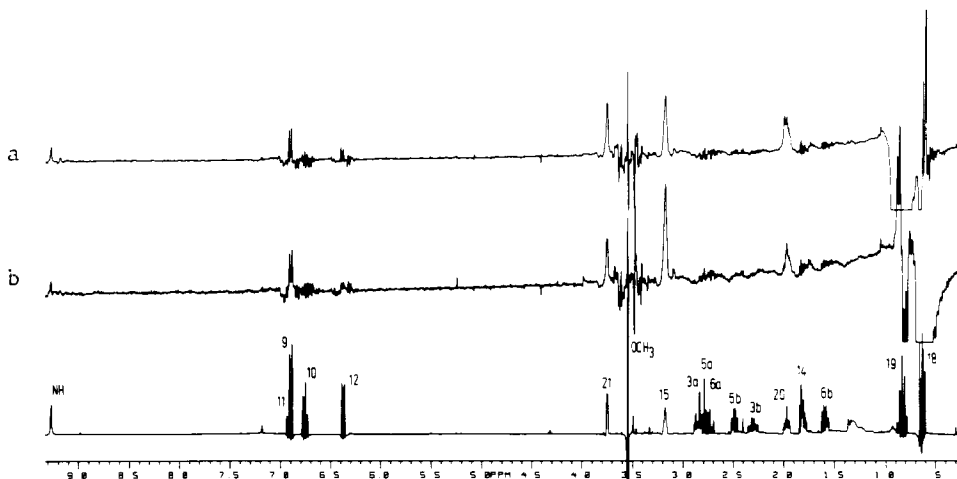
FIGURE 1.   NOe-difference spectra of tubotaiwine (C_6D_6): **a**. irradiated at H-19; **b**. irradiated at H-18

H-20 was also irradiated, but no nOe was observed that could differentiate between the 20 S and the 20 R configuration. The expected enhancement of H-14a could not be detected because the chemical shifts only differed by 0.15 ppm. 2D-NOESY, although less sensitive, is better suited for the detection of such nOes, and, indeed, in the 2D-NOESY spectrum (Figure 3) an nOe was observed between H-20 and H-14. Thus, the nOe measurements showed tubotaiwine to have to 20 S configuration, the same stereochemistry as was originally proposed by Schumann and Schmid (1).

In order to obtain additional proof for the 20 S configuration of tubotaiwine, several other methods were employed. Beside ^{1}H-^{1}H coupling constants, ^{13}C-^{1}H coupling constants can be valuable in solving stereochemical problems. Especially $^3J_{CH}$ seems very interesting because just as for $^3J_{HH}$ a Karplus relation holds (52). In the case of an *anti* conformation, $^3J_{CH}$ is expected to be about 8 Hz, while in the case of a *gauche* con-
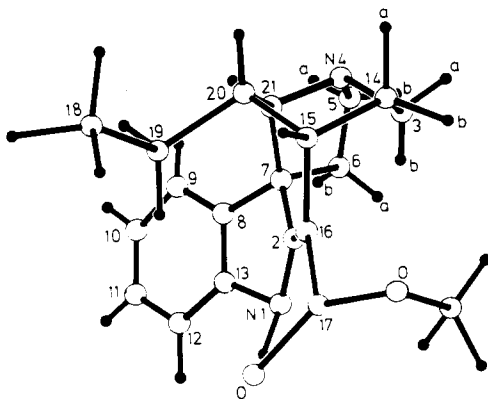

FIGURE 2.   Stereochemistry of tubotaiwine

FIGURE 3.   NOESY-spectrum of tubotaiwine (C_6D_6)

formation $^3J_{CH}$ is only about 2 Hz. Therefore, the C-20 stereochemistry of tubotaiwine should be clearly recognizable from the coupling constants of H-20 with C-7, C-16, and C-14.

Long-range ^{13}C-J resolved 2D-nmr (LRJR) as reported by Bax (53) is intended to observe, selectively, the ^{13}C-^1H long-range couplings of carbons with a specific proton. However, in this case the desired results could not be obtained because of the overlap of the proton signals of interest. Instead, a gated decoupled ^{13}C-nmr spectrum was recorded. In this spectrum all ^{13}C-^1H couplings are present. To verify the assignment of the ^{13}C spectrum by Urrea (54), a CH correlation 2D spectrum was recorded. The assignment of C-3 and C-6 and of C-9 and C-10 had to be interchanged (Table 4). In the gated decoupled ^{13}C spectrum the signals of C-7, C-14, and C-16 were observed. Owing to the large number of couplings present, the signal of C-7 appeared as a complex multiplet from which no indication about the coupling to H-20 could be obtained. The signal of C-14 displayed three couplings: the very large $^1J_{CH}$ of 129 Hz and two small couplings, one of 3 Hz and one of 4 Hz, owing to two-bond ^{13}C-^1H coupling. The absence of a coupling > 6 Hz ruled out the 20 R configuration.

Finally, the signal of C-16 appeared as some kind of pentet, indicating the presence of four couplings: three of 6-7 Hz and one of about 4 Hz. Four couplings were expected; the smallest coupling with H-14b because it is in a *gauche* position. The three remaining couplings with H-20, H-15, and H-14a are, thus, 6-7 Hz each. This large coupling to H-20 also proves the 20 S configuration.

Another method we studied to elucidate the C-20 stereochemistry of tubotaiwine was the application of CF_3COOH as a shift reagent in ^1H-nmr spectroscopy (50). The

TABLE 4. ^{13}C-nmr Spectrum Tubotaiwine (CDCl$_3$)^a

C-2	170.6 s	C-13	143.6 s
C-3	45.2 t	C-14	28.4 t
C-5	53.9 t	C-15	30.9 d
C-6	43.9 t	C-16	95.5 s
C-7	55.0 s	C-18	11.5 q
C-8	137.1 s	C-19	23.8 t
C-9	119.5 d	C-20	41.2 d
C-10	120.9 d	C-21	65.5 d
C-11	127.0 d	C=O	168.8 s
C-12	109.6 d	OCH$_3$	51.0 q

^{a}Splitting pattern in the gated decoupled spectrum: s=singlet; d=doublet; t=triplet; q=quartet.

reason was that we assumed an alkaloid isolated from *Tabernaemontana divaricata* (T.A. van Beek, unpublished results) to be 20-*epi*-tubotaiwine, and CF$_3$COOH shifts seemed suitable for determining the stereochemistry of both compounds. The same alkaloid had previously been isolated from *Tabernaemontana dichotoma* and had been reported as a new alkaloid with an unknown structure (37).

However, addition of CF$_3$COOH to a tubotaiwine solution in CDCl$_3$ revealed that the unknown compound was most likely tubotaiwine containing some sort of acidic impurity, because identical ^{1}H-nmr spectra were obtained upon addition of about 0.4 equivalents of CF$_3$COOH. Indeed, after an additional purification of the unknown compound by an acid-base extraction, pure tubotaiwine was obtained identical in all respects to the reference compound.[4] The change of the ms upon acidification remains unexplained (37).

Although there was only one stereo isomer, the effect of protonation was studied in greater detail. CF$_3$COOH was added stepwise (see Figure 4), and the protonation shifts were determined graphically (Figure 5). The protonation shifts were determined both
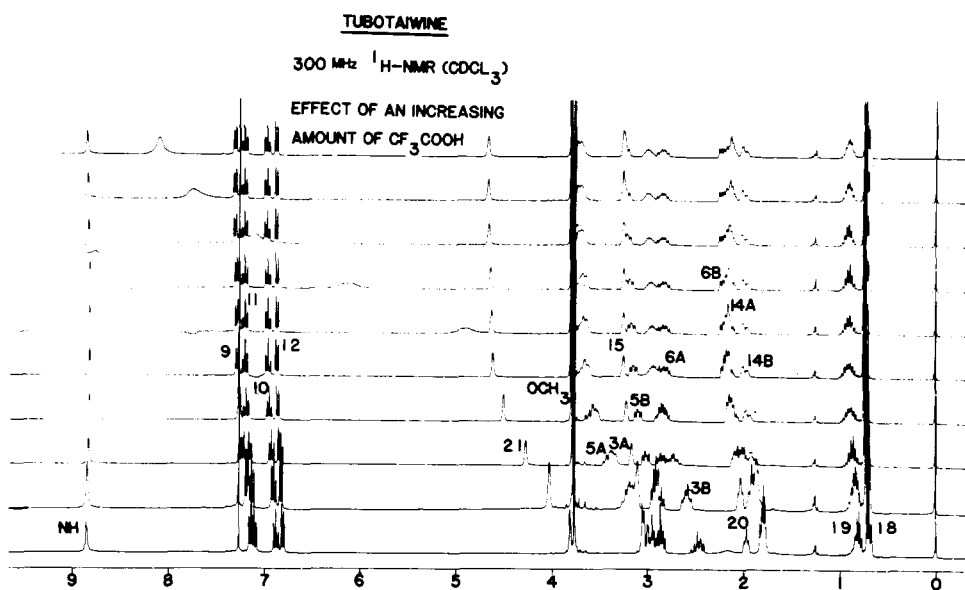

FIGURE 4. ^{1}H-nmr spectra of tubotaiwine with an increasing amount of CF$_3$COOH added (CDCl$_3$)

[4]The ^{1}H- and ^{13}C-nmr data reported for 19,20-dihydrocondylocarpine by Attu-ur-Rahman *et al.* (62) in fact correspond to tubotaiwine containing 0.2 equivalent of an acidic impurity.
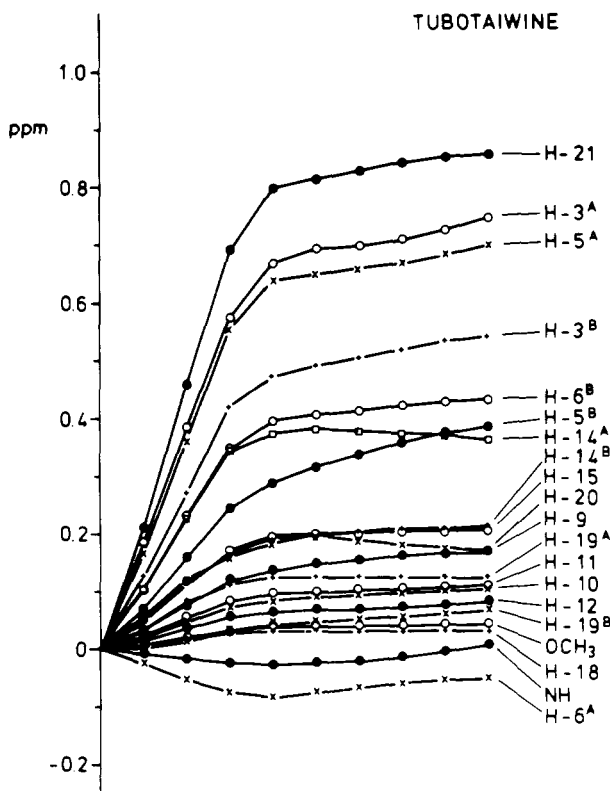
FIGURE 5.   Relation between changes in chemical shifts of the protons in tubotaiwine and the amount of CF₃COOH added (CDCl₃)

in CDCl$_3$ and in C$_6$D$_6$. The interesting observation was made that in CDCl$_3$ the majority of protonation shifts was downfield, while in C$_6$D$_6$ the majority was upfield. This can be explained by the shielding anisotropy and the tendency of C$_6$D$_6$ to form π-complexes. Under the influence of the positive charge on the protonated nitrogen, the C$_6$D$_6$ molecules direct themselves with the shielding zone towards the nitrogen, causing the so-called extra solvent-shift. So from the experiments the following data were obtained for every proton (Table 5): (1) protonation shift in CDCl$_3$ (=A), (2) protonation shift in C$_6$D$_6$ (=B), (3) extra solvent-shift upon protonation in C$_6$D$_6$ (=B-A). The protonation shifts in CDCl$_3$ are expected to be the most indicative of the stereochemistry around the protonated nitrogen because, as explained above, the protonation shifts in C$_6$D$_6$ are the result of two usually opposing effects. In CDCl$_3$ the protons attached to the carbons next to the protonated nitrogen show the largest shifts (Figure 5).

The NH proton displays a very small upfield shift. This indicates the presence of three carbons between both nitrogens in the molecule (50). The shifts of the protons of the ethyl side-chain are as small as those of the aromatic protons, indicating their remoteness from the protonated nitrogen, and, thus, also indicating the 20 *S* configuration for tubotaiwine.

As outlined above, the protonation shifts in C$_6$D$_6$ are not interpretable right away. The extra solvent-shift as deduced from these shifts gives some information about the arrangement of the C$_6$D$_6$ molecules around the molecule. Some correlation is expected between the protonation shifts in CDCl$_3$ and the extra solvent-shifts and such correlation is indeed seen (Figure 6). Some protons, however, show a large deviation. For H-21 and H-5a a smaller extra solvent-shift is observed, as was expected. This can be

TABLE 5.   Protonation Shifts and Extra Solvent Shift[a]

Proton	Protonation shift (ppm)		Extra solvent shift (ppm)
	CDCl$_3$	in C$_6$D$_6$	
NH	−0.03	−0.36	−0.34
H-9	+0.14	+0.05	−0.08
H-10	+0.09	−0.06	−0.14
H-11	+0.10	−0.06	−0.16
H-12	+0.07	−0.12	−0.19
OCH$_3$	+0.04	−0.08	−0.12
H-3a	+0.67	−0.04	−0.71
H-3b	+0.47	−0.47	−0.94
H-5a	+0.64	+0.25	−0.39
H-5b	+0.29	−0.42	−0.71
H-6a	−0.06	−0.86	−0.80
H-6b	+0.40	−0.23	−0.63
H-14a	+0.37	−0.16	−0.53
H-14b	+0.19	−0.47	−0.66
H-15	+0.20	−0.28	−0.48
H-18	+0.03	−0.17	−0.20
H-19a	+0.13	−0.26	−0.39
H-19b	+0.04	−0.30	−0.34
H-20	+0.18	−0.08	−0.26
H-21	+0.80	+0.68	−0.12

[a]+ =downfield; − =upfield.

explained by a sterical hindrance by the trifluoroacetate counter ion preventing the C$_6$D$_6$ molecules from approaching the protonated nitrogen from that direction.

On the other hand, for H-6a a larger extra solvent-shift was observed. This proton is situated just on the opposite side of the nitrogen as compared to the location of the
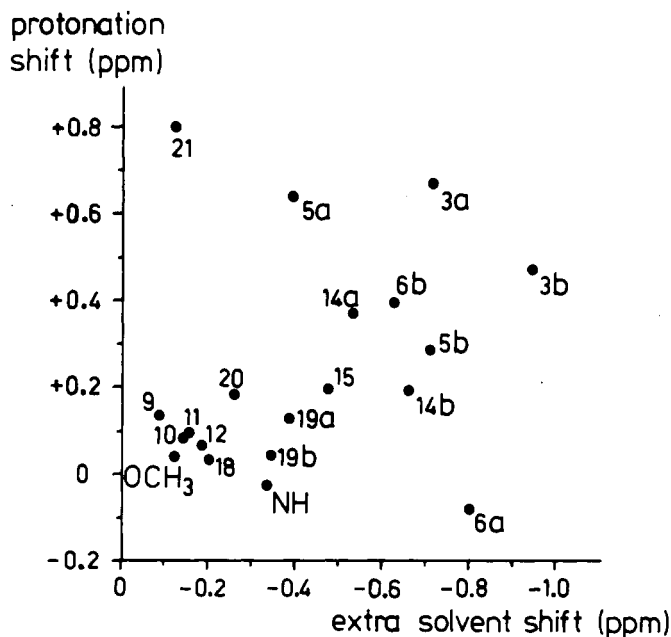

FIGURE 6.   Relation between the protonation shift in CDCl$_3$ and the extra solvent shift, for the different protons in tubotaiwine

counter ion, and more or less on the outside of the molecule. When C_6D_6 molecules approach the protonated nitrogen from that direction, H-6a is situated in the middle of the shielding zone near the C_6D_6 molecule. The extra solvent-shifts of the protons of the ethyl side chain are small, as could be expected for the 20 *S* configuration.

The evidence presented above clearly proves the 20 *S* configuration of the tubotaiwine sample studied (Figure 2 and Structure 1). For most of the previous isolations (Table 1), direct comparison of the samples by tlc and/or ^1H nmr proved that the isolated compound was identical to our sample of tubotaiwine, and that the actual configuration of C-20 is *S*.

Some isolations are thought to concern alkaloids identical with our sample based on the reported data. In these data particularly the chemical shift of H-18 seems of importance, as in the related compound, uleine, a large difference in this shift is observed for the two C-20 isomers, caused by the influence of the aromatic moiety (47).

Finally, several papers do not give sufficient data to relate the isolated compound to the one studied here. Among these the papers describing the original compound, tubotaiwine, by Schmid *et al.* (1-3), who concluded a 20 *S* configuration from chemical evidence (see above), however, did not give any ^1H-nmr data allowing a comparison. Also none of the later publications on the isolation of tubotaiwine reported a direct comparison with this compound.

In fact, in the literature, so far, no evidence has been presented for a 19,20-dihydrocondylocarpine with a 20 *R* configuration. We, therefore, conclude that the structures given by Hesse (55), Glasby (56), Gabetta (57), and the *Chemical Abstracts* should be corrected.

EXPERIMENTAL

ACKNOWLEDGMENTS

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