[Chem. Pharm. Bull. 26(4)1182—1187(1978)]

UDC 547.944.04 : 581.192

Studies on Plants containing Indole Alkaloids. VII.[1] Isolation of Several Aspidosperma- and Vincamine-type Alkaloids from the seeds of *Amsonia elliptica* Roem. et Schult.

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(Received September 14, 1977)

Four known (tabersonine (**1**), tetrahydroalstonine (**2**), Δ^{14}-vincamine (**6**) and 16-epi-Δ^{14}-vincamine (**5**)) and four new indole alkaloids (3-oxo-tabersonine (**3**), 14,15-epoxy-3-oxo-vincadifformine (**4**), 16-carbomethoxy-16-hydroxy-14,15-epoxy-3-oxo-1,2-dehydro-aspidospermidine (**7**) and tabersonine $N_{(b)}$-oxide (**8**)) were isolated from the seeds of *Amsonia elliptica* Roem. et Schult. (Apocynaceae).

Δ^{14}-Vincamine (**6**) and its $C_{(16)}$-epimer (**5**) were partially synthesized from tabersonine (**1**).

Unusual oxidative chlorination was observed when tabersonine hydrochloride was oxidized with *m*-chloroperbenzoic acid.

Keywords——*Amsonia elliptica* Roem. et Schult.; Apocynaceae; indole alkaloids; isolation from seeds; structure determination; chemical conversion; Aspidosperma-type alkaloids; Vincamine-type alkaloids; *m*-chloroperbenzoic acid oxidation of base hydrochloride

Nineteen *Amsonia* species (Apocynaceae) are known in the world, among which each one species distributes in Japan and Asia Minor.[3] *Amsonia elliptica* Roem. et Schult. is a native plant of Japan and its constituents have long been studied in this country; first by Kimoto, *et al.*[4a] and afterwards by Imai, *et al.*[4b] In the recent years many indole alkaloids have been

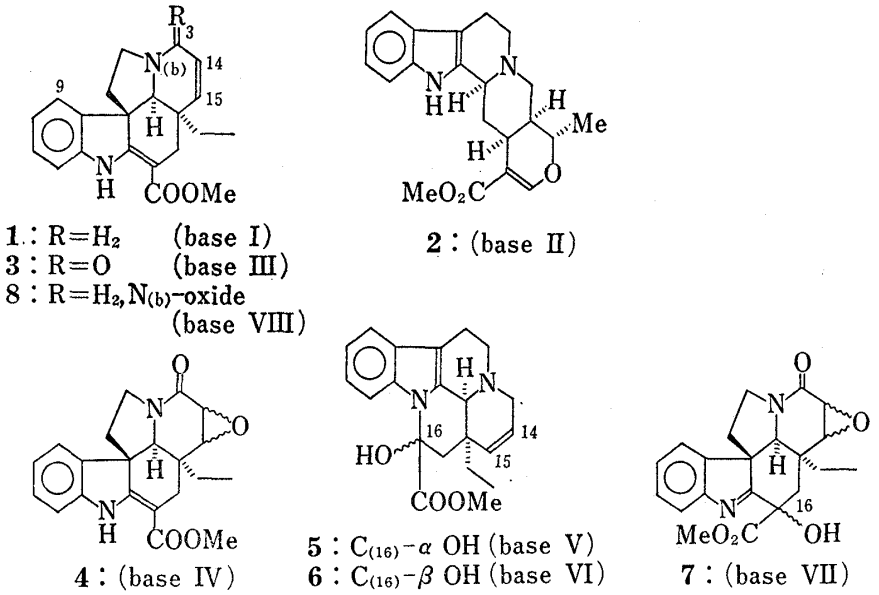

Chart 1

1) Part VI: N. Aimi, E. Yamanaka, N. Shinma, M. Fujiu, J. Kurita, S. Sakai, and J. Haginiwa, *Chem. Pharm. Bull.* (Tokyo), **25**, 2067 (1977).
2) Location: *1–33 Yayoi-cho, Chiba.*
3) "A. Engler's Syllabus der Pflanzen Familien," H. Melchior ed., Band II, Gebruder Borntraeger, Berlin, 1964, p. 413.
4) *a*) S. Kimoto and H. Inoue, *Yakugaku Zasshi*, **65**, 95 (1942); S. Kimoto and M. Okamoto, *Chem. Pharm. Bull.* (Tokyo), **3**, 392 (1955); *b*) K. Imai and A. Ogiso, *Ann. Report Takamine Lab.*, **7**, 35 (1955).

newly isolated from the roots in this laboratory,[5] but the constituents of the seeds have still remained to be studied. This paper describes the structures and chemistry of the seed alkaloids. Some other *Amsonia* spp. are also revealed to contain indole alkaloids in their seeds through the works by the chemists of France,[6] Hungary[7] and Poland.[8]

Ground dry seeds of *Amsonia elliptica* was extracted with hexane and the basic components separated from oil was chromatographed over Al_2O_3. From the early fractions base I (**1**) was obtained as the main constituent. Repeated chromatography of a mixture of the minor bases afforded base II (**2**), base III (**3**), base IV (**4**) and base V (**5**). The mother liquor of crystallization of base V was applied to preparative thin-layer chromatography (preparative TLC) to give base VI (**6**). Further separation of the noncrystallizable fraction of the above chromatography gave two additional minor bases, base VII (**7**) and base VIII (**8**).

Base I (**1**) was found to be (−)-tabersonine (**1**) by the physical properties of its hydrochloride, mp 199—199.5°, $[\alpha]_D$ −333.3°, and the spectral data.[6,9]

Base II (**2**) was crystallized from methanol to colorless needles, mp 216—218°. Its mass spectrum showed the molecular ion peak at *m/e* 352 (100%) accompanied by a strong (M^+-1) peak at 351 (77%) suggesting indoloquinolizidine skeleton. Heteroyohimbinoid nature was evidenced by its infrared spectrum (IR) showing the absorption bands at 1710 and 1630 cm^{-1} ascribable to the conjugated ester carbonyl and double bond, respectively. Direct comparison of base II with an authentic specimen of tetrahydroalstonine[10] proved identity.

Base III (**3**) was obtained as colorless prisms, mp 151—153°, on crystallization from ethyl acetate. From the ultraviolet spectrum (UV) having the absorption maxima at 297 and 331 nm, presence of a chromophore of β-anilino acrylic ester was evident. The molecular formula $C_{21}H_{22}O_3N_2$ suggested that a methylene group of tabersonine (**1**) was replaced by a carbonyl group in this compound, and this assumption was supported by an IR absorption band due to an amide carbonyl at 1665 cm^{-1}. On the proton nuclear magnetic resonance spectrum (NMR) signals of AB quartet were observed at δ 5.94 and δ 6.44 with a coupling constant of 9 Hz ascribable to the vicinal olefinic protons on $C_{(14)}$ and $C_{(15)}$, respectively. This fact strongly suggested that no proton is on the adjacent carbon ($C_{(3)}$) and therefore this base was deduced to be 3-oxo-tabersonine (**3**) which is, as far as we know, a new base. To confirm the structure, (**3**) was catalytically reduced with PtO_2 to the dihydro derivative (**9**), mp 218—220°, $[\alpha]_D$ −326.8°. Le Men, *et al.*[11] reported the synthesis of (**9**) (3-oxo-vincadifformine) as an intermediate in their total synthesis of (±)-vincadifformine. Our sample (**9**) was sent to Prof. Le Men, by whom complete identity except their optical properties was proved. Thus base III was shown to be 3-oxo-tabersonine (**3**). Base III was obtained on direct oxidation of tabersonine (**1**) with $KMnO_4$, further supporting the structure.

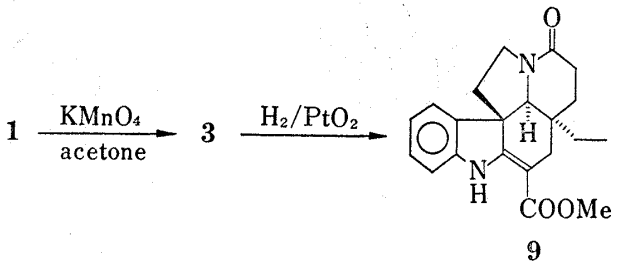

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Chart 2

5) S. Sakai, H. Ohtani, H. Ido, and J. Haginiwa, *Yakugaku Zasshi*, **93**, 483 (1973). S. Sakai, N. Aimi, K. Kato, H. Ido, K. Masuda, Y. Watanabe, and J. Haginiwa, *ibid.*, **95**, 1152 (1975).
6) M.-M. Janot, H. Pourrat, and J. Le Men, *Bull. Soc. Chim. Fr.*, **1954**, 707; M.-M. Janot, J. Le Men, and C. Fan, *C.R. Acad. Sci.*, **248**, 3005 (1959).
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9) "Physical Data of Indole and Dihydroindole Alkaloids," N. Neuss ed., Eli Lilly Co., Indiana, USA, 1960.
10) N. Aimi, E. Yamanaka, J. Endo, S. Sakai, and J. Haginiwa, *Tetrahedron*, **29**, 2015 (1973).
11) J.-Y. Laronze, J. L-Fontaine, J. Lévy, and J. Le Men, *Tetrahedron Lett.*, **1974**, 491.

Base IV (**4**), which was eluted slightly faster than base III (**3**) from the SiO_2 column, was an amorphous powder and showed a similar color reaction towards $Ce(SO_4)_2$ reagent to base III (**3**). Its UV spectrum showed the characteristic absorption curve due to β-anilino acrylic ester suggesting the tabersonine skeleton. The molecular ion peak at *m/e* 366 on its mass spectrum suggested introduction of an additional oxygen atom to base III (**3**). The structure (**4**) having an epoxide ring was evidenced by the NMR spectrum which lacked the vinyl protons of 3-oxo-tabersonine (**3**) and instead clearly showed the AB type quartet due to the vicinal protons on the epoxide ring at 3.46 and 3.60 (J=4 Hz). The configuration of the epoxide ring is not known. This compound is also a new compound.

Base V (**5**), colorless needles of mp 181—182°, showed the characteristic UV absorption of indole chromophore. Its other spectral data, especially the NMR spectrum and mass spectral fragmentation suggested it to be 16-epi-Δ^{14}-vincamine.[12] This assumption was substantiated by its partial synthesis from tabersonine (**1**) according to the method of Le Men[13] as is described later.

The mother liquor of the above crystal was subjected to preparative TLC separation and Δ^{14}-vincamine (**6**) (base VI)[12] was obtained as colorless prisms, mp 221.5—223° (from acetone). The structure of this compound was also confirmed by the direct derivation from (**1**) as follows.

The vincamine type alkaloids are considered to be biosynthesized from aspidosperma type alkaloids in the living plants. In accord to this concept, Le Men, *et al.* published an elegant biogenetic type conversion of aspidosperma to vincamine type alkaloids.[13] Thus vincadifformine (**10**) was converted to a mixture of vincamine (**11**) and 16-epi-vincamine (**12**). In their paper, however, there was no report on the same type conversion of tabersonine (**1**) as the starting material, which would have yielded Δ^{14}-vincamine (**6**) and 16-epi-Δ^{14}-vincamine (**5**). Therefore we tried this conversion.

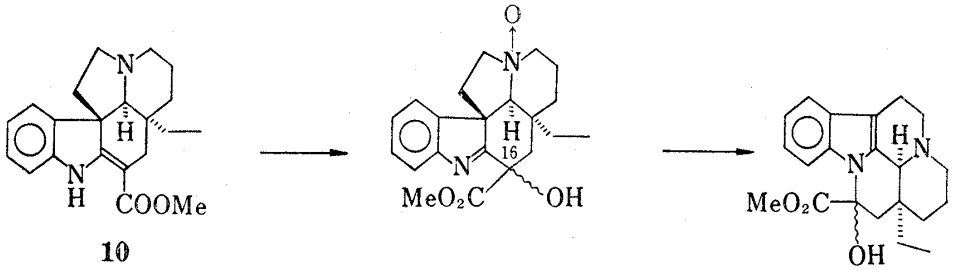

Chart 3

The original procedure[13] employs direct oxidation of (**10**) to $C_{(16)}$-hydroxylated $N_{(b)}$-oxide and therefore in the next step the $N_{(b)}$-oxide function has to be removed to realize the rearrangement. To avoid the extra step of reduction we tried to oxidize tabersonine (**1**) in the form of hydrochloride in which $N_{(b)}$ is considered to be protected from oxidation. The product, however, was $C_{(16)}$-chlorinated compound (**13**)[14] instead of the oxpected $C_{(16)}$-hydroxylated compound. Obviously electrophilic attack of chloronium ion or chlor radical which was produced from oxidation of chloride anion with metachloroperbenzoic acid (*m*-CPBA) must have occurred at the β-position of an enamine system. Generality of this new one step oxidative chlorination was studied and some of the results were reported in a separated paper.[15]

12) A. Cavé, A. Bouquet, and B.C. Das, *C.R. Acad. Sc. Paris* (*C*), **272**, 1367 (1971).
13) G. Hugel, J. Lévy, and J. Le Men, *C.R. Acad. Sc. Paris* (*C*), **274**, 1350 (1972).
14) C. Pierron, J. Garnier, J. Lévy, and J. Le Men, *Tetrahedron Lett.*, **1971**, 1007.
15) N. Aimi, Y. Asada, S. Tsuge, T. Kohmoto, K. Mogi, and S. Sakai, *Heterocycles*, **5**, 267 (1976).

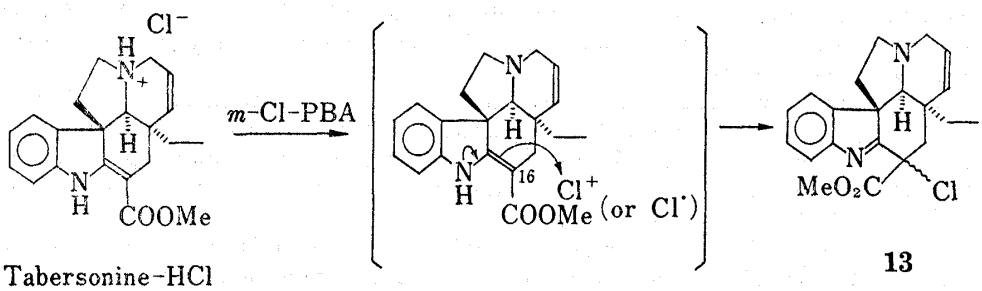

Chart 4

As we failed to obtain the desired $C_{(16)}$-oxygenated compound by *m*-CPBA oxidation of tabersonine hydrochloride, the counter anion of the latter was changed to sulfate by passing the solution through a column of ion exchange resin Amberlite XT-5001 (sulfate form). The salt, without any further purification, was submitted to oxidation with *m*-CPBA. The product was then stirred in acetic acid for 2 hours at room temperature. The usual work-up gave the desired Δ^{14}-vincamine (**6**) (14%) and 16-epi-Δ^{14}-vincamine (**5**) (29%).[16] The structures of the natural specimens (base V and base VI) were thus proved by direct comparison with the partially synthesized specimens. The both compounds have been known to occur in several plants but this seems to be the first time to find it in *Amsonia* spp.

Base VII (**7**) was shown to be $C_{(16)}$-hydroxylated derivative of base IV (**4**) by the UV spectrum having an indolenine type absorption curve and the NMR spectrum revealing a pair of vicinal protons on an epoxide ring at δ 3.24 and 3.50 with a coupling constant of 4 Hz. Possibility of this compound to be an artefact could not be ruled out, for long standing of a chloroform solution of base IV in the air produced a minute amount of base VII (**7**) as was evidenced by TLC.

The last compound isolated was tabersonine $N_{(b)}$-oxide (base VIII, (**8**)) (new compound) whose mass spectrum showed the molecular ion peak at *m/e* 352 (4.3%) and the fragmentation pattern closely similar to that of tabersonine (**1**). In the NMR spectrum the aromatic proton signal ascribable to $C_{(9)}$-H was observed at deshielded position (δ 8.68) as a doublet (J=8 Hz), suggesting anisotropic effect of the N–O bond on the $C_{(9)}$–H. Studying this observation by using a molecular model, α orientation of N-oxide bond was deduced. The same compound (**8**) was obtained when tabersonine (**1**) was oxidized with one molar equivalent of *m*-CPBA.

Experimental

All melting points are uncorrected. IR spectra were measured with Model 215 spectrophotometer (Hitachi Co) and UV spectra with a Model EPS-3T spectrophotometer (Hitachi Co.). A JNM MH-100 NMR instrument (Japan Electron Optics Co.) was used for measurement of NMR spectra using $CDCl_3$ as the solvent unless otherwise stated. Mass spectra were taken with a Model RMU-6E mass spectrometer (Hitachi Co.). Measurement of CD spectra was made with a Model J-20 spectropolarimeter (Japan Electroscopic Co.) for methanol solutions, concentration of which was about 1 mg/10 ml.

Extraction and Separation of Alkaloids from *Amsonia elliptica* Seeds——The powdered seeds (500 g) of *Amsonia elliptica* collected at Tajimagahara, Saitama Pref., was first extracted with hexane and then with MeOH. Hexane extract which contained rich of seed oil was shaken with dilute hydrochloric acid. White precipitate then formed was collected by filtration. The suspended solution of the precipitate in NH_4OH was extracted with $CHCl_3$ and 7.31 g of crude extract (crude extract A) was obtained from the organic layer. The filtrate of the above precipitate was separated to aq. HCl layer and hexane layer. The acid layer was made basified with NH_4OH and extracted with $CHCl_3$ to give 1.42 g of a crude extract (crude extract B).

MeOH extract of the seeds was fractionated as usual and 1.20 g of a crude base was obtained (crude extract C).

16) When this work was carried out in this laboratory, a similar conversion was reported on Chemical Abstracts as a patent article [*Chem. Abstr.*, **83**, 79457*z* (1975)].

Crude extract A was found to be constituted mainly from seed oil and tabersonine (**1**). Column chromatography on Al_2O_3 (Brockmann) gave tabersonine (**1**) which was converted to crystalline hydrochloride (yield 696 mg, 0.13% from the dry seeds).

Crude extracts B and C were shown to contain the main base, tabersonine (**1**), and other minor bases by TLC, and the both fractions were combined and chromatographed over Al_2O_3 (Woelm), from which tabersonine (**1**) was obtained by elution with hexane–benzene (3:1)–(1:2), and was crystallized as the hydrochloride (yield, 710 mg, 0.13% from the dry seeds). From the fraction eluted with benzene–AcOEt (9:1) base II (tetrahydroalstonine) (**2**, 131 mg) was obtained.

Base III (3-oxo-tabersonine) (**3**) (131 mg) was obtained from the fractions eluted with benzene–AcOEt (4:1). Another chromatography of the intermediate fractions gave an additional amount of tabersonine (710 mg as the hydrochloride) and base III (3-oxo-tabersonine) (**3**) (173 mg).

Column chromatography of the residual base mixture on SiO_2 gave base IV (14,15-epoxy-3-oxo-vincadifformine) (**4**) (256 mg, amorphous) and base V (16-epi-Δ^{14}-vincamine) (**5**) (23 mg). Preparative TLC of the mother liquor of the base V afforded three bases, base VI (Δ^{14}-vincamine) (**6**) (4 mg), base VII (16-carbomethoxy-16-hydroxy-14,15-epoxy-3-oxo-1,2-dehydro aspidospermidine) (**7**) (14 mg) and Base VIII (tabersonine $N_{(b)}$-oxide) (**8**), besides a further amount of base V (**5**) (12 mg).

Base I (Tabersonine) (**1**): HCl salt; mp 199—199.5° (Lit. 196°) from EtOH, and $[\alpha]_D^{18}$ −333° (c=2.5, MeOH). Total yield (as the hydrochloride) was 2.11 g (0.36% from the dry seeds).

Base II (**2**) (Tetrahydroalstonine): mp 216—218° (colorless needles from MeOH. UV λ_{max}^{EtOH} nm: 227, 285 and 291. IR ν_{max}^{KBr} cm^{-1}: 3400 (NH), 2850—2760 (Bohlmann Bands), 1710 (conj. ester C=O), and 1630 (conj. C=C). MS *m/e*: 352 (M^+, 100%), 351 (77%) and 156 (39%). Measurement of the melting point on admixture with an authentic tetrahydroalstonine showed no depression.

Base III (**3**) (3-oxo-Tabersonine): Prisms from AcOEt, mp 151.5—153°. UV λ_{max}^{MeOH} nm (log ε): 297 (4.12) and 331 (4.23). IR ν_{max}^{KBr} cm^{-1}: 3350 (NH), 1665 (amide C=O and conj. ester C=O) and 1610 (conj. C=C). MS *m/e*: 350 (M^+, 11%), 227 (100%) and 195 (87%). NMR δ: 0.72 (3H, t, J=7 Hz, $C_{(18)}H_3$); 2.04 (1H, d, J=16 Hz), 2.62 (1H, d, J=16 Hz) ($C_{(17)}H_AH_B$); 3.78 (3H, s, CO_2Me); 4.0 (1H, s, $C_{(21)}$–H); 4.32 (1H, m, $C_{(5)}$–H); 5.94 (1H, d, J=9 Hz, $C_{(14)}$–H); 6.44 (1H, d, J=9 Hz, $C_{(15)}$–H); 6.92—7.22 (4H, m, Arom.H×4); 9.04 (1H, br.s, NH). NMR signals ascribable to crystalline ether were observed at δ 1.20 (CH_3–) and 3.46 (–CH_2–). *Anal.* Calcd. for $C_{21}H_{22}N_2O_3 \cdot 1/2$ether: C, 71.32; H, 6.98; N, 7.24. Found: C, 71.25; H, 7.06; N, 7.27. $[\alpha]_D^{18}$ −77.4°. CD λ_{nm}^{max} ($\Delta\varepsilon$): 316 (−4.7), 297.5 (+2.7), 265 (−13.4), 229 (+15.3) and 214 (−1.3).

Base IV (14,15-epoxy-3-oxo-Vincadifformine) (**4**): Amorphous powder. UV λ_{max}^{MeOH} nm (log ε): 222 (4.18), 297 (3.99) and 328 (4.11). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3375 (NH), 1675 (conj. ester C=O), 1650 (lactam C=O) and 1610 (conj. C=C). MS *m/e* 336 (M^+, 37%), 227 (100%), 195 (61%). NMR δ: 0.80 (deformed t, 3H, J=7 Hz, $C_{(18)}H_3$); 1.90 (1H, d, J=15 Hz, $C_{(17)}H_A$); 2.67 (1H, d.d, J=15, 2 Hz, $C_{(17)}H_B$); 3.46 (1H, d, J=3 Hz), 3.60 (1H, d, J=3 Hz) ($C_{(14)}$H, $C_{(15)}$H); 3.67 (1H, s, $C_{(21)}$H); 3.79 (3H, s, COOMe); 4.46 (1H, m, $C_{(5)}$H); 6.8—7.3 (4H, m, Arom.H×4); 8.96 (1H, br.s, NH). CD λ_{max}^{MeOH} nm ($\Delta\varepsilon$): 325 (−14.5), 288 (+3.2), 265 (+0.4), 231 (+7.9) and 218 (+6.4).

Base V (16-epi-Δ^{14}-Vincamine) (**5**): Elution from the SiO_2 column with benzene–AcOEt (2:1) and subsequent crystallization from acetone gave colorless needles of mp 181—182°. UV λ_{max}^{MeOH} nm (log ε): 226.5 (4.50), 276 (3.89), 281 (3.88), 290 (3.72). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1730 (ester C=O). MS *m/e*: 352 (M^+, 100%), 323 (64%), 250 (64%). NMR δ: 0.92 (3H, t, J=8 Hz, $C_{(18)}H_3$); 2.02, 2.54 (AB doublets, J=14 Hz, $C_{(17)}H_AH_B$); 3.00 (2H, d, J=2 Hz, $C_{(3)}H_2$); 3.46 (3H, s, COOMe); 3.80 (1H, s, $C_{(21)}$H); 4.04 (1H, br.s, OH); 5.22 (1H, d, J=10 Hz), 5.46 (1H, d.t, J=10, 2 Hz) ($C_{(14)}$ and $C_{(15)}$H); 7.0—7.5 (4H, m, Arom.H×4). CD λ_{max}^{MeOH} ($\Delta\varepsilon$): 290 (+2), 237.5 (−18.4) and 211 (+6.8).

Base VI (Δ^{14}-Vincamine) (**6**): Colorless prisms, mp 221.5—223° were obtained from benzene on crystallization of the base obtained by preparative TLC purification of the mother liquor of base V. UV λ_{max}^{MeOH} nm: 228, 276, 282 and 290 (sh). IR ν_{max}^{KBr} cm^{-1}: 3420, 1750 (ester C=O). MS *m/e*: 352 (M^+, 100%), 323 (84%), 250 (49%). CD λ_{max}^{MeOH} nm ($\Delta\varepsilon$): 275 (+2.1), 255 (+1.2) 242 (+2.1) and 227.5 (−11.7). NMR δ: 0.99 (3H, t, J=7 Hz, $C_{(18)}H_3$); 2.33 (2H, s, $C_{(17)}H_2$); 3.10 (2H, br.s, $C_{(3)}H_2$); 4.14 (1H, br.s, $C_{(21)}$H); 5.72, 5.74 (2H, AB doublets, J=10 Hz, $C_{(14)}$, $C_{(15)}H_AH_B$); 7.0—7.6 (4H, m, Arom.H×4).

Base VII (16-Carbomethoxy-16-hydroxy-14,15-epoxy-3-oxo-1,2-dehydroaspidospermidine (**7**): Amorphous powder. UV λ_{max}^{EtOH} nm: 223, 229 (sh) and 284 (sh). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735 (ester C=O), 1650 (lactam C=O), 1600 (C=N). MS *m/e*: 382 (M^+, 100%), 170 (79%), 169 (46%). NMR δ: 0.80 (3H, deformed t, $C_{(18)}H_3$); 2.07 (1H, d, J=14 Hz), 2.65 (1H, d, J=14 Hz) ($C_{(17)}H_AH_B$); 3.24 (1H, d, J=3 Hz), 3.50 (1H, d, J=3 Hz) ($C_{(14)}$, $C_{(15)}H_AH_B$); 3.96 (3H, s, COOMe); 4.04 (1H, s, $C_{(21)}$H); 7.20—7.70 (4H, m, Arom. H×4).

Base VIII (Tabersonine $N_{(b)}$-oxide) (**8**): Amorphous powder. UV λ_{max}^{EtOH} nm: 230.5, 298 and 335. IR $\nu_{max}^{CHCl_3}$ 3375 (NH), 1680 (conj. C=O), 1610 (conj. C=C). MS *m/e*: 352 (M^+, 4%).

Catalytic Reduction of Base III (3) to 3-oxo-Vincadifformine (9)——Base III (**3**) (50 mg) was reduced catalytically in EtOH (10 ml) with PtO_2 at room temperature. The product was crystallized from AcOEt to give the desired dihydro derivative (**9**) (19 mg), mp 218—220°. UV λ_{max}^{MeOH} nm (log ε): 225.5 (4.11), 297.5 (4.14), 328 (4.24). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3370 (NH); 1640 (conj. ester C=O), 1605 (conj. C=C). MS *m/e*: 352 (M^+, 42%), 227 (100%), 195 (40%). NMR δ: 0.70 (3H, m, $C_{(18)}H_3$); 2.64 (1H, d, J=16 Hz, $C_{(17)}$H); 3.48 (1H, s, $C_{(21)}$H); 3.76 (3H, s, COOMe); 4.16 (1H, d.d, J=11, 6 Hz, $C_{(5)}$H); 6.80—7.25 (4H, m, Arom. H×4); 8.96

(1H, br.s, NH). CD λ_{nm}^{max} ($\Delta\varepsilon$); 326 (−21.6), 287 (+4.4), 262 (+0.58), 237.5 (+12.2), 220 (+4.4). $[\alpha]_D^{21}$ −327°. This sample was sent to Prof. Le Men, Univ. of Reims, by whom identity with his synthetic (±)-3-oxo-vincadifformine was proved excepting their optical properties.

Oxydation of Tabersonine with $KMnO_4$——To a solution of tabersonine (**1**) (48 mg) in dry acetone (3 ml), powdered $KMnO_4$ (28 mg) was added and the solution was stirred in an ice-salt bath. After 1 hr, 5 mg of $KMnO_4$ was added and stirring was continued for 40 min. EtOH was added to the solution, MnO_2 was filtered off and evaporation of the solvent gave a residue (47 mg). Benzene and benzene–AcOEt elution fractions of Al_2O_3 column (neutral, activity III, 25 g) afforded 16 mg of 3-oxo-tabersonine (32%). Crystallization from AcOEt gave crystals of mp 146—148°. Mixed fusion with the above natural specimen proved complete identity.

***m*-CPBA Oxydation of Tabersonine Hydrochloride**——Tabersonine hydrochloride (200 mg) in dry CH_2Cl_2 (10 ml) was cooled in an ice-salt bath, to which 97 mg of *m*-CPBA was added. After 35 min, $NaHSO_3$ was added and the solution was stirred for a short time (5 min). Dilution of the reaction solution with $CHCl_3$ followed by successive washing with dil. NH_4OH and water afforded 207 mg of a crude material, which showed a single spot on TLC. UV λ_{max}^{EtOH} nm: 228.5 and 288. IR ν_{max}^{KBr} cm^{-1}: 1738 (ester (C=O), 1610 (C=N), no OH. High resolution mass spectrum, *m/e*: 372.1416 (Calcd. for $C_{21}H_{23}N_2O_2Cl$*; 372.1416); 370.1453 (Calcd. for $C_{21}H_{23}N_2O_2Cl$; 370.1446). The above data strongly suggested that the product was 16-chlorinated compound (**13**), and correctness of this assumption was proved by direct comparison with an authentic specimen prepared from tabersonine (**1**) by a known method.[14]

Conversion of Tabersonine (1) to Δ^{14}-Vincamine (6) and 16-epi-Δ^{14}-Vincamine (5)——Tabersonine hydrochloride (50 mg) was passed through a column of ion exchange resin Amberlite XT-500 (sulfate form) and the eluate was concentrated *in vacuo*. to dryness. To the cooled solution (ice-salt bath) of the above sulfate in dry CH_2Cl_2 (2 ml), 23.6 mg of *m*-CPBA was added and the solution was stirred for 20 min. The solution was diluted with $CHCl_3$ and washed with 5% $NaHCO_3$ and water. Removal of the solvent afforded 51 mg of a residue. Acetic acid (1.5 ml) solution of the above material was stirred for 2 hr at room temperature. Evaporation of the solvent under reduced pressure gave 51 mg of a residue which was submitted to preparative TLC (benzene–$CHCl_3$–$NHEt_2$ 85: 10: 5). Δ^{14}-Vincamine (**6**) (6.5 mg) and 16-epi-Δ^{14}-vincamine (**5**) (13.5 mg, 28.5%) were obtained, and they were proved to be completely identical with the respective natural compounds.

Acknowledgement We are grateful to Prof. J. Le Men, Université de Reims, Faculté de Pharmacie, France, for his kind comparison of our sample with his synthetic 3-oxo-vincadifformine. This work was supported in part by a Grant-in-Aid for Cancer Research from the Ministry of Health and Welfare.