Tetrahedron. Vol. 32, pp. 1973 to 1977. Pergamon Press 1976. Printed in Great Britain

REACTIONS OF PROTOBERBERINE-TYPE ALKALOIDS—XI[1]

SYNTHESIS OF OPTICALLY ACTIVE OCHOTENSANES

J. IMAI, Y. KONDO and T. TAKEMOTO*
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai, Japan

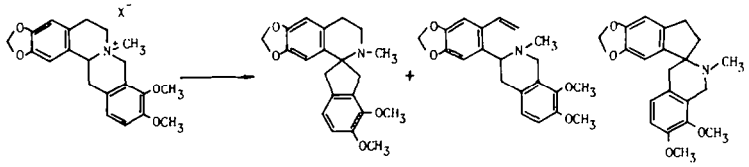
(*Received in Japan* 20 *September* 1975; *Received in UK for publication* 9 *October* 1975)

Abstract—Treatment of *l*(14S)-β-canadine methochloride (**1b**) and *d*(14R)-β-canadine methochloride (**1c**) with organometals gave *d*- (**2b**) and *l*-2,3-methylenedioxy-9,10-dimethoxyochotensanes (**2c**), respectively. The structures of these derivatives were proved by chemical and spectral means. The CD spectra of **2b** showed Davydov split extrema centered at 284 nm with a positive first Cotton effect, while **2c** showed the antipodal curve of **2b**. Consequently, the absolute configurations of **2b** and **2c** were concluded the 14R and 14S, respectively.

Application of the anionic rearrangement to N-methylthalictricavine chloride (**15**) led to 2,3 - methylenedioxy - 9,10 - dimethoxy - 13 - methylochotensane (**18**) together with the Hofmann methines **16** and **17**. The stereochemistry of **18** was confirmed in terms of the nuclear Overhauser effects.

Several light- and base-induced rearrangements of the protoberberinium salts into the ochotensine type alkaloids have been reported.[2-6] These rearrangements[2-5] include an *o*-quinodimethide as the general intermediate. Although the Hofmann degradation of the protoberberinium salts is quite commonly employed, the non-phenolic protoberberinium salts are comparatively stable for cold alkali.[2-4] We now report the first synthesis of optically active ochotensanes which include an anionic rearrangement of the non-phenolic protoberberinium salts.

Compound **2a** showed the composition $C_{21}H_{23}O_4N$, which was established by mass spectral and elemental analysis, and gave a picrate, m.p. 237–238° (dec), $C_{27}H_{26}O_{11}N_4$. **2a** revealed absorption maxima in the UV spectrum at 230 nm (sh. log ε 4·24) and 287 nm (log ε 3·77) showing the presence of the tetrahydroisoquinoline nucleus. In the NMR spectrum of **2a** in $CDCl_3$, although signals at δ 2·29 (3H, s), 3·85 (6H, s), 5·81 (2H, s), 6·42 (1H, s), 6·47 (1H, s), 6·62 (1H, d, J = 16 Hz) and 6·83 (1H, d, J = 16 Hz) were readily assignable to the N-Me group,



Scheme 1.

When *dl*-N-methyltetrahydroberberinium salts **1a** (X = I, Cl, and CH_3SO_4) were subjected to Stevens rearrangement with phenyllithium, a tertiary base **2a**, m.p. 117–118°, was obtained in addition to the normal Hofmann methine[7] **3a**, m.p. 111–112°. Compound **2a** was also obtained on treatment of **1a** with other organometalic reagents, butyllithium, lithium aluminium hydride and sodium methylsulfinylmethanide as well as 3% sodium amalgam.[8] Yields are given in Table 1.

Table 1.

	Yield (%)				
X	n-Butyl Li	Phenyl Li	$NaCH_2SOCH_3$	$LiAlH_4$	Na/Hg
I	–	–	29.1	62.4	–
Cl	54.5	–	63.3	–	3.5
sulfate	–	25.0	–	61.0	–

two OMe groups, methylenedioxy group, $C_{1(or\,4)}$, $C_{4(or\,1)}$, $C_{11(or\,12)}$ and $C_{12(or\,11)}$ ring protons, respectively, a multiplet at δ 2·68–3·60 was difficult to assign because of the relative complexity of the pattern. In practice, however, the spectrum was well separated on addition of a shift reagent, Eu(fod)$_3$, and all signals were assigned satisfactorily to 2,3 - methylenedioxy - 9,10 - dimethoxyochotensane[9] **2a** with the aid of double resonance technique. Typical spectra are shown in Fig. 1.

2a readily reacted with methyl iodide or dimethyl sulfate to yield a dimethyl quarternary salt **4** (X = I or SO_4CH_3) as amorphous solid. **4** on treatment with caustic alkali solution led successively to a Hofmann methine base **5**, m.p. 118–119°, $C_{22}H_{25}O_4N$ (M⁺ 367). **5** showed an absorption maximum at 298 nm (log ε 4·23) which resembled that of stilbene.

The methine base **5**, in spite of homogeneous spot on the TLC and sharp m.p., revealed split signals attributable to one of OMe groups. The fact suggests that the methine base is a mixture of double-bond isomers. **5** was

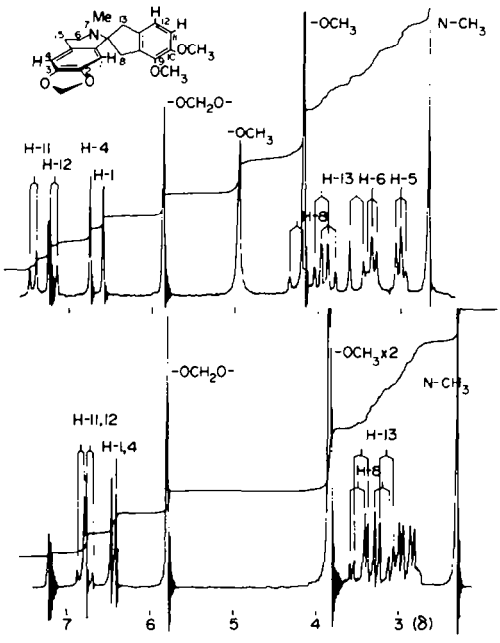


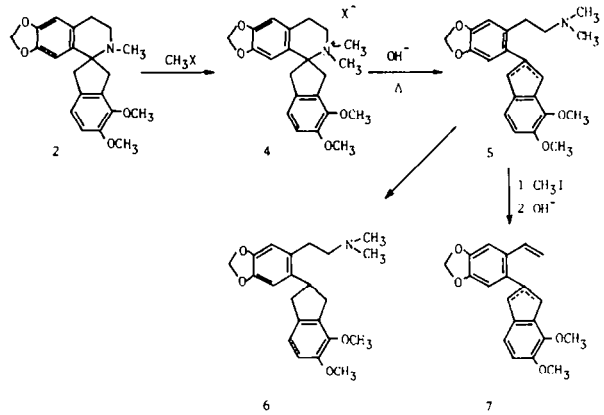
Fig. 1. ^{1}H NMR spectrum of 2,3 - methylenedioxy - 9,10 - dimethoxyochotensane (**2**) before and after the addition of 0·15 molar equiv of the shift reagent, Eu(fod)$_3$.

hydrogenated with Adams catalyst to yield 2 - (2' - dimethylaminoethyl - 4',5' - methylenedioxy) - 4,5 - dimethoxyindane **6**, $C_{22}H_{27}O_4N$ (M^+ 369), oil, in good yield. **6** revealed, as was expected, a sharp singlet at 3·84 ppm (6H) due to two OMe groups.

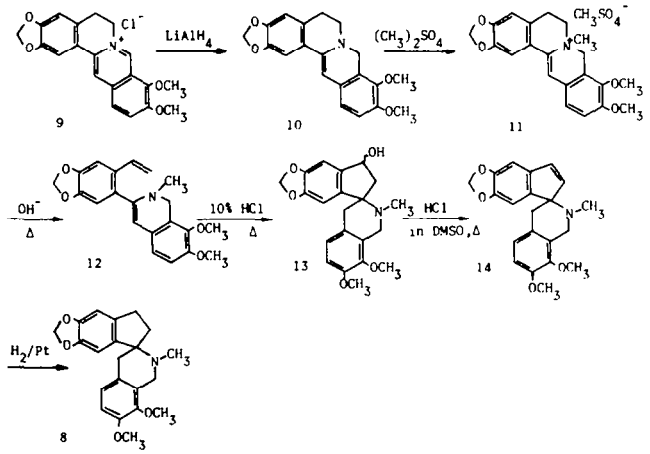
When the methine base **5** was subjected to second Hofmann degradation, a nitrogen-free substance **7**, $C_{20}H_{18}O_4$ (M^+ 322), m.p. 155–156°, was obtained. **7** showed absorption maxima at 224 nm (log ϵ 4·25), 265 nm (3·88), 301 nm (4·02) and 313 nm (3·99) in the UV spectrum. Although **7** was anticipated to be an admixture of double-bond isomers, its NMR spectrum revealed newly appeared signals attributed to the vinyl group at 5·15 ppm (1H dd, J = 11 Hz, J ≃ 1 Hz, $H\diagdown C{=}C\diagup_{H}^{H}$) and 5·53 ppm (1H dd, J = 17 Hz, J ≃ 1 Hz, $H\diagdown C{=}C\diagup_{H}^{H}$). These observations led to the conclusion that **2a** is 2,3 - methylenedioxy - 9,10 - dimethoxyochotensane. Another possible structure **8** could be ruled out by synthetic manner which involves schematically the sequence 9→10→11→12→13→14→8 (Scheme 3).

Compound **8**, $C_{21}H_{23}O_4N$, m.p. 147–148°, was not identical with the rearrangement product **2a**.

As an extension of the utility of this rearrangement, treatment of *l*-(14S)-β-canadine methochloride **1b** (m.p.

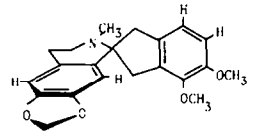


Scheme 2.

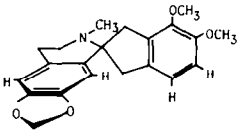


Scheme 3.

262°, $[\alpha]_D^{16} - 161°$) and *d*-(14R)-β-canadine methochloride **1c** (m.p. 262°, $[\alpha]_D^{16} + 161°$) with sodium methylsulfinylmethanide afforded *d* - 2,3 - methylenedioxy - 9,10 - dimethoxyochotensane **2b** (m.p. 104–105°, $[\alpha]_D^{16} + 60°$) and *l* - 2,3 - methylenedioxy - 9,10 - dimethoxyochotensane **2c** (m.p. 104–105°, $[\alpha]_D^{16} - 60°$), respectively. Since this rearrangement was rationalized by an S_Ni mechanism,[10] **2b** derived from *l*-β-canadine methochloride was dextrorotatory and must have the R configuration. The CD of **2b**, as was expected, showed Davydov split extrema centered at 284 nm, corresponding to the $L_b \leftarrow A$ band, with a positive first Cotton effect.[11] Therefore, the absolute configuration of *d* - 2,3 - methylendioxy - 9,10 - dimethoxyochotensane **2b** is represented as **2B**. **2c** derived from *d*-β-canadine methochloride was levorotatory and its CD spectrum showed the antipodal curve of **2b**, corresponding to the S configuration **2C**.



2B (EtOH) λmax 287nm (log 4.24)
cd 292nm (Δε +1.6)
276nm (Δε -1.0) Davydov split



2C (EtOH) λmax 287nm (log ε 4.24)
cd 292nm (Δε -1.6)
276nm (Δε +1.0) Davydov split

The Stevens rearrangement of **1b** or **1c** to give optically active ochotensanes is understood as an S_Ni mechanism which involved initially a tight ion pair as the obligatory intermediate. Organolithium bases, LAH and sodium methylsulfinylmethanide were usually used for preparation of carbanions. It is of interest to note that ochotensane was also obtained in poor yield even when N-methyltetrahydroberberinium salts were treated with sodium amalgam in aqueous solution.[8]

Analogously, treatment of *dl*-N-methylthalictricavine chloride **15** with sodium methylsulfinylmethanide in THF afforded two normal Hofmann methines **16**, m.p. 116–117° (24%), **17**, m.p. 166–167° (54%), and a rearrangement product **18**, oil (6%). Attempts to improve the yield of **18** by means of application of some organometals (sodium methylsulfinylmethanide, phenyllithium, n-butyllithium) and solvents (THF, DMSO) were not achieved.

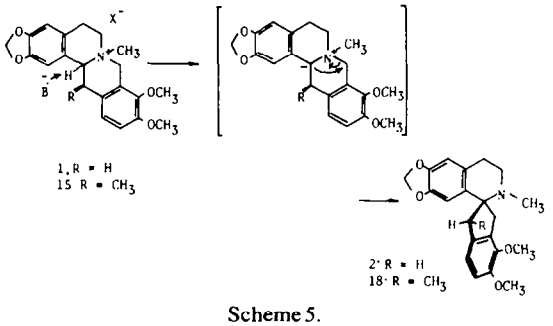
The composition $C_{22}H_{25}O_4N$ of **18** was confirmed on the basis of the molecular ion peak at *m/e* 367 in the mass spectrum and formation of a picrate, m.p. 207–209° (dec), $C_{28}H_{28}O_{11}N_4$. The UV absorption spectrum of **18** showed maxima at 230 nm (sh. log ε 4·20), 286 nm (3·80) and 294 nm (3·74), and the NMR spectrum exhibited signals at δ 1·24 (3H, d, J = 7 Hz), 2·18 (3H, s), 2·66–3·10 (4H, m), 3·06 (1H, d, J = 16 Hz), 3·44 (1H, d, J = 16 Hz), 3·39 (1H, d, J = 7 Hz), 3·85 (6H, s), 5·78 (2H, s), 6·44 (1H, s), 6·46 (1H, s) and 6·72 (2H, s) which were satisfactorily assigned to 2,3 - methylenedioxy - 9,10 - dimethoxy - 13 - methylochotensane (Fig. 2).

The C-13 Me doublet of **18** appeared in lower magnetic field than that of dihydroochotensimine[12,2b,4b] **19** (δ 0·95, J = 7·2 Hz). This fact suggests that C-13 Me group is pointing to the nitrogen side and deshieled by the lone pair of the nitrogen. The observation of the nuclear Overhauser effects[13–16] between C-1H and C-13H as well as C-1H and C-8H_A offered final proof of the stereochemistry. The results are given in Table 2.

Table 2. Nuclear Overhauser effects in **18**.

Observed proton	δ (ppm)	Irradiated protons	δ (ppm)	% area increase
C-8H	6.48	C-5H	2.76	26
C-1H	6.45	C-13H	3.36	14
C-1H	6.45	C-8H_A	3.43	9
C-13H	3.36	C-1H	6.45	8

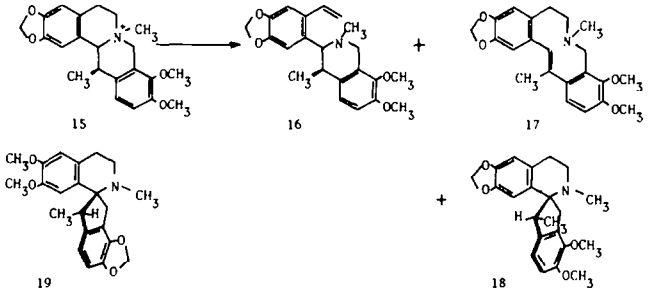
The S_Ni mechanism depicted in Scheme 5 is further supported by the fact that the rearrangement of thalictricavine methochloride **15** proceeded with retention of the 13-Me configuration to give **18**.



1, R = H
15 R = CH_3

2·R = H
18·R = CH_3

Scheme 5.



15 16 17 19 18

Scheme 4.

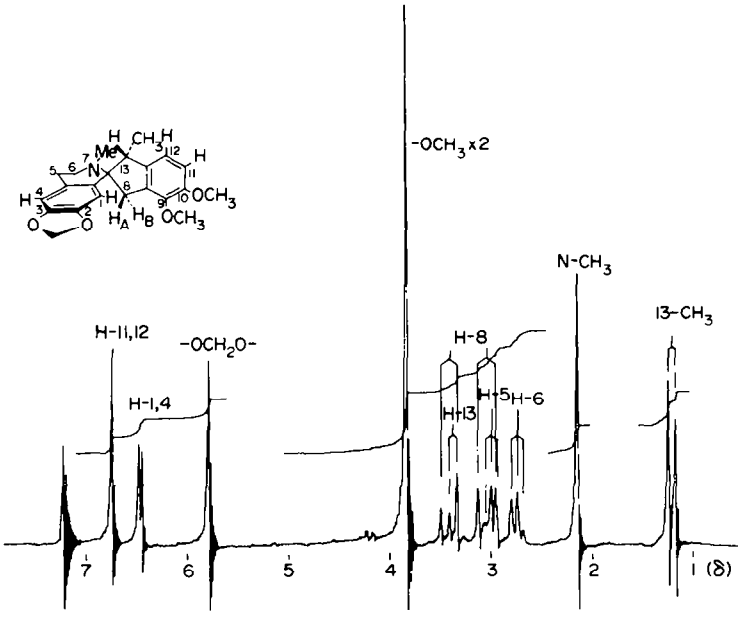


Fig. 2. ^{1}H NMR spectrum of 2,3 - methylendioxy - 9,10 - dimethoxy - 13 - methylochotensane (**18**).

Although several conversions[2-5] of the protoberberinium salts into the ochotensine alkaloids have been reported, these conversions which included an *o*-quinodimethide intermediate were inadequate as the synthetic strategy for the optically active ochotensanes. The anionic rearrangement **1**→**2** or **15**→**18**, represents a new stereospecific method for the synthesis of the optically active ochotensane alkaloids.

EXPERIMENTAL

All m.ps were determined on a Yamato Model MP-21 apparatus and uncorrected. IR spectra were recorded on a Shimazu IR-27G grating spectrophotometer, and UV spectra were measured on a Hitachi 124 spectrometer. The NMR data were obtained using Hitachi H-60 and JNM PS-100 spectrometers. The chemical shifts (δ) were calculated on the basis of TMS as an internal standard. Mass spectra were obtained on a Hitachi RMU-7 spectrometer. CD spectra were determined on a Jasco J-20A spectropolarimeter. The samples for the measurement of the nuclear Overhauser effects were dissolved in deuterio-solvent and degassed by at least five freeze-thaw cycles under high vacuum.

Reaction of N-*methyl tetrahydroberberinium salts with carbanion reagents*

General procedure. Well dried and powdered N-methyltetrahydroberberinium salts (X = I, Cl, and $MeSO_4$) was suspended in dry THF and carbanion reagent (3·0 molar equiv) was added with a vigorous stirring under a dry N_2. The mixture became a clear yellowish brown soln as the reaction proceeded. After stirring at room temp. for 30 min, the mixture was poured into ice-water and extracted with AcOEt three times. The combined extracts were washed once with water, dried over K_2CO_3, and evaporated.

Reaction of β-tetrahydroberberine methochloride **1** *with n-buthyllithium*

A. To a suspension of **1a** (1·02 g, 2·62 m mole) in 20 ml dry THF, 6 ml of 20% n-BuLi in hexane was added. The mixture was treated as described to yield a reddish brown oil, which was chromatographed on active II alumina column. The initial benzene eluate gave crystals of **3a**, m.p. 111–112° (85 mg) which were identical with the Hofmann degradation product[7] of **1a**. Further elution with benzene-AcOEt (9:1) afforded **2a** (500 mg) which was recrystallized from EtOH to give colorless needles, m.p. 117–118° (Found: C, 71·57; H, 6·64; N, 4·05. $C_{21}H_{23}O_4N$ requires: C, 71·37; H, 6·56; N, 3·96%); UV (nm) EtOH: 230 (sh log ϵ 4·24), 287 (3·77); NMR (δ) $CDCl_3$: 2·29 (3H, s, N-CH_3), 2·68 to 3·08 (4h, m, -CH_2-CH_2-), 3·13 and 3·45 (1H × 2, d, J = 16 Hz, -CH_2-), 3·19 and 3·49 (1H × 2, d, J = 16 Hz, -CH_2-), 3·85 (6H, s, -OCH_3), 5·81 (2H, s, -O-CH_2-O-), 6·42 and 6·47 (1H × 2, s, Ar-H), 6·72 and 6·83 (1H × 2, d, J = 8 Hz, Ar-H). MS (*m/e*): 353 (M^+), 338, 322.

B. Compound **1b** (222 mg; 0·571 mmole) was suspended in 4·4 ml dry THF and sodium methylsulfinylmethanide (0·55 ml) added. The mixture was treated as described. The residual oil was chromatographed on alumina column (8 g) with benzene: AcOEt. The initial eluate gave **3b** m.p. 103–104° (21 mg). The second eluate afforded **2b** (132 mg) which was recrystallized from EtOH to give colorless prisms, m.p. 104–105° $[\alpha]_D^{16}$ + 60° (*c* = 0·19). (Found: C, 71·41; H, 6·50; N, 3·93. $C_{21}H_{23}O_4N$ requires: C, 71·37; H, 6·56; N, 3·96%); NMR, UV and MS data were identical with those of **2a**.

C. Compound **1c** (231 mg; 0·592 mmole) was suspended in 4·6 ml dry THF and sodium methylsulfinylmethanide (0·56 ml) added. The mixture was treated as described to yield **3c**, m.p. 103–104° (24 mg), and **2c** (120 mg) which was recrystallized from EtOH to give colorless prisms, m.p. 104–105°, $[\alpha]_D^{16}$ - 60° (*c* = 0·14), (Found: C, 71·29; H, 6·70; N, 3·88. $C_{21}H_{23}O_4N$ requires: C, 71·37; H, 6·56; N, 3·96%); NMR, UV and MS date were identical with those of **2a**.

Hofmann degradation of dl - 2,3 - *methylenedioxy* - 9,10 - *dimethoxyochotensane* **2a**

To a soln of **2a** (480 mg; 1·36 mmole) 1·0 ml $CHCl_3$ (0·5 ml) MeI was added. The mixture was allowed to stand at room temp for 1 hr and then evaporated to give a pale yellow residue. The residue was dissolved in 10 ml MeOH and Ag_2O added (newly prepared from 1·03 g $AgNO_3$). The mixture was heated on a boiling water bath for 15 min and the ppt was filtered off. After the filtrate was evaporated under reduced pressure, 10% NaOH (6·0 ml) was added to the residue and refluxed on a water bath for 5 hr. The oil was exhaustively extracted with ether. The pooled ether layers were washed with sat NaCl aq, dried over K_2CO_3, and evaporated to give colorless needles **5** (420 mg), m.p. 118–119° (EtOH). (Found: C, 71·84; H, 6·98; N, 3·59. $C_{22}H_{25}O_4N$ requires: C, 71·91; H, 6·86; N, 3·81%); UV (nm) EtOH: 298 (log ϵ 4·24); NMR (δ) $CDCl_3$: 2·12 (3H, s, N-CH_3), δ 2·35 to 2·96 (4H, m, -CH_2CH_2-N), 3·64 (2H, m, -CH_2-), 3·85 (3H, s, -OCH_3), 3·89 and 3·93 (3H, each s, -OCH_3), 5·90 (2H, s, -O-CH_2-O-), 6·64–7·15 (5H, m, Ar-H). MS (*m/e*): 367 (M^+), 58 (CH_2=$N^+(CH_3)_2$).

Reduction of the methine base **5**

Compound **5** (100 mg, 0·272 mmole) in mixture of 15 ml MeOH

and 0·5 ml AcOH was hydrogenated over PtO_2 (100 mg) at atmospheric pressure and room temp. for 2 hr. After removal of the catalyst, the filtrate was made alkaline with ammonia. Extraction with ether yielded an oil. The oil was chromatographed on a silica gel column (6·0 g). The eluate with $CHCl_3$–MeOH (20:1) afforded **6** (oil) (82·5 mg) (Found: C, 71·41; H, 7·50; N, 3·70; $C_{22}H_{27}O_4N$ requires: C, 71·52; H, 7·37; N, 3·79%); UV (nm) EtOH: 230 (log ϵ 4·07), 285 (3·71), 292 (3·67); NMR (δ) $CDCl_3$: 2·30 (6H, s, N–CH_3), 2·40 to 3·52 (9H, m), 3·84 (6H, s, –OCH_3), 5·84 (2H, s, –O–CH_2–O–), 6·65 and 6·67 (1H × 2, s, Ar–H), 6·74 and 6·88 (1H × 2, d, J = 8 Hz, Ar–H). MS (*m/e*): 369 (M^+), 324, 127, 86, 84, 58.

Second Hofmann degradation

To a soln of methine base **5** (105 mg, 0·266 mmole) in 0·22 ml $CHCl_3$ MeI (0·15 ml) was added and allowed to stand at room temp. for 3 hr. After removal of the solvent, 1·5 ml of 25% KOH–MeOH was added and then refluxed under N_2 for 15 min. The crude product (76·9 mg) was isolated in the usual manner. Recrystallization from acetone gave colorless needles **7** (60·3 mg), m.p. 155–156° (Found: C, 74·68; H, 5·50. $C_{20}H_{18}O_4$ requires: C, 74·52; H, 5·63%); UV (nm) EtOH: 224 (sh. log ϵ 4·25), 265 (3·88), 301 (4·02), 313 (3·99); *NMR* (δ) $CDCl_3$: 2·70 (2H, m, –CH_2–), 3·88 (3H, s, –OCH_3), 3·93 and 3·95 (3H, each s, –OCH_3), 5·15 (1H, dd, J = 11 Hz, J = 1 Hz, $\overset{H}{\backslash}C{=}C\overset{H}{\underset{H}{/}}$), 5·53 (1H, dd, J = 17 Hz, J = 1 Hz, $\overset{H}{\backslash}C{=}C\overset{H}{\underset{H}{/}}$), 5·96 (2H, s, –O–$CH_2$–O), 6·70–7·40 (6H, m). MS (*m/e*): 322 (M^+), 307, 291, 275.

N - *Methyl* - 7,8 - *dimethoxy* - 1,2,3,4 - *tetrahydroisoquinoline* - 3 - *spiro* - 1′ - 5′,6′ - *methylenedioxyindane* **8**

Compound **14**[17] (243 mg, 0·693 mmole) in 15 ml MeOH was hydrogenated over PtO_2 (60 mg) at atmospheric pressure and room temp. for 1 hr. After removal of the catalyst, the filtrate was evaporated to dryness. The residue was chromatographed on an alumina column (25 g). The eluate with benzene-AcOEt (9:1) afforded **8** (204 mg) which was recrystallized from EtOH to give colorless needles, m.p. 147–148°, (Found: C, 71·30; H, 6·60; N, 3·81; $C_{21}H_{23}O_4N$ requires: C, 71·37; H, 6·56; N, 3·96%); UV (nm) EtOH: 228 (sh, log ϵ 4·07), 288 (3·75), 294 (3·77); NMR (δ) $CDCl_3$: 1·69 and 2·20 (1H × 2, m, –CH_2–CH_2–), 2·20 (3H, s, N–CH_3), 2·52–3·12 (4H, m), 3·52 and 4·00 (1H × 2, d, J = 17 Hz, Ar–CH_2–N), 3·81 (6H, s, –OCH_3), 5·89 (2H, m, –O–CH_2–O–), 6·60 and 6·65 (1H × 2, s, Ar–H), 6·70 (2H, s, Ar–H). MS (*m/e*): 338, 322, 164.

Reaction of dl-*thalictricavine methochloride* **15** *with sodium methylsulfinylmethanide*

To a suspension of **15** (1·43 g, 3·56 mmole) in 28·4 ml THF sodium methylsulfinylmethanide (4·5 ml) was added. The following treatment was carried out in the general procedure mentioned above. To the resulting residue MeOH was added to give colorless crystals. The crystalline mass was filtered off and recrystallized from MeOH to afford colorless fine needles (710 mg, 1·93 mmole) m.p. 166–167° (lit.[18] m.p. 162–163°) which was found to be identical with **17** (Found: C, 71·91; H, 6·90; N, 3·71; requires: C, 71·91; H, 6·86; N, 3·81%); UV (nm) EtOH: 234 (log ϵ 4·18), 294 (3·94). NMR (δ) $CDCl_3$: 1·77 (3H, d, J = 1 Hz, $\overset{H}{\backslash}C{=}C\underset{CH_3}{\diagdown}$), 2·20 (3H, s, N–$CH_3$), 2·74 (4H, broad s, Ar–CH_2–CH_2–N), 3·70 (2H, broad s, Ar–CH_2–N), 3·80 (3H, s, –OCH_3), 3·87 (3H, s, –OCH_3), 5·91 (2H, s, –O–CH_2–O–), 6·42 (1H, broad s, $\overset{H}{\backslash}C{=}C\underset{CH_3}{\diagdown}$), 6·67 (1H, s, Ar–H), 6·74 (1H, s, Ar–H), 6·80 (1H, d, J = 8 Hz, Ar–H), 6.96 (1H, d, J = 8 Hz, Ar–H). MS (*m/e*): 367 (M^+): 352, 336, 309.

The mother liquor was evaporated *in vacuo* and the residue was chromatographed on a silica gel column (42 g). The initial eluate with $CHCl_3$–MeOH (100:1) gave **16** (317 mg, 24%). Recrystallization from EtOH gave colorless prisms, m.p. 116–117°. (Found: C, 71·94; H, 7·02; N, 3·75. $C_{22}H_{25}O_4N$ requires: C, 71·91; H, 6·86; N, 3·81%); UV (nm) EtOH: 264 (log ϵ 4·05), 300 (3·69); NMR (δ) $CDCl_3$: 1·05 (3H, d, J = 7 Hz, CH–CH_3), 2·29 (3H, s, N–CH_3), 2·96 (1H, octet, J_1 = 5 Hz, J_2 = 7 Hz, Ar–CH–CH_3), 3·50 (1H, d, J = 16 Hz, Ar–CHH–N), 4·16 (1H, d, J = 16 Hz, Ar–CHH–N), 3·86 (6H, s, 2 × –OCH_3), 3·92 (1H, d, J = 5 Hz, Ar–CH–CH–CH_3), 5·16 (1H, dd, J_1 = 11 Hz, J_2 = 2 Hz, $\overset{H}{\backslash}C{=}C\overset{H}{\underset{H}{/}}$), 5·42 (1H, dd, J_1 = 18 Hz, J_2 = 2 Hz, $\overset{H}{\backslash}C{=}C\overset{H}{\underset{H}{/}}$), 5·90 (2H, s, –O–$CH_2$–O–), 6·74 (1H, s, Ar–H), 7·95 (1H, s, Ar–H), 6·80 (2H, s, 2 × Ar–H), 7·05 (1H, dd, J_1 = 11 Hz, J_2 = 18 Hz, $\overset{H}{\backslash}C{=}C\overset{H}{\underset{H}{/}}$). MS (*m/e*): 367 ($M^+$), 352, 336.

The second eluate with $CHCl_3$–MeOH (100:1) afforded **18** as an oil (82 mg, 6·3%). The analytical data was obtained as a picrate, m.p. 207–209° (dec) (MeOH). (Found: C, 56·22; H, 4·80; N, 9·61: $C_{22}H_{25}O_4N$, $C_6H_3O_7N_3$ requires: C, 56·3; H, 4·69; N, 9·39%); UV (nm) EtOH: 230 (sh. log ϵ 4·20), 286 (3·80), 294 (3·74); NMR (δ) $CDCl_3$: 1·24 (3H, d, J = 7 Hz, CH–CH_3), 2·18 (3H, s, N–CH_3), 2·75 (2H, t, J = 6 Hz, Ar–CH_2–CH_2–N), 3·00 (2H, m, Ar–CH_2–CH_2–N), 3·06 (1H, d, J = 16 Hz, –CHH–), 3·44 (1H, d, J = 16 Hz, –CHH–), 3·39 (1H, d, J = 7 Hz, CH–CH_3), 3·85 (6H, s, 2 × –OCH_3), 5·78 (2H, s, –O–CH_2–O–), 6·44 (1H, s, Ar–H), 6·46 (1H, s, Ar–H), 6·72 (2H, s, 2 × Ar–H). MS (*m/e*): 367 (M^+), 352, 336.

Acknowledgements—The authors are grateful to Miss Harumi Koizumi, Mrs. Aiko Sato, Mrs. Ayako Sato, Mrs. Chieko Koyanagi, Mr. Kazuyoshi Kawamura, Miss Hideko Ono and Miss Mayumi Ohotani, Pharmaceutical Institute, Tohoku University, for microanalysis and spectral measurements.

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