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Studies on the Constituents of *Picrasma quassioides* BENNET. II.[1] On the Alkaloidal Constituents

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Two new alkaloids, 4,9-dimethoxy-1-vinyl-β-carboline (XI) and β-carbolin-1-yl 3-(4,8-dimethoxy-β-carbolin-1-yl)-1-methoxypropyl ketone (XII) were isolated from the wood of *Picrasma quassioides* BENNET (Simaroubaceae) together with known alkaloids, 1-ethyl-4-methoxy-β-carboline (VI), 4-methoxy-1-vinyl-β-carboline (VII), 4,8-dimethoxy-1-vinyl-β-carboline (VIII), canthin-6-one (IX), and 5-methoxycanthin-6-one (X). The structures of these alkaloids were elucidated on the basis of spectroscopic evidence.

Keywords——*Picrasma quassioides*; Simaroubaceae; β-carboline alkaloid; 4,9-dimethoxy-1-vinyl-β-carboline; β-carbolin-1-yl 3-(4,8-dimethoxy-β-carbolin-1-yl)-1-methoxypropyl ketone

In the previous paper,[1] we reported the isolation and structural elucidation of alkaloids (I—V) in the root-wood of *Picrasma quassioides* BENNET (Simaroubaceae, Japanese name "Nigaki"). Further investigation on the alkaloids of *Picrasma quassioides* has been carried out in order to compare the alkaloids of different parts of this plant. Two new alkaloids (XI) and (XII), together with known alkaloids (VI, VII, VIII, IX, and X), were isolated from the wood of this plant. This paper deals with the isolation and structural elucidation of these compounds.

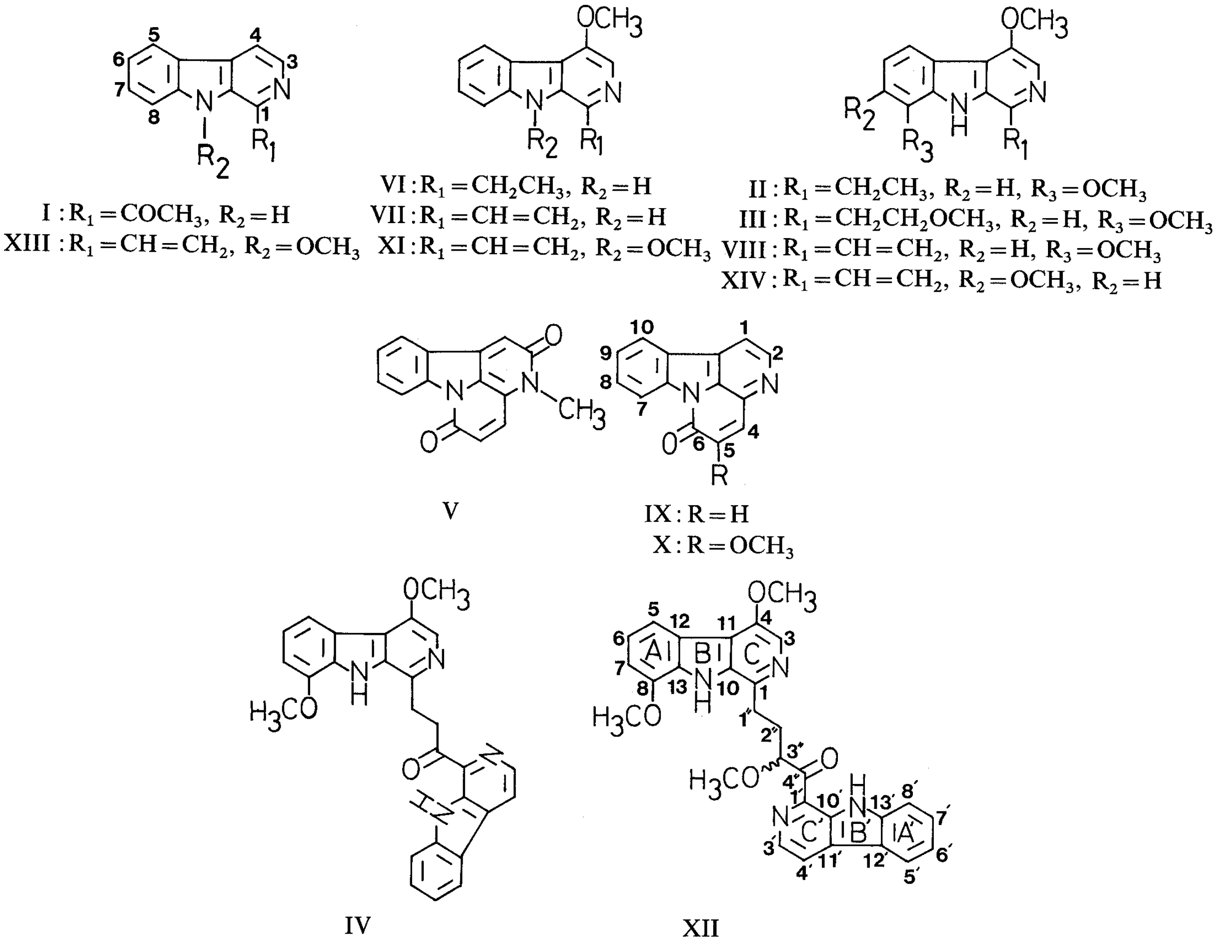
The dried wood of *Picrasma quassioides* was extracted with methanol, and the basic fraction was collected as described in the experimental section. The basic components were then fractionated by silica gel column chromatography, which yielded compounds VI, VII, VIII, IX, X, XI, and XII, each in a pure state.

Compounds VI, VII, and VIII gave positive Dragendorff tests, and their ultraviolet (UV) spectra exhibited typical absorption of a β-carboline skeleton.[1,2] It was concluded that VI, VII, and VIII were 1-ethyl-4-methoxy-β-carboline,[3] 4-methoxy-1-vinyl-β-carboline,[4] 4,8-dimethoxy-1-vinyl-β-carboline,[5] respectively, from the infrared (IR), proton nuclear magnetic resonance (^{1}H-NMR), and mass spectra.

Compounds IX and X gave positive Dragendorff tests, and their UV spectra exhibited typical absorption of a canthin-6-one skeleton.[6] Compounds IX and X were identified as canthin-6-one[6] and 5-methoxycanthin-6-one,[7] respectively, by direct comparison with authentic samples [thin-layer chromatography (TLC), IR spectra and mixed mp determination].

Compound XI, colorless needles, mp 191—192 °C, showed a positive Dragendorff test. The MS of XI gave a molecular ion peak (M^+) at m/z 254 and the high resolution MS of XI gave $M^+ - OCH_3$ at m/z 223.0875 (Calcd for $C_{14}H_{11}N_2O$, m/z 223.0924). These spectra suggested the molecular formula to be $C_{15}H_{14}N_2O_2$. The UV spectrum of XI exhibited typical absorption of a β-carboline skeleton,[1,2] and its IR spectrum indicated the presence of an ether linkage (1270, 1250, and 1050 cm^{-1}). This time, however, the IR spectrum of XI lacked the absorption of the amino group of β-carboline.

The ^{1}H-NMR spectrum of XI (Table I) showed two methoxy groups at δ 4.00 and 4.13,



I : $R_1=COCH_3$, $R_2=H$
XIII : $R_1=CH=CH_2$, $R_2=OCH_3$

VI : $R_1=CH_2CH_3$, $R_2=H$
VII : $R_1=CH=CH_2$, $R_2=H$
XI : $R_1=CH=CH_2$, $R_2=OCH_3$

II : $R_1=CH_2CH_3$, $R_2=H$, $R_3=OCH_3$
III : $R_1=CH_2CH_2OCH_3$, $R_2=H$, $R_3=OCH_3$
VIII : $R_1=CH=CH_2$, $R_2=H$, $R_3=OCH_3$
XIV : $R_1=CH=CH_2$, $R_2=OCH_3$, $R_2=H$

V

IX : R=H
X : R=OCH_3

IV

XII

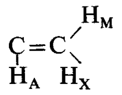
Chart 1

vinyl group signals (AMX-type protons) at δ 5.48, 6.22, and 7.15, one singlet at δ 8.10, two *ortho* coupled doublets at δ 7.53 and 8.25, and two triplets at δ 7.30 and 7.50. The location of the two methoxyl groups and vinyl group on XI was supported by comparison with the spectra of 9-methoxy-1-vinyl-β-carboline (XIII),[8] 4-methoxy-1-vinyl-β-carboline (VII),[4] and 4,7-dimethoxy-1-vinyl-β-carboline (XIV),[9] and 4,8-dimethoxy-1-vinyl-β-carboline (VIII).[5] Chemical shift values of the protons of XI were very similar to those of 4-methoxy-1-vinyl-β-carboline (VII). These results suggested that XI has the same dispositions as regards the location of one methoxyl group and the vinyl group on XI, and the other methoxyl group must be attached at the *N*-position of the B-ring.

Thus, the structure of XI was elucidated as 4,9-dimethoxy-1-vinyl-β-carboline.

Compound XII, pale yellow granular crystals, mp 121—122 °C, gave a positive Dragendorff test. The elemental analysis and MS of XII gave a molecular formula of $C_{29}H_{26}H_4O_4$ (M^+, *m/z* 490). The UV spectrum of XII exhibited typical absorption of a β-carboline skeleton,[1,2] and its IR spectrum showed absorption bands due to an amino group (3460 cm^{-1}), conjugated carbonyl group (1680 cm^{-1}), and ether linkages (1285, 1250, 1115, and 1060 cm^{-1}). The ^1H-NMR spectrum of XII (Table II) showed signals of three methoxyl groups [one (at δ 3.51) attached to an aliphatic carbon and the others attached to aromatic carbon] at δ 3.51, 3.95, and 4.01, multiplet and triplet signals due to two methylene protons at δ 2.59 and 3.29, respectively, a doublet of doublets due to a methine proton at δ 5.55, one singlet at δ 8.07, four *ortho*-coupled doublets at δ 6.93, 7.53, 7.82, and 8.05, three triplets at δ 7.17, 7.32, and 7.49, and two broad singlets due to indolic NH protons at δ 9.38 and 10.18 (both of which disappeared with D_2O). The MS of XII showed significant fragment ion peaks

TABLE I. ^{1}H-NMR Spectral Data$^{a)}$ for VII, VIII, XI, XIII, and XIV

Position		XI	VII	VIII	XIII	XIV
3H		8.10 (s)	8.06 (s)	8.03 (s)	8.45 (d, $J=5.1$ Hz)	8.00
4H					7.84 (d, $J=5.1$ Hz)	
5H		8.25 (d, $J=8.0$ Hz)	8.30 (d, $J=8.0$ Hz)	7.86 (d, $J=8.0$ Hz)	8.06 (d, $J=8.0$ Hz)	8.20 (d, $J=9.5$ Hz)
6H		7.30 (t, $J=8.0$ Hz)	7.23 (t, $J=8.0$ Hz)	7.15 (t, $J=8.0$ Hz)	7.85 (t, $J=8.0$ Hz)	6.88 (dd, $J=9.5$, 2.0 Hz)
7H		7.50 (t, $J=8.0$ Hz)	7.40 (t, $J=8.0$ Hz)	6.87 (d, $J=8.0$ Hz)	$\left.\begin{array}{l}7.29\\7.58\end{array}\right\}$ (m)	
8H		7.53 (d, $J=8.0$ Hz)	7.48 (d, $J=8.0$ Hz)			6.88 (d, $J=2.0$ Hz)
NH			9.65 (br s)$^{b)}$	9.85 (br s)$^{b)}$		9.40 (br s)$^{b)}$
	H_A	7.15 $J_{AM}=17.5$ Hz	7.15 $J_{AM}=17.5$ Hz	7.15 $J_{AM}=17.5$ Hz	7.71 $J_{AM}=17.0$ Hz	7.16 $J_{AM}=17.2$ Hz
	H_M	6.22 $J_{AX}=11.0$ Hz	6.22 $J_{AX}=11.0$ Hz	6.22 $J_{AX}=11.0$ Hz	6.60 $J_{AX}=10.6$ Hz	6.17 $J_{AX}=11.0$ Hz
	H_X	5.48 $J_{MX}=2.0$ Hz	5.48 $J_{MX}=2.0$ Hz	5.40 $J_{MX}=2.0$ Hz	5.64 $J_{MX}=2.1$ Hz	5.46 $J_{MX}=1.5$ Hz
C_4-OCH_3		4.13 (s)	4.10 (s)	4.08 (s)		4.08 (s)
C_7-OCH_3						3.80 (s)
C_8-OCH_3				3.92 (s)		
N-OCH_3		4.00 (s)			3.99 (s)	

a) In $CDCl_3$ solution. *b)* Disappeared with D_2O.

Table II. ^{1}H-NMR Spectral Data for IV[a] and XII[b]

Position	IV	XII
3H	7.87 (s)	8.07 (s)
5H	7.78 (d, J=8.0 Hz)	7.53 (d, J=7.5 Hz)
6H	7.18 (t, J=8.0 Hz)	7.17 (t, J=7.5 Hz)
7H	7.11 (d, J=8.0 Hz)	6.93 (d, J=7.5 Hz)
N_9H	11.99 (br s)[c]	9.38 (br s)[c]
3'H	8.54 (d, J=5.0 Hz)	8.45 (d, J=4.8 Hz)
4'H	8.46 (d, J=5.0 Hz)	8.05 (d, J=4.5 Hz)
5'H	8.31 (d, J=8.0 Hz)	8.07 (d, J=7.9 Hz)
6'H	7.31 (t, J=8.0 Hz)	7.32 (t, J=7.9 Hz)
7'H	7.59 (t, J=8.0 Hz)	7.49 (t, J=7.9 Hz)
8'H	7.78 (d, J=8.0 Hz)	7.82 (d, J=7.9 Hz)
$N_{9'}$H	12.06 (br s)[c]	10.18 (br s)[c]
1''Hx2	3.60 (t, J=5.0 Hz)	3.29 (t, J=7.0 Hz)
2''Hx2	3.92 (t, J=5.0 Hz)	2.59 (m, $W_{1/2}$=9.0 Hz)
3''H		5.55 (dd, J=4.8, 6.2 Hz)
C_4-OCH_3	4.04 (s)	4.01 (s)
C_8-OCH_3	4.03 (s)	3.95 (s)
C_3-OCH_3		3.51 (s)

a) In DMSO-d_6 solution.
b) In $CDCl_3$ solution.
c) Disappeared with D_2O.

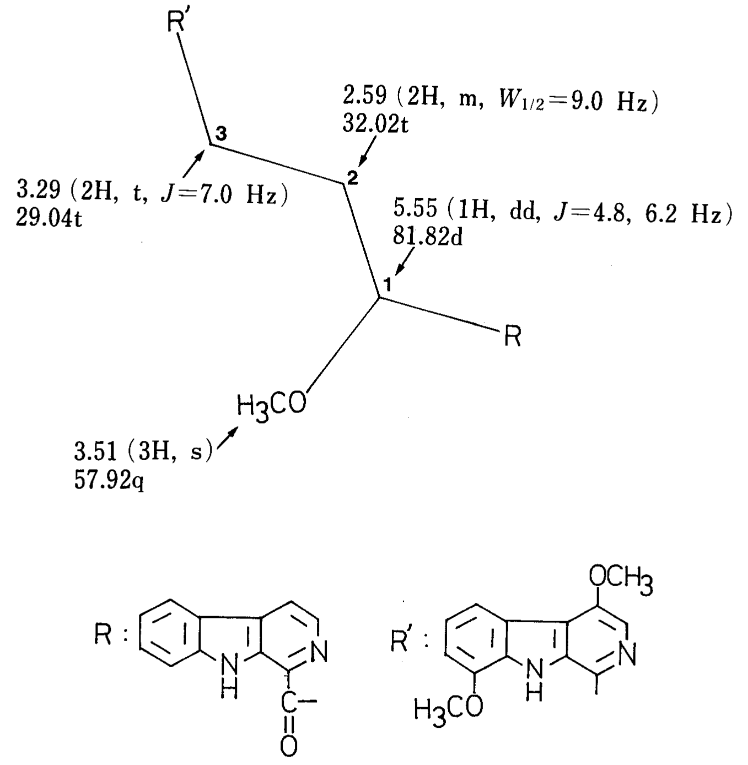


Chart 2. ^{1}H and ^{13}C NMR Spectral Data for 1-Methoxy-1,3-disubstituted Propane Grouping of XII

Table III. ^{13}C NMR Spectral Data for VI and XII

Carbon	IV[a]	XII[b]
C-1	138.49	138.65
C-3	120.07	120.55
C-4	149.91	150.68
C-5	115.46	116.38
C-6	120.07	120.82
C-7	107.28	106.95
C-8	146.01	146.01
C-10	130.90	131.66
C-11	117.03	117.03
C-12	121.53	121.53
C-13	134.80	134.80
C-1′	141.79	141.79
C-3′	137.30	137.30
C-4′	119.14	119.14
C-5′	121.63	122.45
C-6′	128.73	129.33
C-7′	119.38	120.55
C-8′	112.97	112.10
C-10′	133.99	134.64
C-11′	119.85	120.39
C-12′	129.93	130.09
C-13′	135.83	135.67
C-1″	27.09	29.04
C-2″	35.01	32.02
C-3″	202.20	81.82
C-4″	—	202.85
C_4-OCH_3	55.91	55.86
C_8-OCH_3	55.34	55.59
$C_{3''}$-OCH_3	—	57.92

a) In DMSO-d_6 solution.
b) In $CDCl_3$ solution.

at *m*/*z* 490 (M^+), 299 (α-cleavage of M^+), 255 ($299-CH_2{}^+$, base ion peak), 241 ($255-CH_2{}^+$), and 240 (β-cleavage of M^+ with McLafferty rearrangement). These findings suggested that compound XII is a β-carboline dimer alkaloid.

In the ^{1}H-NMR spectrum (Table II) and carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum (Table II) of VI,[1)] the proton and carbon atoms of XII showed similar chemical shift values to those of IV, except for the >CH–OCH_3 grouping of XII. These results suggested that XII has the same dispositions as regards the location of two methoxyl groups and the linkage moiety of the two β-carbolines of XII.

The ^{1}H-NMR and ^{13}C-NMR spectra of XII (Chart 2) also showed the signals of a 1-methoxy-1,3-disubstituted propane grouping at δ 2.59, 3.29, and 5.55. These results suggested that 1-methoxy-1,3-disubstituted propane grouping acts as a cross-link at C-1 of the two β-carbolines of XII. Thus, the chemical shift values of the proton and carbon atoms of XII were assigned by comparison with those of IV.[1)]

On the basis of these data, compound XII, except for the configuration at C-3″ position, is β-carbolin-1-yl 3-(4,8-dimethoxy-β-carbolin-1-yl)-1-methoxypropyl ketone.

This is the first time that compounds VI, VII, VIII, IX, and X and the two new compounds XI and XII have been isolated from the wood of *Picrasma quassioides* Bennet. To our knowledge, there is no earlier report in the literature of dimeric alkaloids such as IV and XII as natural products.

Experimental

All melting points were determined with a micro-melting point apparatus and are uncorrected. The UV spectra were recorded with a Hitachi 340 spectrometer and the IR spectra with a Hitachi 295 machine. Elemental analyses were carried out at the microanalytical laboratory of this university. The ^{1}H-NMR and ^{13}C-NMR spectra were recorded with JEOL FX-90Q and Hitachi R-900 spectrometers, and chemical shifts are given on the δ (ppm) scale with tetramethylsilane as an internal standard (s, singlet; d, doublet; dd, doublet of doublets; t, triplet; m, multiplet; and br s, broad singlet). The mass spectra were measured with JEOL JMS-01SG-2 mass spectrometer.

Column chromatography was carried out on Wako gel C-200 (Wako Pure Chemical Ind., Ltd.). Thin layer chromatography was performed on pre-coated Silica gel K6 plates (Whatman), and the developing solvent was $CHCl_3$–MeOH (10 : 1). The spots on the plates were detected with the Dragendorff reagent.

Extraction and Isolation——Dried wood chips (50 kg) of *P. quassioides* collected at Yachiyo City, Chiba prefecture in December 1981, were extracted with MeOH at 50 °C for 48 h. The extracts were evaporated to dryness and the residue was suspended in water and extracted with $CHCl_3$. The $CHCl_3$ solution was shaken with 5% H_2SO_4. The aqueous layer was basified with 5% NH_4OH and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with water, and dried over Na_2SO_4, then concentrated to give a basic fraction (50 g), which was passed through a column packed with silica gel. The column was eluted successively with benzene, $CHCl_3$, and MeOH. 4,9-Dimethoxy-1-vinyl-β-carboline (XI, 4 mg) was first eluted with benzene. Elution with $CHCl_3$ then afforded canthin-6-one (IX, 26 mg), 5-methoxycanthin-6-one (X, 10 mg, 1-ethyl-4-methoxy-β-carboline (VI, 25 mg), and 4-methoxy-1-vinyl-β-carboline (VII, 20 mg). Finally elution with $CHCl_3$–MeOH (99 : 1) gave 4,8-dimethoxy-1-vinyl-β-carboline (VIII, 44 mg) and β-carbolin-1-yl 3-(4,8-dimethoxy-β-carbolin-1-yl)-1-methoxypropyl ketone (XII, 31 mg).

1-Ethyl-4-methoxy-β-carboline (VI)——Crystallization from MeOH gave colorless needles, mp 177—178 °C (lit.[3] mp 177—179 °C). MS *m/z*: 226 (M^+). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 238 (4.81), 244 (4.84), 259 (4.07), 288 (4.32), 336 (4.00), 350 (4.07). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3240, 1620, 1580, 1330, 1270, 1080.

4-Methoxy-1-vinyl-β-carboline (VII)——Crystallization from MeOH gave pale yellow prisms, mp 145—146 °C (lit.[4] mp 145—146 °C). MS *m/z*: 224 (M^+). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 228 (4.15), 246 (4.15), 270 (3.98), 358 (3.55). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3440, 2920, 1639, 1575, 1285, 1045. ^{1}H-NMR: Table I.

4,8-Dimethoxy-1-vinyl-β-carboline (VIII)——Crystallization from MeOH gave pale yellow prisms, mp 157—158 °C (lit.[5] mp 156 °C). MS *m/z*: 254 (M^+). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 234 (4.09), 256 (4.16), 272 (3.89), 360 (3.46). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3440, 1630, 1575, 1290, 1270, 1050. ^{1}H-NMR: Table I.

Canthin-6-one (IX)——Crystallization from acetone gave pale yellow prisms, mp 155—156 °C (lit.[6] mp 155—156 °C). MS *m/z*: 220 (M^+). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε); 252 (4.08), 261 (4.05), 271 (4.00), 294 (3.85), 364 (4.02), 381 (3.97). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1677, 1640, 1609, 1142. This compound was identified by direct comparison (TLC, IR spectra and mixed mp) with an authentic sample.[6]

5-Methoxycanthin-6-one (X)——Crystallization from MeOH gave colorless needles, mp 239—240 °C (lit.[7] mp 239—240 °C). MS *m/z*: 250 (M^+). UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 252 (4.08), 261 (4.05), 271 (4.00), 294 (3.85), 364 (4.02), 381 (3.97). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1680, 1640, 1440, 1290, 1250, 1050. This compound was identified by direct comparison (TLC, IR spectra and mixed mp) with an authentic sample.[7]

4,9-Dimethoxy-1-vinyl-β-carboline (XI)——Crystallization from acetone gave colorless needles, mp 191—192 °C. UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 234 (4.41), 244 (4.36), 270 (4.03), 350 (3.60). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1610, 1550, 1270, 1250, 1050. ^{1}H-NMR: Table I. MS *m/z* (%): 254 (M^+, 60), 226 (12), 223 (100), 208 (65), 197 (18), 181 (10), 179 (10), 167 (7), 153 (25). High resolution MS, Calcd for $C_{14}H_{11}N_2O$ (M^+-OCH_3), *m/z* 223.0924. Found: *m/z* 223.0875.

β-Carbolin-1-yl 3-(4,8-Dimethoxy-β-carbolin-1-yl)-1-methoxy-propyl Ketone (XII)——Crystallization from MeOH gave granular crystals, mp 121—122 °C. UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 221 (4.85), 244 (4.93), 270 (4.20), 287 (4.45), 330 (3.99), 385 (3.91). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3460, 2930, 1680, 1630, 1570, 1490, 1430, 1285, 1250, 1115, 1060. ^{1}H-NMR: Table II. ^{13}C-NMR: Table III. MS *m/z* (%): 494 (M^+, 6), 463 (2), 462 (5), 408 (7), 299 (5), 255 (100), 242 (20), 241 (16), 240 (16), 225 (15), 197 (5), 168 (8), 167 (7). *Anal.* Calcd for $C_{28}H_{26}N_4O_4$, C, 70.43; H, 5.30; N, 11.33. Found: C, 69.66; H, 5.23; N, 11.12.

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