with a cold 3 N hydrochloric acid solution to pH 3 and extracted with diethyl ether. The combined extracts were washed with saturated sodium chloride solution, dried ($MgSO_4$), and concentrated to give a mixture of diastereomers **10a** and **13b** (0.3 g, oil, 55% yield), which were separated by HPLC (Perkin-Elmer SiO_2/23% EtOAc/hexane/5% formic acid/20 mL/min/at 260 nm). **10a** (0.137 g): ^1H NMR ($CDCl_3$) δ 1.2–1.75 (m, 12 H), 2.5–2.8 (m, 8 H), 3.30 ns, 3 H), 4.06 (d, J = 8.2 Hz, 1 H), 4.45 (d, J = 8.2 Hz, 1 H), 7.1–7.3 (m, 8 H), 7.35–7.57 (m, 1 H); MS, m/e (DCI, NH_3) 472; HPLC t_R = 6.44 min (Dynamax/SiO_2/30% EtOAc/hexane/0.5% formic acid/2 mL/min). Anal. Calcd for $C_{27}H_{36}O_5S \cdot {}^1/_8H_2O$: C, 68.29; H, 7.69. Found: C, 68.17; H, 7.63. **13b** (0.154 g): ^1H NMR ($CDCl_3$) δ 1.2–1.8 (m, 12 H), 2.45–2.85 (m, 8 H), 3.38 (s, 3 H) 4.0 (d, J = 3.0 Hz, 1 H), 4.75 (d, J = 3.0 Hz, 1 H), 7.1–7.35 (m, 8 H), 7.7–7.9 (m, 1 H); HPLC t_R = 5.93 min (Dynamax/SiO_2/30% EtOAc/hexane/0.5% formic acid/2 mL/min). Anal. Calcd for $C_{27}H_{36}O_5S \cdot {}^1/_2H_2O$: C, 67.33; H, 7.53. Found: C, 68.17; H, 7.54.

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Supplementary Material Available: ^1H NMR spectra of compounds **2**, **3**, and **5–13** (15 pages). Ordering information is given on any current masthead page.

Limalongine, a Modified Hasubanan Type Alkaloid, and Clolimalongine, Its Chlorinated Derivative

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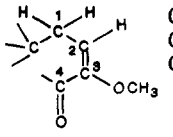
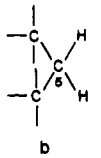
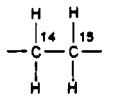
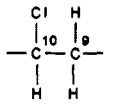
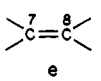
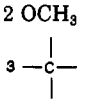
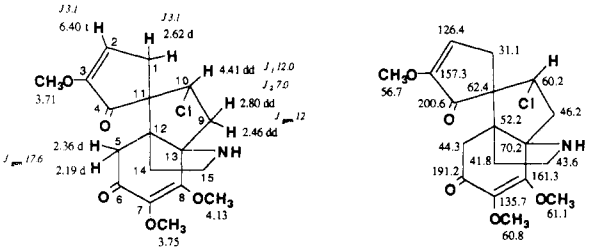
The hasubanan alkaloids are a small group of about 30 compounds, found mainly in *Stephania* species.[1,2] In this investigation, two new alkaloids related to this structural type have been obtained from *Limacia oblonga* (Miers) Hook. f. & Thoms. (Menispermaceae). (+)-Clolimalongine (1) and (+)-limalongine (2) differ from each other only by the presence of a chlorine atom in the first compound.

The UV spectra of both species are simple and show a maximum at 265 nm. The IR spectra indicate the presence of two carbonyls (1715, 1660 cm^{-1}). The formula $C_{18}H_{22}NO_5Cl$ of (+)-clolimalongine (1) is deduced from the mass spectrum, which has a molecular ion at m/z 367 and a base peak at m/z 195. The m/z 369 ion, corresponding to $[M + 2]^+$, has one third of the intensity of the molecular ion. This isotopic pattern is characteristic of the presence of a chlorine atom. The high-resolution mass spectrum confirms this conclusion (Experimental Section).

Table I. Structural Components of (+)-Clolimalongine (1)

structural fragments	^1H NMR: δ, ppm	^{13}C NMR: δ, ppm
 a	CH_2-1: 2.62 (d, 2 H, J = 3.1 Hz) CH-2: 6.40 (t, 1 H, J = 3.1 Hz) OCH_3: 3.71 (s)	C-1: 31.1 C-2: 126.4 C-3: 157.3 C-4: 191.2 OCH_3: 56.7
 b	2.19 (d, 1 H, J = 17.6 Hz), 2.36 (d, 1 H, J = 17.6 Hz)	C-5: 44.3
 c	CH_2-14: 2.85 (ddd, 1 H, J = 11, 12, 4 Hz), 3.05 (dd, 1 H, J = 11, 7 Hz) CH_2-15: 1.97 (ddd, 1 H, J = 12, 12, 7 Hz), 1.61 (dd, 1 H, J = 12, 4 Hz)	C-14: 43.6 C-15: 41.8
 d	CH-10; 4.41 (dd, 1 H, J = 11.9, 7 Hz) CH_2-9: 2.80 (dd, 1 H, J_{gem} = 12, J = 11.9 Hz), 2.46 (dd, 1 H, J_{gem} = 12, J = 7 Hz)	C-10: 60.2 C-9: 46.2
 e		C-7: 135.7 C-8: 161.3
2 OCH_3	4.13, 3.75	61.1, 60.8
		52.2, 62.4, 70.2
		200.6

The ^1H NMR spectrum of (+)-clolimalongine incorporates three methoxyl singlets and is summarized in the accompanying drawing of 1. Particularly important is the fact that no signal due to an aromatic proton is present, while the most downfield signal is a triplet at δ 6.40 (J = 3.1 Hz). The signals of other protons appear between δ 1.60 and 4.41 ppm. A complete homodecoupling study of the ^1H NMR spectrum, and ^{13}C NMR spectrum complemented by a ^1H–^{13}C direct correlation, led to the determination of the various structural components of the molecule presented in Table I. The triplet at δ 6.40 is due to the C-2 vinylic proton, and the two C-1 methylene protons have the same δ value.



(+)-clolimalongine (1)

The results are in agreement with a structural network closely related to a hasubanan or morphinan skeleton.

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0022-3263/89/1954-3491$01.50/0

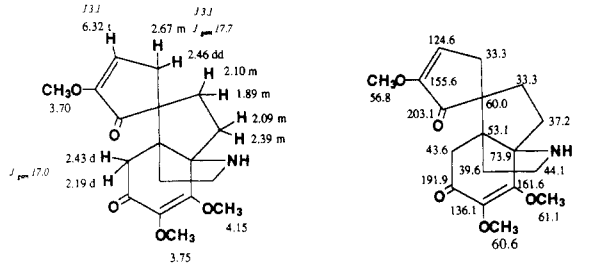
However, the ^{13}C NMR spectrum summarized in the accompanying drawing of 1 and the ^1H NMR signals due to a $-CHClCH_2-$ group are in accordance only with a hasubanan skeleton. The chemical shift of C-5 (δ 44.3) strongly suggests that the carbonyl group is at C-6. The same carbon would appear at $\delta \approx 34.0$ if the carbonyl group had been at C-8.[3]

The proximity of the methylene group to the proton geminal to the chlorine atom (δ 4.41) is indicated by reciprocating NMR NOE's.

The isolation of two chlorine-containing products from a menispermaceous plant has previously been reported.[4-6] (−)-Acutumine and (−)-acutumidine possess a hasubanan-related skeleton with rearranged rings A and B. The spectral data of 1 are closely related to those for (−)-acutumidine.[4,5] The differences between the two compounds include the absence of an alcoholic function in compound 1 and the presence of the methoxyl group at C-3 instead of at C-2.

The structure and absolute configuration of (−)-acutumidine have been determined by X-ray analysis. However, the presence of the alcoholic hydroxyl at C-10 results in a supplementary asymmetric center in (−)-acutumidine by comparison with clolimalongine. This fact precludes the establishment of the absolute configuration of (+)-clolimalongine (1) by simple comparison of the specific rotations of the two products. The relative configuration at C-10 and C-11 (spiro carbon) can be deduced from the NOE study. Irradiation of the C-1 methylene group (δ 2.62) enhances the H-10 signal (δ 4.41), and irradiation at δ 4.41 enhances the δ 2.62 signal. These results show that the proton geminal to the chlorine atom is on the same side as the methylene group.

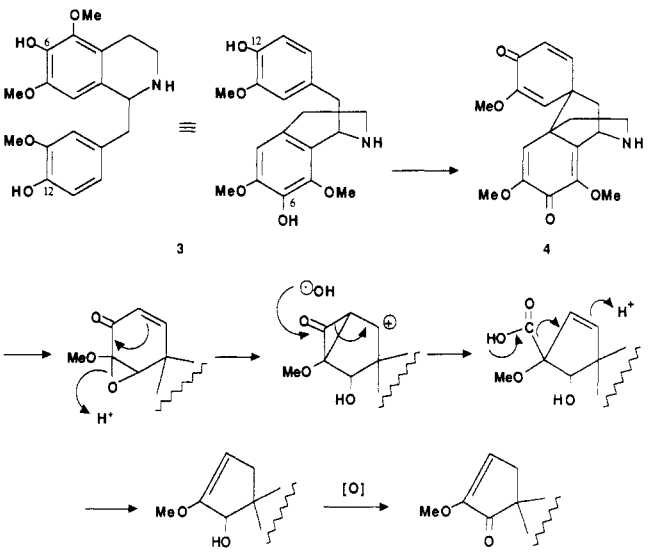
(+)-Limalongine (2) is structurally very close to (+)-



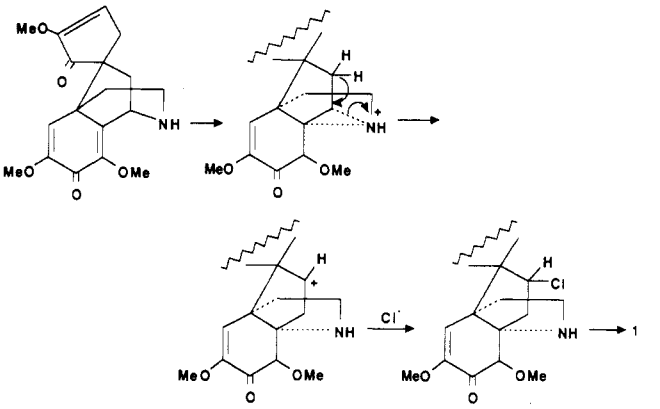
(+)-limalongine (2)

clolimalongine (1). Its mass spectrum has a molecular ion at m/z 333, which is 34 daltons less than for (+)-clolimalongine (1) but the fragmentation patterns presented by the two spectra are similar. The ^1H NMR spectrum for 2 shows several differences due to the absence of the chlorine atom. A $-CH_2CH_2-$ group instead of the $-CHClCH_2-$ appears as four multiplets at δ 1.89, 2.09, 2.10, and 2.39. The C-1 methylene group assumes the form of two doublets of doublets at δ 2.46 and 2.67, so the expected ABX pattern for this system is observed in the case of limalongine instead of the A_2B spin system presented by the same protons in the spectrum of clolimalongine. The specific rotation of 2 is close to that of (+)-clolimalongine (1).

Scheme I



Scheme II



A biogenetic scheme related to the one presented for acutumine[6] is suggested for our two products. The precursor might be a 5,6,7,11,12-pentasubstituted tetrahydrobenzylisoquinoline such as 3 bearing hydroxyl groups at C-6 and C-12. Intramolecular oxidative coupling would lead to bisdienone 4. Further oxidation to an oxirane, followed by a Favorski-type rearrangement, decarboxylation, and oxidation would then afford the cyclopentenone system (Scheme I).

Furthermore, the dienone system of ring C can undergo reductive rearrangement to supply the hasubanan system as indicated in Scheme II. The chloride ion addition in clolimalongine (1) might occur during this transformation. Ring C of limalongine (2) and clolimalongine (1) could be formed by the same reaction sequence as described for the conversion of sinoacutine to sinomenine.[7]

Alkaloids incorporating a chlorine atom are rather unusual. As in the case of acutumine, it is likely that 1 is a real metabolite in the plant.[6]

In addition to (+)-clolimalongine and (+)-limalongine, five known alkaloids were isolated from *L. oblonga* stem bark, one proaporphine, (+)-stepharine, and four oxoaporphines, namely lysicamine, homomoschatoline, imenine, and splendidine. The last two, which are O-methylated at C-4, had been previously isolated only from another menispermaceous species, *Abuta rufescens*.[8]

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Experimental Section

^1H NMR spectra are at 360 MHz (FT) in $CDCl_3$ solution and ^{13}C NMR spectra at 50 MHz on a Bruker SY 200 instrument. The NOE experiments were carried out by FT NOE difference spectroscopy with previously degassed samples.

Alkaloid Extraction and Purification. *L. oblonga* (Miers) Hook. f. & Thoms. was collected in Malaysia, in Jerantut (Pahang), by one of us (B.D.). Vouchers have been preserved at the Bogor Herbarium in Indonesia and at the Museum National d'Histoire Naturelle (Paris) (no. KL 292). Ground stem barks (10 kg) were first extracted with petroleum ether. After drying, the powder was basified with NH_4OH and extracted by methylene chloride using a Soxhlet apparatus. The organic solution was concentrated and extracted with dilute hydrochloric acid. The aqueous solution was basified and reextracted with methylene chloride to furnish 18.6 g of crude alkaloids.

An initial separation was achieved on a Sephadex LH20 column using $CHCl_3$–CH_3OH (30:70) as eluent. Four fractions were collected. (+)-Clolimalongine (1) and (+)-limalongine (2) were abundant in the two first fractions. Further separations were realized by column chromatography, and preparative TLC on Kieselgel 60 Merck article no. 7734, using C_6H_6–$CHCl_3$–CH_3OH (30:60:10) in an NH_3-saturated tank, furnished 1.2 g of 1 and 0.2 g of 2. Purification of the following fractions led to the isolation of (+)-stepharine (0.9 g), lysicamine (4.5 g), homomoschatoline (5.0 g), imenine (0.3 g), and splendidine (0.1 g).

(+)-Clolimalongine (1): $[\alpha]_D$ +300° (c = 0.1, $CHCl_3$); EIMS, m/z (relative intensity) 369 [$(M + 2)^+$, 1.4], 367 (M^+, $C_{18}H_{22}NO_5Cl$, 4), 332 (18), 304 (6), 196 (12), 195 (100), 194 (20), 152 (30); HR EIMS, m/z 367.1164 ($C_{18}H_{22}NO_5Cl$, calcd 367.1187), 332.1536 ($C_{18}H_{12}NO_5$, calcd 332.1498), 304.1557 ($C_{17}H_{22}NO_4$, calcd 304.1750), 208.0998 ($C_{11}H_{14}NO_3$, calcd 208.0974), 196.0923 ($C_{10}H_{14}NO_3$, calcd 196.0973), 195.0873 ($C_{10}H_{13}NO_3$, calcd 194.0799), 152.0698 ($C_8H_{10}NO_2$, calcd 152.0712); UV (MeOH) λ_{max} 265 (log ϵ = 4.10); IR (KBr) (cm^{-1}) 2920, 1715, 1660, 1620, 1450, 1320, 1300, 940, 820; ^1H NMR and ^{13}C NMR (see around structure 1).

Principal NOEs were H-14 (δ 1.97) to H-14 (δ 1.61) (9.8%), H-14 (δ 1.61) to H-14 (δ 1.97) (9.8%), H-5 (δ 2.19) to H-14 (δ 1.61) (3%), H-14 (δ 1.61) to H-5 (δ 2.19) (3%), H-14 (δ 1.61) to H-15 (δ 2.85) (4%), H-15 (δ 2.85) to H-14 (δ 1.61) (3%), H-14 (δ 1.97) to H-15 (δ 3.05) (1.5%), H-14 (δ 1.97) to H-10 (2.9%), H-10 to H-14 (δ 1.97) (2.7%), H-5 (δ 2.36) to H-5 (δ 2.19) (4.4%), H-5 (δ 2.19) to H-5 (δ 2.36) (2.2%), H-9 (δ 2.80) to H-9 (δ 2.46) (8.8%), H-9 (δ 2.46) to H-9 (δ 2.80) (7.3%), H-9 (δ 2.46) to H-10 (2%), H-10 to H-9 (δ 2.46) (2%), H-1 to H-2 (9%), H-2 to H-1 (2.4%), H-9 (δ 2.80) to H-15 (δ 3.05) (2.5%), H-15 (δ 3.05) to H-9 (δ 2.80) (2.5%), H-15 (δ 2.85) to H-15 (δ 3.05) (5%), H-2 to OMe-3 (9.3%), OMe-3 to H-2 (8.8%).

(+)-Limalongine (2): $[\alpha]_D$ +290° (c = 0.15, $CHCl_3$); EIMS, m/z (relative intensity) 333 (M^+, 73), 332 (12), 318 (90), 305 (41), 304 (5), 290 (69), 289 (11), 262 (43), 260 (42), 234 (29), 195 (90), 194 (100), 167 (45), 152 (83), 134 (30); UV (MeOH) λ_{max} 265 (log ϵ = 3.95); IR (KBr) (cm^{-1}) 2920, 1715, 1660, 1620, 1450, 1320, 1300, 940; ^1H NMR and ^{13}C NMR (see around structure 2).

Principal NOE's were OMe-3 to H-2 (8%), H-2 to OMe-3 (9%), H-15 (δ 3.11) to H-15 (δ 2.89) (5%), H-15 (δ 2.89) to H-15 (δ 3.11) (5%), H-15 (δ 3.11) to H-9 (δ 2.09) (3%), H-9 (δ 2.09) to H-15 (δ 3.11) (2.5%), H-1 (δ 2.67) to H-1 (δ 2.46) (5%), H-1 (δ 2.46) to H-1 (δ 2.67) (7%), H-1 (δ 2.67) to H-2 (10%), H-2 to H-1 (δ 2.67) (9%), H-1 (δ 2.46) to H-2 (8%), H-5 (δ 2.19) to H-5 (δ 2.43) (3%), H-5 (δ 2.43) to H-5 (δ 2.19) (3%), H-5 (δ 2.19) to H-14 (δ 1.56) (4%), H-14 (δ 1.56) to H-5 (δ 2.19) (2.5%), H-10 (δ 1.89) to H-9 (δ 2.09) (2%), H-9 (δ 2.09) to H-10 (δ 1.89) (3%), H-10 (δ 2.10) to H-9 (δ 2.39) (3%), H-9 (δ 2.39) to H-10 (δ 2.10) (2%), H-14 (δ 2.02) to H-14 (δ 1.56) (10%), H-14 (δ 1.56) to H-14 (δ 2.02) (10%), H-14 (δ 2.02) to H-15 (δ 3.11) (5%), H-15 (δ 3.11) to H-14 (δ 2.02) (4%), H-10 (δ 1.89) to H-10 (δ 2.10) (5%), H-10 (δ 2.10) to H-10 (δ 1.89) (6%), H-14 (δ 2.02) to H-10 (δ 1.89) (3%), H-10 (δ 1.89) to H-14 (δ 2.02) (2.8%), H-14 (δ 1.56) to H-1 (δ 2.67) (2.5%), H-1 (δ 2.67) to H-14 (δ 1.56) (2.5%).

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Synthesis and Nuclear Magnetic Resonance Spectroscopic Properties of Some 5,10-Dihydrophenophosphazine Derivatives

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The 5,10-dihydrophenophosphazine ring system is easily constructed, and its derivatives were among the first heterocyclic phosphorus compounds to be synthesized. A recent review[1] of the chemistry of this ring system reveals that much of the fundamental work was performed some years ago, without significant use of the powerful techniques of ^{13}C and ^{31}P NMR spectroscopy. The only ^{13}C NMR spectral data reported were obtained for the 5,10-dimethyl derivative and its *P*-oxide.[2] The ^{31}P NMR spectra of the same compounds, as well as of the 2,8-dinitro derivative of the former, have been reported,[3] as have data for some thiophosphoryl derivatives[4] and a spirobisphenophosphazinium salt.[5]

In the present work, ^{13}C and ^{31}P NMR techniques were employed effectively in structural studies of the 5,10-dihydrophenophosphazine system. Some new reactions are reported where the spectroscopic properties of the products are used to prove their structure. Information on solution conformations of heterocyclic phosphorus compounds can be obtained with the aid of the stereospecificity in ^{13}C–^{31}P coupling constants,[6] and analysis of the ^{13}C NMR spectra of several derivatives with tricovalent P has provided the first indications of the conformational preferences at phosphorus for this ring system.

5,10-Dihydrophenophosphazine 10-oxide (2) (Scheme I) is the most important member of the family; it is easily synthesized by first reacting diphenylamine with phosphorus trichloride at 220 °C, followed by hydrolysis of the mixture with hot water. The 10-chloro derivative 1 has been proposed as the intermediate that is being hydrolyzed to the secondary phosphine oxide 2. This has been supported by the formation of tertiary phosphines when alkylmetallics are added to such reaction mixtures before hydrolysis,[7] but the phosphinous chloride 1 has never been directly observed in the medium. We have now accomplished this by examination of the reaction mixture with ^{31}P NMR before the hydrolysis. The only significant signal appeared at δ +59.8 (THF), which can be assigned to 1. Addition of *tert*-butyllithium in THF to the mixture resulted in disappearance of this signal and formation of the tertiary phosphine 3, with ^{31}P NMR δ −20.1 ($CDCl_3$). Proof

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