acetone–water to give 3.5 g (97%) of pure material. A sample for analysis was chromatographed on aluminum oxide (Woelm, neutral, activity grade II) and eluted with ether to afford colorless crystals: mp 54.5–55°; ir (CCl_4), 1575, 1480, 1460, 1390, 1150, 1060, 890, 730 cm^{-1}; nmr (CCl_4), 2.20 (6 H s), 6.41 (2 H d, J = 2), 7.53 (2 H d, J = 2).

Anal. Calcd for $C_{10}H_{10}O_2Hg$: C, 33.08; H, 2.77. Found: C, 32.83; H, 2.76.

3-Methyl-2-(3-methylbutene-2)furan (Rosefuran) (1).—2,2′-Di(3-methylfuryl)mercury (**12**) (5.50 g) in absolute ether (10 ml) was dropped, during 1 hr, into a suspension (−20°) of lithium sand (0.36 g, >50% excess) in ether (10 ml). After the addition was complete the reaction mixture was stirred at −20° for 1 hr. This mixture was then allowed to warm to room temperature and was then stirred for an additional 30 min. The solution of the organolithium compound was forced by helium pressure through a sintered glass disk into a second reaction vessel kept at −20°. 1-Bromo-3-methylbutene (4.50 g) in absolute ether (6 ml) was added through a dropping funnel in the course of 30 min. After the reaction mixture had reached room temperature it was poured into ice cold 15% ethanolic potassium hydroxide (20 ml). The ether was carefully distilled off, and after the mixture had been allowed to reflux for 1.5 hr the hydrolysis of unreacted bromide was complete. To the cold reaction mixture was added ether (30 ml) and the ether solution was washed with water until neutral and free of ethanol. After the solvent had been removed *in vacuo* the residue was distilled giving 1.64 g (36% yield) of rosefuran (**1**): bp 39–40° (1.0 mm); ir absorptions, 1675, 1625, 1510, 1460, 1380, 1160, 1090, 900, 860, 730 cm^{-1}; nmr ($CDCl_3$), 1.74 (6 H d, J = 1), 1.98 (3 H s), 3.31 (2 H d, J = 7.5), 5.34 (1 H t of heptet, J = 7.5, J' = 1), 6.22 (1 H d, J = 2), 7.28 (1 H d, J = 2), mass spectrum, M^+ 150, intense peak at 135.

Anal. Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 79.99; H, 9.45.

Registry No.—**1,** 15186-51-3; **2,** 6138-88-1; **6,** 15135-45-2; **9,** 15135-46-3; **11,** 15136-36-4; **12,** 15136-37-5.

Acknowledgment.—We are indebted to Firmenich et Co., Geneva for generous financial support.

Greenheart Alkaloids. III. Sepeerine (Ocoteamine) and Demerarine[1,2]

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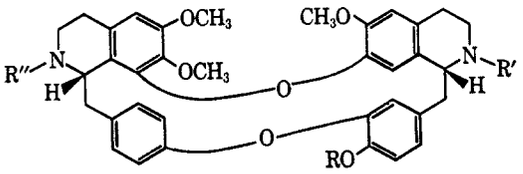
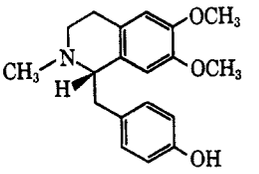
The seven alkaloids which had been isolated from the ether-soluble alkaloids of greenheart bark (*Ocotea rodiaei*) had properties pointing to biscoclaurine structures. Three of these alkaloids, rodiasine, norrodiasine, and dirosine, appeared to have one diphenyl ether linkage[1] and such a structure has recently been determined for rodiasine.[3] The four other alkaloids, ocoteamine, otocamine, demerarine, and ocodemerine, appeared to have two diphenyl ether linkages.[1] The latter alkaloids each had one secondary amino group and ocoteamine and demerarine each had one free phenolic group.

Ocoteamine has an infrared spectrum very similar to that of oxyacanthine (I), a phenolic alkaloid with no secondary amino groups. Methylation with formaldehyde and formic acid gave N-methylocoteamine whose hydrochloride was indistinguishable from that of oxyacanthine (based on infrared spectral comparisons, specific rotations, and distribution coefficients in acetate buffer–chloroform). Ocoteamine is thus a de-N-methyloxyacanthine (II or III).



	R	R′	R″	
I	H	CH_3	CH_3	oxyacanthine
II	H	H	CH_3	ocoteamine, sepeerine
III	H	CH_3	H	
IV	CH_3	H	CH_3	dimethyldaphnoline
V	CH_3	CH_3	H	hydroepistephanine-A

Methylation of the phenolic group of ocoteamine with diazomethane should give O-methylocoteamine of structure IV or V. The hydrochloride of O-methylocoteamine differed from that of authentic hydroepistephanine-A (V)[4] (in specific rotation, distribution coefficient, and R_f in paper chromatography). O-Methylocoteamine, therefore, had to be the same as O,O-dimethyldaphnoline (O,O-dimethyltrilobamine, IV)[5,6] and the specific rotation of the hydrochloride was indeed the same as that reported in the literature. The structure of O-methylocoteamine (IV) was further confirmed by reductive cleavage with sodium in liquid ammonia. This cleavage gave armepavine (VI), which can be obtained from a structure such as IV, but not from V.



VI

Ocoteamine therefore has structure II and is identical with sepeerine, which Grundon and McGarvey isolated from Greenheart.[7] Ocoteamine has a higher melting point (222.5° *vs.* 199°), but the specific rotations are the same and the infrared spectra are practically indistinguishable. The name ocoteamine should therefore be superseded by sepeerine.

Turning now to demerarine, this alkaloid has several properties closely resembling those of ocoteamine. These include the molecular composition, the distribution coefficients in acetate buffer and chloroform, the R_f values in multibuffer chromatography, the infrared spectrum of the phenolic peak,

(1) Part II: P. J. Hearst, *J. Org. Chem.*, **29**, 466 (1964).

(2) Presented in part at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept 1963.

(3) M. F. Grundon and J. E. B. McGarvey, *J. Chem. Soc., Sect. C*, 1082 (1966).

(4) M. Tomita and Y. Watanabe, *Pharm. Bull.* (*Tokyo*), **4**, 124 (1956); and H. Furukawa, *Yakugaku Zasshi*, **86** (3), 253 (1966).

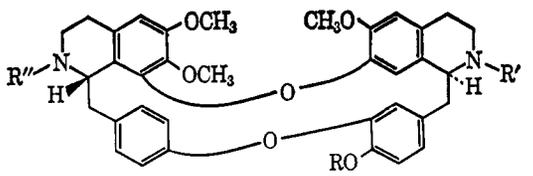
(5) Y. Inubushi, *Pharm. Bull.* (Tokyo), **3**, 384 (1955).

(6) I. R. C. Bick, P. S. Clezy, and M. J. Vernengo, *J. Chem. Soc.*, 4928 (1960).

(7) M. F. Grundon and J. E. B. McGarvey, *ibid.*, 2739 (1960); 2077 (1962).

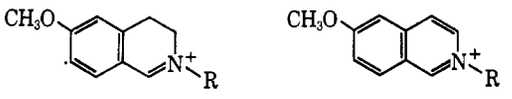
and the number of functional groups (OH, NH, and CH_3O).[1] It therefore appeared that the difference between the two bases could be due simply to a different configuration of one of the two asymmetric carbon atoms.

To clarify this point, demerarine was N-methylated by the Clarke–Eschweiler method and the N-methyldemerarine obtained was found to be identical with repandine (VII) (as shown by corresponding infrared spectra, practically identical mass spectra, and identical R_f values in thin layer chromatography using 12 different solvent systems). Demerarine is thus a de-N-methylrepandine (VIII or IX).



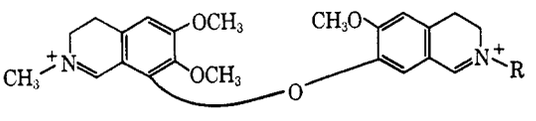
	R	R′	R″	
VII	H	CH_3	CH_3	repandine
VIII	H	H	CH_3	demerarine
IX	H	CH_3	H	

The mass spectrum of demerarine has an important peak at *m/e* 160 which is due to fragment X (R = H) less a hydrogen atom, or possibly XI (R = H). Either fragment could have been obtained from demerarine or from the moiety XII (R = H). The presence of this *m/e* 160 fragment shows that the secondary nitrogen of demerarine must be on the right-hand side of the molecule so that demerarine is VIII and not IX.

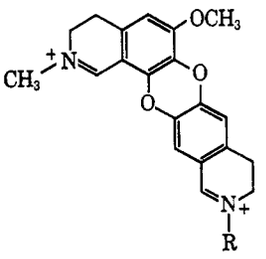


X XI

Other peaks in the mass spectrum of demerarine are consistent with structure VIII and include a molecular ion peak at *m/e* 594 ± 1 (calcd for VIII, 594.7) and a base peak at *m/e* 191 with an isotope peak at *m/e* 191.5. The latter must be due to the doubly charged species XII (R = H) and the corresponding singly charged species gives a peak at *m/e* 382 and also at 381 through loss of a hydrogen atom. Doubly charged fragments of type XII are known to cyclize with elimination of CH_3OCH_3 to



XII



XIII

give XIII[8] and the resultant peak at *m/e* 168 (XIII, R = H) is evident.

The above assignments are confirmed by the mass spectrum of N-methyldemerarine (repandine, VII). This spectrum gives peaks at *m/e* 608 (calcd for VII, 608.7), at 198 and 198.5 (XII, R = CH_3), at 396 and 395, at 175 and 175.5 (XIII, R = CH_3), and at 174. The latter peak probably is due to the fragment X (R = CH_3), less a hydrogen atom, or possibly XI (R = CH_3). These spectral values are all 14 mass units higher than those of the corresponding singly charged fragments from demerarine and 7 mass units higher than those of the corresponding doubly charged fragments from demerarine.

Experimental Section[9]

Ocoteamine.—Ocoteamine hydrochloride[1] had $[\alpha]^{25}D$ + 250° and $[\alpha]^{25}_{5461}$ + 303° (*c* 1.0, water). Treatment of an aqueous solution with ammonium hydroxide gave ocoteamine, which on crystallization from acetone or from benzene melted in a broad range near 180°; recrystallization from methanol gave platelets: mp 221.5–222.5°; $[\alpha]^{25}D$ + 392° (*c* 0.29, chloroform). The infrared spectrum of ocoteamine in chloroform was similar to that of oxyacanthine but lacked a peak at 1380 cm^{-1} and a doublet at 1360 cm^{-1}.

Anal. Calcd for $C_{36}H_{38}N_2O_6$: C, 72.7; H, 6.44; N, 4.71; O, 16.1; $4CH_3O$, 15.7; $1NCH_3$, 2.5. Found: C, 72.7; H, 6.49; N, 4.81; O, 16.7; CH_3O, 15.4; NCH_3, 2.3.

N-Methylocoteamine Hydrochloride.—Ocoteamine (350 mg) was dissolved in 1 ml of 90% formic acid and 1 ml of 37% formalin and was heated on a steam bath under reflux for 3 hr. Water and ammonium hydroxide were added to the reaction mixture and the resultant precipitate was freeze-dried to give 332 mg of crude product. The infrared spectrum of the product in chloroform was very similar to that of oxyacanthine. The product in very dilute hydrochloric acid was treated with saturated sodium sulfate solution and the resultant crystalline product was recrystallized to give 248 mg of the hydrogen sulfate salt. Recrystallization from dilute hydrochloric acid gave 161 mg of long needles of the hydrochloride: $[\alpha]^{25}D$ + 186° (*c* 1.0, water); *K* = 2.59.

O-Methylocoteamine Hydrochloride.—Ocoteamine (1.5 g) in methanol was treated with ethereal diazomethane for 2 days. The product was dissolved in dilute hydrochloric acid and washed with ether. Further addition of hydrochloric acid produced 951 mg (54%) of crystalline product. Recrystallization to constant specific rotation gave 685 mg of long platelets: $[\alpha]^{25}D$ + 263° (*c* 1.0, water); $[\alpha]^{26}D$ + 268° (*c* 0.50, water); $[\alpha]^{26}D$ + 279° (*c* 0.27, water) (lit.[4] $[\alpha]^{20}D$ + 272°, *c* 0.47, water); *K* = 0.47; R_f 0.62 for the free alkaloid with the system amyl alcohol–pyridine–water (110:110:90) on paper impregnated with potassium dihydrogen phosphate.[10]

Anal. Calcd for $C_{37}H_{40}N_2O_6 \cdot 2HCl \cdot H_2O$: C, 63.5; H, 6.34; O, 16.0; $4CH_3O$, 17.8. Found: C, 63.4; H, 6.34; O, 16.4; CH_3O, 17.6.

Cleavage with Sodium in Liquid Ammonia.—O-Methylocoteamine (300 mg obtained from the hydrochloride) in 10 ml of benzene–toluene (1:1) was added in seven portions to 150 ml of liquid ammonia at −40° to which a total of 500 mg of sodium was added to maintain a lasting blue color. Extraction with ether and 5% sodium hydroxide solution gave 21 mg of nonphenolic product and 279 mg of phenolic product. The latter product in 2 ml of ethanol was treated with 2 ml of a saturated alcoholic solution of oxalic acid. Obtained were 196 mg of crystals, which were recrystallized to give 165 mg of armepavine oxalate, mp 215–216° dec. A similar cleavage of cycleanine, mp 274–276°, which had been prepared by the O-methylation[10]

(8) D. C. DeJongh, S. R. Shrader, and M. P. Cava, *J. Amer. Chem. Soc.*, **88**, 1052 (1966).

(9) Melting points were corrected and were determined in evacuated capillaries or on a hot stage under a blanket of nitrogen; microanalyses were performed by Dr. W. Zimmermann, University of Melbourne, Australia; distribution coefficients, *K*, were determined according to the method of ref 1, using 0.5 *M* acetate buffer, pH 4.15, and chloroform. The mass spectra were obtained on a Nuclide single beam spectrometer, 12-90-G1.1.

(10) D. A. A. Kidd and J. Walker, *J. Chem. Soc.*, 669 (1954).

of isochondrodendrine[11] in benzene–methanol, gave armepavine oxalate, mp 211–213° (lit. mp 211–212° uncor[5] and mp 209° [6]).

Demerarine.—Demerarine hydrochloride[1] had $[\alpha]^{25}D$ − 181°, $[\alpha]^{25}_{5461}$ − 219° (*c* 1.0, water). Treatment of an aqueous solution with ammonium hydroxide gave demerarine which crystallized in needles from methanol: mp 222–223°; $[\alpha]^{25}D$ − 162° (*c* 0.35, 5% methanol in chloroform). The mass spectrum exhibited a molecular ion peak at *m/e* 594 ± 1 in accord with the molecular formula $C_{36}H_{38}N_2O_6$. Other important peaks were at *m/e* 168, 191, 381, and 382.

N-Methyldemerarine.—Demerarine (100 mg) in 0.5 ml of formic acid and 0.5 ml of formalin was heated in a steam bath for 4 hr. Treatment with water and ammonia gave a precipitate which on drying weighed 91 mg. The infrared spectrum in a KBr pellet was the same as that of a sample of repandine. In thin layer chromatographic comparisons on silica gel (Adsorbosil-1), using 12 different solvent systems, N-methyldemerarine and repandine had the same R_f values. The mass spectra of the two alkaloids were identical showing a molecular ion peak at *m/e* 608 ± 1 in accord with the molecular formula $C_{37}H_{40}N_2O_6$.

Oxyacanthine Hydrochloride.—The addition of saturated sodium sulfate solution to a solution of commercial "oxyacanthine hydrochloride tetrahydrate" (Fluka AG. Buchs, Switzerland) gave platelets of oxyacanthine sulfate. The product was recrystallized from water and was converted into oxyacanthine hydrochloride by the addition of hydrochloric acid to an aqueous solution: $[\alpha]^{25}D$ + 188° (*c* 1.0, water); K = 2.36.

Hydroepistephanine-A Hydrochloride.—A sample of epistephanine in sulfuric acid and ethanol was reduced with zinc dust by the method of Tomita and Watanabe.[4] Hydroepistephanine-A hydrochloride was obtained in small, long rods: $[\alpha]^{24}D$ + 300° (*c* 0.27, water) (lit.[4] $[\alpha]^{29}D$ + 298°, *c* 0.24, water); K = 1.03; R_f 0.58 for the free alkaloid with the system amyl alcohol–pyridine–water (110:110:90) on buffered paper.[10]

Registry No.—II, 6787-93-5; VIII, 15353-21-6; N-methylocoteamine HCl, 15352-74-6; O-methylocoteamine HCl, 15352-75-7; N-methyldemerarine, 15352-76-8.

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(11) H. McKennis, Jr., P. J. Hearst, R. W. Drisko, T. Roe, Jr., and R. L. Alumbaugh, *J. Amer. Chem. Soc.*, **78**, 245 (1956).

Solvent Effects in the Chlorination of Isobutyl Chloride and *t*-Butyl Chloride[1]

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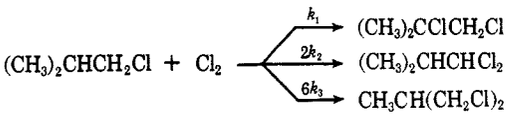
Russell[2] reported that in the photochlorination of 2,3-dimethylbutane at 25° the relative reactivities of the primary and tertiary hydrogen atoms varied from 4.2 in pure carbon tetrachloride to 225 in 12 *M* carbon disulfide. The relative reactivities of covalently bound hydrogen atoms to photochlorination in different solvents have been determined for other compounds such as *n*-pentane,[3] *n*-butyl chloride,[4] hexanoyl chloride,[5] *n*-heptane,[6] octanoyl chloride,[6] and chlorocyclopentane;[7] relationships between the nature of the solvent and the relative reactivities of the hydrogen atoms being abstracted have been developed. Our purpose in this investigation was to apply these principles to the chlorination of isobutyl chloride in order to obtain a better understanding of the transition state.

Isobutyl chloride in mixed solvents of different compositions was allowed to react photochemically with a small amount of chlorine and the products were separated and measured quantitatively by gas chromatography. The results are shown in Table I.

TABLE I
SOLVENT EFFECTS IN THE CHLORINATION OF ISOBUTYL CHLORIDE[a]



Solvents	Concn of second solvent, mol/l.	k_1/k_2[b]	k_1/k_2[b]	k_3/k_2[b]
CCl_4	...	4.5	6.1	1.35[c]
CCl_4–CS_2	1.2	8.8	8.7	0.99
CCl_4–CS_2	2.2	11.4	10.2	0.90
CCl_4–CS_2	3.8	14.4	11.6	0.81
CCl_4–CS_2	6.2	19.7	13.6	0.69
CCl_4–CS_2	8.5	24.3	14.6	0.60
CCl_4–CS_2	9.2	24.3	14.8	0.61
CCl_4–CS_2	11.2	27.2	15.0	0.55
CS_2	...	29.1	15.3	0.53
CCl_4–C_6H_6	1.3	8.4	9.2	1.10
CCl_4–C_6H_6	2.5	11.2	10.6	0.95
CCl_4–C_6H_6	3.7	13.3	11.7	0.88
CCl_4–C_6H_6	5.0	15.7	12.5	0.80
CCl_4–C_6H_6	6.3	17.4	12.6	0.72
CCl_4–C_6H_6	7.4	19.6	*d*	*d*

[a] Each solution contained 0.87 g of isobutyl chloride and 0.024 g of chlorine in a total volume of 4.2 ml. [b] Each value is the result of four or five determinations; the average deviation of each value is ±3%. [c] E. M. Hodnett and P. S. Juneja, *J. Org. Chem.*, **32**, 4114 (1967). [d] Not determined because of experimental difficulties.

For further comparison, mixtures of isobutyl chloride and *t*-butyl chloride were chlorinated in the same solvents under the same conditions; the results are shown in Table II.

Russell[2,8] has suggested that relative reactivities that are determined mainly by the availability of electrons in the carbon–hydrogen bond are not particularly sensitive to solvent effects while relative reactivities that are determined mainly by the stabilities of the incipient free radicals are very sensitive to changes in solvent. This is because in solvents which complex chlorine atoms the transition state has more radical character and therefore is influenced

(1) Abstracted in part from the Ph.D. dissertation of P. S. J., Oklahoma State University, May 1967.
(2) G. A. Russell, *J. Amer. Chem. Soc.*, **80**, 4987 (1958).
(3) G. A. Russell, *ibid.*, **80**, 4997 (1958).
(4) C. Walling and M. F. Mayahi, *ibid.*, **81**, 1485 (1959).
(5) H. J. den Hertog and P. Smit, *Proc. Chem. Soc.*, 132 (1959).
(6) P. Smit and H. J. den Hertog, *Rec. Trav. Chim.*, **83**, 891 (1964).
(7) G. A. Russell, A. Ito, and R. Konako, *J. Amer. Chem. Soc.*, **85**, 2988 (1963).
(8) G. A. Russell, *Tetrahedron*, **8**, 101 (1960).