# Structures of Ememogin and Trichorabdonin, Minor Diterpenoids from *Rabdosia trichocarpa*

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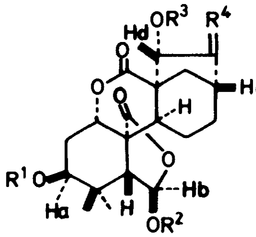
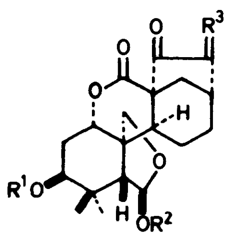
The structures of ememogin and trichorabdonin, minor constituents of the leaves of *Rabdosia trichocarpa*, have been elucidated from spectroscopic and chemical evidence. Enmein has been converted into trichorabdonin diacetate and trichorabdonin.

*Rabdosia trichocarpa* Kudo[1] leaves contain in addition to many diterpenoids of known structure,[2] *e.g.* enmein (6), dihydroenmein (7), and the trichorabdals A—G,[3] many compounds of unknown structure, *e.g.* the diterpene ememogin (1). Much information on the biological activity of these compounds has been accumulated in recent years.[4]

In the course of our studies on the biologically active substances of the *Rabdosia* (Labiatae) plants, we examined the minor constituents of *Rabdosia trichocarpa* collected in Ishikawa Prefecture, Japan and isolated a new diterpene, trichorabdonin (16), together with ememogin (1). Here we describe the isolation and structural elucidation of these two diterpenes.



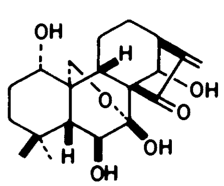

(1) $R^1 = R^2 = R^3 = H$, $R^4 = C{<}^{He}_{Hf}$
(2) $R^1 = R^2 = R^3 = Ac$, $R^4 = C{<}^{He}_{Hf}$
(3) $R^1 = R^2 = R^3 = Ac$, $R^4 = \alpha$-Me, $\beta$-H
(4) $R^1 = R^2 = R^3 = H$, $R^4 = \alpha$-Me, $\beta$-H
(5) $R^1 = R^2 = Ac$, $R^3 = H$, $R^4 = \alpha$-Me, $\beta$-H



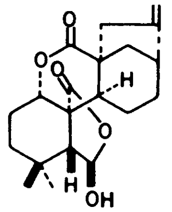

(6) $R^1 = R^2 = H$, $R^3 = \alpha$-Me, $\beta$-H
(7) $R^1 = R^2 = H$, $R^3 = CH_2$
(8) $R^1 = R^2 = Ac$, $R^3 = CH_2$
(9) $R^1 = R^2 = Ac$, $R^3 = \alpha$-Me, $\beta$-H

Dried *R. trichocarpa* leaves were extracted with methanol and the enmein (7) almost completely removed from the extract; from the remaining extract two diterpenes, ememogin (1) (0.0015%) and trichorabdonin (16) (0.0005%), together with the known dihydroenmein (6) and oridonin (10), were obtained.

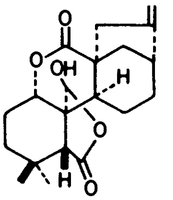
Ememogin (1) was assigned the molecular formula $C_{20}H_{26}O_7$ on the basis of its elemental analysis and high resolution mass spectrum. It contains a γ-lactone ($\nu_{max.}$ 1 745 $cm^{-1}$), a δ-lactone ($\nu_{max.}$ 1 705 $cm^{-1}$), an *exo*-methylene [$\nu_{max.}$ 1 650 $cm^{-1}$; $\delta_H$ 5.48 and 5.60 (each 1 H, m); $\delta_C$ 108.8 (t) and 159.2 (s)], and a hemiacetal group [$\delta_H$ 5.89 (1 H, s); $\delta_C$ 98.6 (d)]. The $^1H$ and $^{13}C$ n.m.r. spectra showed the presence of two secondary hydroxy-bearing carbons [$\delta_H$ 3.79 (m) and 5.12 (m); $\delta_C$ 77.9 and 74.5 or 70.6 (each d)] and two tertiary methyl groups [$\delta_H$ 1.00 and 1.40; $\delta_C$ 22.7 and 26.6 (each q)]. On the other hand, the $^1H$ n.m.r. spectrum of (1) did not show AB type signals characteristic of *Rabdosia* diterpenoids such as enmein (7) and oridonin (10). From these spectral data we deduced that ememogin (1) is pentacyclic and has an enmein structure of the *ent*-6,7-secokaurane type, (11) or (12), to which two secondary hydroxy groups have been added (considering the structures of diterpenoids isolated so far from the genus *Rabdosia*). Acetylation of (1) with acetic anhydride and pyridine gave the triacetate (2) [$\delta_H$ 2.06 (3 H, s) and 2.10 (6 H, s)] whose i.r. spectrum showed an absorption at $\nu_{max.}$ 1 800 $cm^{-1}$ due to the γ-lactone carbonyl group, supporting the assumption that (1) contains the lactonol function as a partial structure. Thus, the dihydro triacetate (3), which was obtained by catalytic hydrogenation followed by acetylation, was subjected to Jones oxidation to give an acid anhydride (13) ($\nu_{max.}$ 1 860, 1 790, and 1 750 $cm^{-1}$). The location of secondary hydroxy groups including the lactonol hydroxy group were determined as follows. The chemical shift of $H_a$ (δ 3.79) was very similar to that of 3α-H in enmein (7) and the corresponding signals in ememogin triacetate (2) (δ 4.88) showed almost the same chemical shift and coupling pattern as those of enmein diacetate (8). These results suggest that a hydroxy group is located at the 3β-position. This was verified by n.O.e. experiments with dihydroememogin triacetate (3). On irradiation at the frequency of 19-$H_3$ (δ 1.01), a n.O.e. (7.4%) was observed for $H_a$ (δ 4.90). Another hydroxy group was assigned to C-15 from the results of spin-spin decoupling experiments for ememogin triacetate (2). On irradiation of $H_d$ (δ 6.18) and $H_e$ (δ 5.14), the signals of $H_e$ and $H_f$ (δ 4.96), and those of $H_d$ and $H_c$ (δ 2.84), respectively, sharpened. Further, on irradiation of $H_c$, the signals of $H_e$ and $H_f$ collapsed to a doublet (*J* 2 Hz). Accordingly, $H_d$ was assigned to 15-H which can undergo allylic coupling with protons of the *exo*-methylene group. On irradiation at the frequencies of 18-$H_3$ (δ 1.12), 19-$H_3$ (δ 1.02), and 5-H (δ 2.52), n.O.e.'s (16.7, 17.5, and 7%, respectively) for $H_b$ (δ 6.32) were observed for ememogin triacetate (2). These results support the assignment of the structure (14) for ememogin. The configuration of the 15-hydroxy group and the absolute stereochemistry were determined from the fact that a dihydro ketone (15), m.p. 255—257 °C, was obtained on treatment of (14) with 15% HCl–MeOH (the conditions for the garryfoline-cuauchichicine rearrangement[5]), and that this compound showed a negative Cotton effect in the o.r.d. spectrum. On the basis of these findings, the structure and absolute stereochemistry of ememogin should be represented as (**1**).



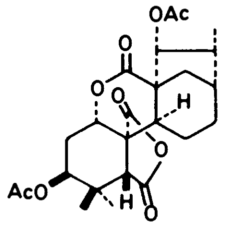
(**10**)



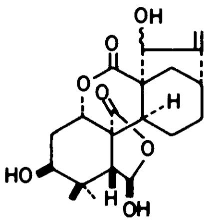
(**11**)



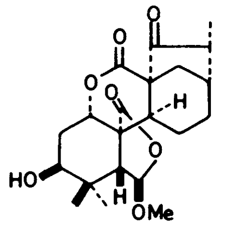
(**12**)



(**13**)



(**14**)



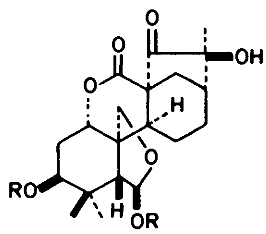
(**15**)

Trichorabdonin (**16**) was obtained and assigned the molecular formula $C_{20}H_{28}O_7$ on the basis of elemental analysis and its high resolution mass spectrum. Trichorabdonin (**16**) contains a five-membered ketone group [$\nu_{max.}$ 1 750 cm$^{-1}$; $\delta_C$ 212.7 (s)], δ-lactone [$\nu_{max.}$ 1 700 cm$^{-1}$; $\delta_H$ 5.46 (1 H, dd, *J* 10 and 6 Hz)], and a hemiacetal group [$\delta_H$ 5.89 (1 H, s); $\delta_C$ 102.9 (d)]. The $^1$H n.m.r. spectrum of (**16**) further showed the presence of a secondary carbinyl proton (δ 3.80, 1 H, m), an oxygenated methyl group [δ 4.37 and 4.57 (1 H, d, *J* 9 Hz)] adjacent to a quaternary carbon, and three tertiary methyl groups (δ 1.06, 1.36, and 1.48). These data suggest that trichorabdonin (**16**) is an enmein type diterpenoid of pentacyclic 6,7-*seco*-*ent*-kaurane type. However, the compound does not show an absorption maximum above 220 nm in the u.v. spectrum, suggesting the absence of a five-membered ketone conjugated with the *exo*-methylene. The $^1$H n.m.r. spectrum of trichorabdonin (**16**) is very similar to that of dihydroenmein (**6**) except for a signal at δ 1.48 (3 H, s) due to a tertiary methyl group, which was observed at δ 0.98 (3 H, d, *J* 6 Hz) in (**6**). Considering the chemical shift of this methyl signal, and the elemental composition of trichorabdonin, trichorabdonin was assigned structure (**16**) which corresponds to the 16-hydroxydihydroenmein except for the stereochemistry at C-16. Further, the $^{13}$C n.m.r. spectra of trichorabdonin (**16**) and dihydroenmein (**6**) (Table) were compatible except for the signals due to the carbons of the D-ring. Acetylation of (**16**) with acetic anhydride–pyridine (room temperature, 10 h) gave only the diacetate (**17**) [$\delta_H$ 2.11 and 1.99 (each 3 H, s)] which still contains a hydroxy group ($\nu_{max.}$ 3 500 cm$^{-1}$). Since the scarcity of the sample prevented us from further characterization, we tried to convert enmein (**7**), the absolute

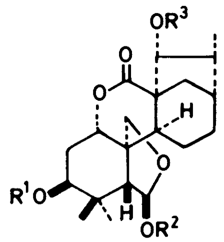
**Table.** $^{13}$C N.m.r. data[a] for trichorabdonin (**16**) and dihydroenmein (**6**).

| Carbon | (**16**) | (**6**) |
|---|---|---|
| 1 | 74.4 | 74.2 |
| 2 | *b* | *b* |
| 3 | 75.1 | 75.6 |
| 4 | 36.3 | 35.8 |
| 5 | 51.7 | 50.9 |
| 6 | 102.9 | 102.3 |
| 7 | 172.9 | 172.8 |
| 8 | 57.7 | 57.3 |
| 9 | 48.4 | 49.2 |
| 10 | 50.5 | 49.8 |
| 11 | *b* | *b* |
| 12 | *b* | *b* |
| 13 | 41.8 | 32.9 |
| 14 | *b* | *b* |
| 15 | 212.7 | 215.2 |
| 16 | 78.6 | 47.1 |
| 17 | 20.4 | 10.6 |
| 18 | 28.8 | 28.3 |
| 19 | 23.7 | 23.3 |
| 20 | 75.0 | 74.6 |
| *b* | 32.0, 31.4 | 34.5, 30.8 |
| | 22.5, 20.0 | 19.4, 19.2 |

[a] Measured for $C_5D_5N$ solutions. [b] These signals were not assigned.

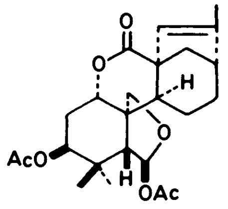


(**16**) R = H
(**17**) R = Ac

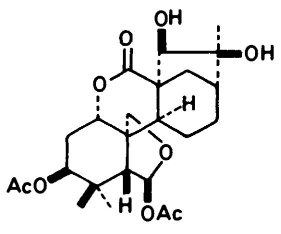


(**18**) $R^1 = R^2 = R^3 = H$
(**19**) $R^1 = R^2 = Ac$, $R^3 = H$
(**20**) $R^1 = R^3 = H$, $R^2 = Ac$
(**21**) $R^1 = R^2 = R^3 = Ac$

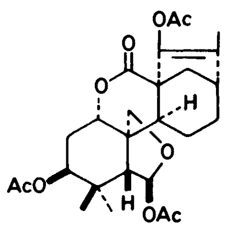
stereochemistry of which has already been established, into the trichorabdonin derivative by two routes. Tetrahydroenmein (**18**)[2a] was partially acetylated with acetic anhydride–pyridine to give the 3,6-diacetate (**19**) which was then dehydrated with phosphoryl chloride–pyridine to give an olefin (**22**) [$\delta_H$ 1.74 (3 H, s, 16-Me)]. The olefin was oxidized with osmium tetraoxide–pyridine to give a *cis*-glycol (**23**) [$\delta_H$ 3.68 (1 H, s, 15-H); $\nu_{max.}$ 3 450, 3 400sh, and 3 300 cm$^{-1}$]. From inspection of a Dreiding model, the reagent could be expected to attack from the less hindered β-side. Thus, the configuration of the resulting glycol should be β. Oxidation of (**23**) with dimethyl sulphoxide–acetic anhydride gave a hydroxy ketone which was identical with trichorabdonin diacetate (**15**). This result proved that the configuration of the 16-hydroxy group is β and that the structure and absolute stereochemistry of trichorabdonin (**16**) should be represented as shown. We also tried an alternative route which requires fewer steps and results in a higher yield of product. Thus, dihydroenmein (**6**) was treated with acetic anhydride–boron trifluoride–diethyl ether to give two compounds, together with the known dihydroenmein diacetate (**9**) in the proportion 9:3:4. The major product, $C_{26}H_{34}O_9$, was found to be the enol triacetate (**24**) from the fact that the signal due to the 16-methyl group was observed at δ 1.57 (3 H, s) in the $^1$H n.m.r. spectrum, and that the signals due to C-15 and C-16 were observed at δ 147.5 (s) and 132.5 (s) in the $^{13}C$ n.m.r. spectrum. A further product, $C_{26}H_{34}O_9$, showed signals due to two acetoxy groups (δ 2.01 and 2.10), an acetyl group (δ 2.32), and three tertiary methyl groups (δ 1.05, 1.07, and 1.33) together with signals due to 6-H, 3-H, 1-H, and 20-$H_2$ in the $^1H$ n.m.r. spectrum. The $^{13}C$ n.m.r. spectrum of this compound showed an additional signal (δ 203.7 p.p.m.) in the carbonyl region when compared with the spectrum of dihydroenmein diacetate (**6**). From these data, this compound was assigned structure (**25**). The configuration at C-16 was tentatively assigned as shown, by considering the reaction mechanism. Oxidation of the enol triacetate (**24**) with *m*-chloroperbenzoic acid gave a β-epoxide (**26**) as a result of less hindered side attack of the reagent. Alkaline hydrolysis of (**26**) gave trichorabdonin (**16**), the physical properties of which were identical with those of the naturally occurring substance.



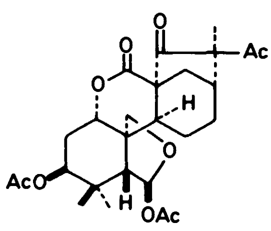

(**22**)



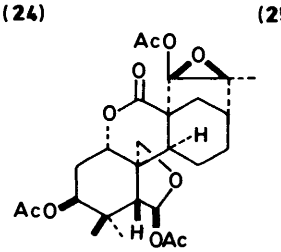

(**23**)




(**24**)




(**25**)




(**26**)

## Experimental

M.p.s were taken on a Yanagimoto melting point apparatus and are uncorrected. I.r. spectra were recorded on Hitachi EPI-S2 or Hitachi 215 spectrometers. $^1H$ and $^{13}C$ N.m.r. spectra were taken with JEOL PS 100, FX 100, or JNM FX 200 spectrometers. Chemical shifts are given in δ (p.p.m.) from tetramethyl silane as internal standard. Mass spectra were determined on a JEOL JMS D-300 spectrometer. Optical rotations and o.r.d. were taken on a spectrophotometer, JASCO Model ORD/UV-5. Kieselgel 60 (0.05—0.2000 mm, Merck) was used for column chromatography and precoated silica gel plates $F_{254}$ (0.25 mm and 0.5 mm in thickness) were used for t.l.c. Extracts were dried over anhydrous sodium sulphate or magnesium sulphate.

*Isolation of Diterpenoids from* Rabdosia trichocarpa.—Dried leaves of *R. trichocarpa* (27.5 kg) were refluxed three times with tenfold volumes of methanol. The methanolic extract was concentrated under reduced pressure, the resulting precipitate filtered off, and the mother liquor evaporated. The addition of further methanol resulted in crude crystalline enmein (162 g) which was filtered off. The mother liquor was concentrated under reduced pressure and the residue partitioned between ethyl acetate and water. The ethyl acetate layer was dried and evaporated under reduced pressure to give a syrup (614.7 g) which was chromatographed on a silica gel (2.5 kg) column with chloroform–acetone as eluant, with increasing acetone content. The eluate from 10% acetone–chloroform was recrystallized from methanol to give dihydroenmein (**6**) (864 mg) [which was contaminated ($^1H$ n.m.r.) with 25% of enmein (**5**)]. The eluate (15.55 g) from 15—20% acetone–chloroform was recrystallized three times to give ememogin (**1**) (409 mg). The eluate (60.5 g) from 20% acetone–chloroform showed an $R_F$ value near that of oridonin (**10**). The eluate was rechromatographed on a silica gel (1.5 kg) column with chloroform–methanol with increasing methanol content. The eluate from 5% methanol–chloroform which showed an $R_F$ value of 0.12 (chloroform–acetone 7:3) gave trichorabdonin (**16**) (132 mg). The mother liquor of ememogin and trichorabdonin, and the fractions which contained mainly oridonin (**10**) were combined and evaporated under reduced pressure. The residue (17 g) was rechromatographed on a silica gel (400 g) column with chloroform and acetone with increasing acetone content. The eluate from 20% acetone–chloroform was recrystallized from methanol to give oridonin (**10**) (1.66 g). The physical properties of the isolated diterpenoids are as follows.

*Dihydroenmein* (**6**). Colourless needles, m.p. 288—290 °C (from methanol); $\nu_{max.}$(KBr) 3 400, 1 750, and 1 705 $cm^{-1}$; $\delta_H$ ($C_5D_5N$) 0.98 (3 H, d, *J* 6 Hz, 16-Me), 1.04 and 1.34 (each 3 H, s, tert. $Me_2$), 2.70 (1 H, s, 5-H), 2.88 (1 H, dd, *J* 6 and 10 Hz, 9-H), 3.80 (1 H, m, 3-H), 4.32 and 4.55 (each 1 H, AB d, *J* 8 Hz, 20-$H_2$), 5.87 (1 H, s, 6-H), 6.80 (1 H, d, *J* 4 Hz, OH), and 8.24 (1 H, br s, OH).

*Ememogin* (**1**). Colourless needles, m.p. > 300 °C (from methanol), $[\alpha]_D^{24}$ −145.8° (*c* 0.20 in pyridine); $\nu_{max.}$(KBr) 3 400, 3 250, 1 745, 1 705, and 1 650 $cm^{-1}$; $\delta_H$($C_5D_5N$) 1.00 and 1.36 (each 3 H, s, tert. $Me_2$), 3.05 (1 H, s, 5-H), 3.79 (2 H, m, 3-H + 1 H), 5.12 (1 H, m, 15-H), 5.52 and 5.63 (each 1 H, br s, 17-$H_2$), 5.55 (1 H, dd, *J* 6 and 12 Hz, 1-H), 6.12 (1 H, s, 6-H), 7.00 (1 H, d, *J* 4 Hz, OH), and 7.36 (1 H, s, OH); $\delta_C$($C_5D_5N$) 176.5 (C-20), 175.2 (C-7), 159.2 (C-16), 108.8 (C-17), 98.6 (C-6), 77.9 (C-15), 74.5 and 70.6 (C-3 and/or C-1), 52.2 (C-8), 48.7 (C-5), 46.9 (C-10), 37.3 and 37.0 (C-13 and/or C-9), 36.3 (C-4), 34.1 (t), 32.6 (t), 32.5 (t), 26.6 (C-18), 22.7 (C-19), and 17.8 (t) (Found: C, 63.5; H, 7.1. $C_{20}H_{26}O_7$ requires C, 63.48; H, 6.93%). This compound was identified by comparison with the i.r. spectrum of an authentic sample of ememogin.

*Trichorabdonin* (**16**). Colourless needles, m.p. > 300 °C (from methanol), $[\alpha]_D^{24}$ −75.0° (*c* 0.12 in methanol); $\nu_{max.}$(KBr) 3 300, 1 750, and 1 700 $cm^{-1}$; $\delta_H$($C_5D_5N$) 1.06 and 1.36 (each 3 H, s, tert. $Me_2$), 1.48 (3 H, s, 16-Me), 2.75 (1 H, s, 5-H), 3.82 (1 H, m, 3-H), 4.37 and 4.57 (each 1 H, ABd, *J* 9 Hz, 20-$H_2$), 5.46 (1 H, dd, *J* 6 and 10 Hz, 1-H), 5.89 (1 H, s, 6-H), 6.80 (1 H, br s, OH), and 8.24 (1 H, br s, OH); $^{13}C$ n.m.r. data are listed in the Table (Found: C, 63.2; H, 7.6. $C_{20}H_{28}O_7$ requires C, 63.14; H, 7.42%).

*Oridonin* (**10**). Colourless needles, m.p. 238—242 °C (from methanol); $\nu_{max.}$(KBr) 3 270, 3 190, 1 700, and 1 635 $cm^{-1}$; $\delta_H$($C_5D_5N$) 1.12 and 1.28 (each 3 H, s, tert. $Me_2$), 3.20 (1 H, d, *J* 8 Hz, 13-H), 3.64 (1 H, t, *J* 8 Hz, 1-H), 4.24 (1 H, dd, *J* 7 and 10 Hz, 6-H), 4.38 and 4.76 (each 1 H, ABd, *J* 10 Hz, 20-$H_2$), 5.30 (1 H, br s, 14-H), 5.48 and 6.25 (each 1 H, br s, 17-$H_2$), 5.90 (1 H, m, OH), 6.90 (1 H, d, *J* 10 Hz, 6-OH), 7.38 (1 H, m, OH), and 9.06 (1 H, m, OH). This compound was identified by comparison with an authentic sample of oridonin (mixed m.p. and i.r. and $^1H$ n.m.r. spectra).

*Ememogin Triacetate* (**3**).—Ememogin (**1**) (20 mg) dissolved in anhydrous pyridine (0.4 ml) and acetic anhydride (0.4 ml) was kept overnight at room temperature. Excess of methanol was added to the reaction mixture and the solvent was removed under reduced pressure. The residue (28 mg) was purified on a silica gel (5 g) column, with diethyl ether as eluant, to give a syrupy triacetate (**2**) (23.8 mg); $\nu_{max.}$($CHCl_3$) 1 800, 1 760, and 1 660w cm$^{-1}$; $\delta_H$($CDCl_3$) 1.02 and 1.12 (each 1 H, s, tert. $Me_2$), 2.06 (3 H, s, Ac), 2.12 (6 H, s, $Ac_2$), 2.52 (1 H, s, 5-H), 2.84 (1 H, 13-H), 4.78 (1 H, dd, *J* 6 and 10 Hz, 1-H), 4.88 (1 H, m, 3-H), 4.96 and 5.14 (each 1 H, m, 17-$H_2$), 6.18 (1 H, m, 15-H), and 6.32 (1 H, s, 6-H) (Found: $M^+$, 504.1967. $C_{26}H_{32}O_6$ requires *M*, 504.1995).

*Dihydroememogin* (**4**).—$PtO_2$ (1 mg) was added to a solution of ememogin (20 mg) dissolved in methanol (2 ml), and the mixture was hydrogenated for 1 h. The catalyst was filtered off and the solvent evaporated under reduced pressure to give a residue (20.4 mg) which was recrystallized from methanol to give dihydroememogin (**4**) as colourless needles, m.p. 272—275 °C; $\nu_{max.}$(KBr) 3 400, 1 750, and 1 705 cm$^{-1}$; $\delta_H$($C_5D_5N$) 0.97 and 1.34 (each 3 H, s, tert. $Me_2$), 1.05 (3 H, d, *J* 8 Hz, 16-Me), 3.00 (1 H, s, 5-H), 3.72 (1 H, m), 3.80 (1 H, m), 5.36 (1 H, d, *J* 10 Hz, 15-H), 5.46 (1 H, dd, *J* 6 and 11 Hz, 1-H), 6.02 (1 H, s, 6-H), and 6.84 (1 H, s, OH); *m/z* 380 ($M^+$).

*Dihydroememogin Diacetate* (**5**).—Dihydroememogin (30 mg) dissolved in anhydrous pyridine (0.3 ml) and acetic anhydride (0.3 ml) was kept for 4 h at room temperature. Work-up as before gave a residue (43.5 mg) which was purified on a silica gel (4 g) column with diethyl ether as eluant to give the diacetate (**5**) (19.6 mg) as a syrup; $\nu_{max.}$($CHCl_3$) 3 600, 3 400, 1 790, and 1 740 cm$^{-1}$; $\delta_H$($CDCl_3$) 0.88 (3 H, d, *J* 7 Hz, 16-Me), 1.00 and 1.10 (each 3 H, s, tert. $Me_2$), 2.10 and 2.14 (each 3 H, s, $Ac_2$), 2.50 (1 H, s, 5-H), 2.98 (1 H, dd, *J* 4 and 12 Hz, 9-H), 4.74 (1 H, dd, *J* 6 and 12 Hz, 1-H), 4.80 and 4.90 (each 1 H, m, 3-H and/or 15-H), and 6.36 (1 H, s, 6-H) (Found: $M^+$, 464.2041. $C_{24}H_{32}O_9$ requires *M*, 464.2045).

*Dihydroememogin Triacetate* (**3**).—Dihydroememogin diacetate (**5**) (20 mg) dissolved in anhydrous pyridine (0.2 ml) and acetic anhydride (0.2 ml) was stirred at 30 °C for 5.5 days. Work-up as before gave a residue (20.7 mg) which was purified on a silica gel (2.5 g) column with diethyl ether as eluant to give the triacetate (**3**) (18.9 mg) as a syrup; $\nu_{max.}$($CHCl_3$) 1 795, 1 750, and 1 740 cm$^{-1}$; $\delta_H$($CDCl_3$) 0.80 (3 H, d, *J* 8 Hz, 16-Me), 1.01 and 1.10 (each 3 H, s, tert. $Me_2$), 2.02, 2.11, and 2.15 (each 3 H, s, $Ac_3$), 2.50 (1 H, s, 5-H), 4.74 (1 H, s, dd, *J* 6 and 12 Hz, 1-H), 4.90 (1 H, dd, *J* 2 and 4 Hz, 3-H), and 5.80 (1 H, d, *J* 11 Hz, 15-H) (Found: $M^+$, 506.2147. $C_{26}H_{34}O_{10}$ requires *M*, 506.2151).

*Jones Oxidation of Dihydroememogin Triacetate* (**3**).—Jones reagent (0.1 ml) was added to a solution of dihydroememogin triacetate (**3**) (14.2 mg) dissolved in acetone (1 ml), and the mixture was stirred for 11.5 days; further Jones reagent (total 0.5 ml) was added during this period. Subsequently, excess of water was added to the mixture which was then extracted with chloroform (12 ml × 3). The chloroform extract was washed with saturated aqueous sodium hydrogen carbonate and water, dried, and evaporated to give a residue (7.0 mg) which was purified on a silica gel plate (solvent: chloroform–acetone 20:1, developed twice) to give the anhydride (**13**) (3.2 mg). Recrystallization from chloroform–methanol gave colourless needles, m.p. 127—130 °C, $\nu_{max.}$($CHCl_3$) 1 860, 1 790, and 1 750 cm$^{-1}$; $\delta_H$($CDCl_3$) 0.79 (3 H, d, *J* 8 Hz, 16-Me), 1.09 and 1.18 (each 3 H, s, tert. $Me_2$), 2.05 and 2.14 (each 3 H, s, $Ac_2$), 3.02 (1 H, s, 5-H), 4.07 (1 H, dd, *J* 6 and 12 Hz, 1-H), 5.03 (1 H, dd, *J* 2 and 4 Hz, 3-H), and 5.83 (1 H, d, *J* 11 Hz, 15-H) (Found: $M^+$, 462.1888. $C_{24}H_{30}O_9$ requires *M*, 462.1889).

*Rearrangement of Ememogin* (**1**) *with Acid*.—20% Aqueous HCl (6 ml) was added to a solution of ememogin (20 mg) dissolved in methanol (2 ml), and the mixture was stirred for 2 days at room temperature. The reaction mixture was extracted with ethyl acetate (4 × 20 ml) and the extract washed successively with saturated aqueous sodium chloride and saturated aqueous sodium carbonate and then dried and evaporated under reduced pressure. The residue was purified on a silica gel plate (solvent: chloroform–acetone 7:3) to give the dihydro ketone (**15**) (11 mg) which was recrystallized from chlofom–diethyl ether to give colourless needles, m.p. 255—257 °C, $[\alpha]_D^{27}$ −160° (*c* 0.1 in methanol); $\nu_{max.}$($CHCl_3$) 3 400—3 300, 1 760, and 1 715 cm$^{-1}$; $\delta_H$($C_5D_5N$) 0.92 and 1.33 (each 3 H, s, tert. $Me_2$), 1.03 (3 H, d, *J* 7 Hz, 16-Me), 2.76 (1 H, s, 5-H), 3.29 (3 H, s, 6-OMe), 3.77 (1 H, m, 3-H), 5.30 (1 H, m, 1-H), 5.38 (1 H, s, 6-H), and 7.12 (1 H, br s, OH); o.r.d. $\lambda_{max.}$(MeOH) nm (φ): 323 (−4 728) and 292 (−3 034) (Found: $M^+$, 392.1848. $C_{21}H_{28}O_7$ requires *M*, 392.1835.

*Trichorabdonin Diacetate* (**17**).—Trichorabdonin (**16**) (22 mg) dissolved in anhydrous pyridine (0.3 ml) and acetic anhydride (0.3 ml) was stirred at room temperature for 10 h. Work-up as before gave a residue (30 mg) which was purified on a silica gel plate (solvent: diethyl ether) to give the diacetate (**17**) (21.7 mg) as a syrup; $\nu_{max.}$($CHCl_3$) 3 450, 1 765, and 1 640 cm$^{-1}$; $\delta_H$($CDCl_3$) 1.04 and 1.06 (each 3 H, s, tert. $Me_2$), 1.40 (3 H, s, 16-Me), 2.00 and 2.12 (each 3 H, s, $Ac_2$), 2.23 (1 H, s, 5-H), 3.96 and 4.08 (each 1 H, ABd, *J* 9 Hz, 20-$H_2$) 4.64 (1 H, dd, *J* 6 and 10 Hz, 1-H), 4.87 (1 H, m, 3-H), and 6.14 (1 H, s, 6-H) [Found: $(M - H_2O)^+$, 446.1920. $C_{24}H_{30}O_8$ requires *M*, 446.1938].

*Acetylation of Tetrahydroenmein* (**18**) *with Acetic Anhydride and Pyridine*.—Tetrahydroenmein (**18**) (4.5 g) dissolved in anhydrous pyridine (16.5 ml) and acetic anhydride (9 ml) was stirred for 14 h at room temperature. Work-up as before gave a residue (5.4 g) which was chromatographed on a silica gel (200 g) column with chloroform–acetone (19:1) as eluant to give the monoacetate (**20**) (1.6 g), the diacetate (**19**) (2.8 g), and the triacetate (**21**) (1 g).

*Monoacetate* (**20**). $\nu_{max.}$($CHCl_3$) 3 630, 3 500, and 1 740—1 720 cm$^{-1}$; $\delta_H$($CDCl_3$) 0.90 (3 H, d, *J* 8 Hz, 16-Me), 0.98 and 1.12 (each 3 H, s, tert. $Me_2$), 2.04 (3 H, s, Ac), 2.34 (1 H, s, 5-H), 3.64 (1 H, m, 3-H), 3.92 and 4.04 (each 1 H, ABd, *J* 10 Hz, 20-$H_2$), 4.80 (1 H, d, *J* 11 Hz, 15-H), 4.91 (1 H, dd, *J* 6 and 12 Hz, 1-H), and 6.16 (1 H, s, 6-H); $\delta_C$($CDCl_3$) 177.3 (C-7), 170.0 (MeCO–O), 102.3 (C-6), 75.7 (d), 75.2 (d), 74.6 (C-20), 71.9 (d), 54.2 (C-8), 49.6 (C-5), 48.6 (C-10), 38.0 (d), 36.1 (d), 36.0 (d), 35.5 (C-4), 34.8 (t), 29.6 (t), 27.5 (C-18), 23.0 (C-19), 21.4 ($CH_3$CO–O–), 20.6 (t), 17.6 (t), and 11.9 (C-17) (Found: $M^+$, 408.2156. $C_{22}H_{32}O_7$ requires *M*, 408.2148).

*Diacetate* (**19**). $\nu_{max.}$($CHCl_3$) 3 500, 1 730, 1 380, and 1 230 cm$^{-1}$; $\delta_H$($CDCl_3$) 0.92 (3 H, d, *J* 8 Hz, 16-Me), 1.08 (6 H, s, tert. $Me_2$), 2.08 and 2.14 (each 3 H, s, $Ac_2$), 2.36 (1 H, s, 5-H), 3.98 and 4.10 (each 1 H, ABd, *J* 10 Hz, 20-$H_2$), 4.72 (1 H, dd, *J* 6 and 12 Hz, 1-H), 4.84—4.90 (2 H, m, 15-H and 3-H), and 6.20 (1 H, s, 6-H); $\delta_C$($CDCl_3$) 176.3 (C-7), 169.8 and 169.7 (MeCOO), 102.0 (C-6), 77.4 (d), 75.2 (d), 74.6 (C-20), 71.3 (d), 54.2 (C-8), 50.2 (C-5), 48.7 (C-10), 37.9 (d), 36.3 (d), 36.1 (d), 34.8 (t), 27.4 (C-18), 27.2 (t), 22.8 (C-19), 22.8 and 21.0 (*Me*CO–O–), 21.4 (t), 20.6 (t), 17.7 (t), and 11.9 (C-17) (Found: $M^+$, 450.2268. $C_{24}H_{34}O_8$ requires *M*, 450.2253).

*Triacetate* (**21**): $\nu_{max.}$($CHCl_3$) 1 750, 1 740, 1 388, and 1 370 cm$^{-1}$; $\delta_H$($CDCl_3$) 0.84 (3 H, d, *J* 6 Hz, 16-Me), 1.07 and 1.09 (each 3 H, s, tert. $Me_2$), 2.08, 2.09, and 2.12 (each 3 H, s, $Ac_3$), 2.36 (1 H, s, 5-H), 3.96 and 4.06 (each 1 H, ABd, *J* 9 Hz, 20-$H_2$), 4.76 (1 H, dd, *J* 6 and 12 Hz, 1-H), 4.94 (1 H, m, 3-H), 5.77 (1 H, d, *J* 10 Hz, 15-H), and 6.21 (1 H, s, 6-H).

*Dehydration of Tetrahydroenmein Diacetate* (**19**).—Phosphoryl chloride (0.2 ml) was added to a solution of tetrahydroenmein diacetate (**19**) (48.7 mg) dissolved in anhydrous pyridine (1 ml), with ice cooling and the mixture was stirred at 60 °C for 12 h. The reaction mixture was then poured into ice–water and the resulting precipitate was extracted with ethyl acetate (2 × 20 ml). The ethyl acetate extract was washed with saturated aqueous sodium hydrogen carbonate and water, dried, and evaporated under reduced pressure to give a residue (32.3 mg) which was purified twice on a silica gel plate [solvent: chloroform–acetone (9:1); benzene–diethyl ether (8:2)] to give a dehydrated product (**22**) (12.3 mg) as a syrup; $\nu_{max.}(CHCl_3)$ 1 750, 1 730, and 1 643 $cm^{-1}$; $\delta_H(CDCl_3)$ 1.02 (6 H, s, tert. $Me_2$), 1.74 (3 H, s, 16-Me), 2.00 and 2.07 (each 3 H, s, $Ac_2$), 3.66 and 4.06 (each 1 H, ABd, *J* 9 Hz, 20-$H_2$), 4.73 (1 H, dd, *J* 6 and 11 Hz, 1-H), 4.83 (1 H, m, 3-H), 5.70 (1 H, s, 15-H), and 6.11 (1 H, s, 6-H) (Found: $M^+$, 432.2133. $C_{24}H_{32}O_7$ requires *M*, 432.2145).

cis-*Glycol* (**23**).—The olefin (**22**) (28.6 mg) was dissolved in anhydrous pyridine (0.5 ml) and osmium tetraoxide (25.6 mg) was added to the solution. The reaction mixture was kept at room temperature for 76 h in the dark. After addition of water (1 ml) and sodium hydrogen sulphite (50 mg), the mixture was stirred for 30 min and extracted with chloroform (2 × 20 ml). The chloroform extract was washed successively with 2M-HCl and saturated aqueous sodium hydrogen carbonate, dried, and evaporated under reduced pressure. The residue (44.8 mg) was purified on a silica gel plate (solvent: diethyl ether) to give a *cis*-glycol (**23**) (12 mg) as a syrup; $\nu_{max.}(CHCl_3)$ 3 450—3 400, 3 300, 1 715, and 1 698 $cm^{-1}$; $\delta_H(CDCl_3)$ 1.02 and 1.04 (each 3 H, s, tert. $Me_2$), 1.32 (3 H, s, 16-Me), 2.02 and 2.07 (each 3 H, s, $Ac_2$), 2.26 (1 H, s, 5-H), 3.68 (1 H, s, 15-H), 3.76 and 4.04 (each 1 H, ABd, *J* 12 Hz, 20-$H_2$), 4.38 (0.5 H, m, OH), 4.64 (1 H, dd, *J* 6 and 10 Hz, 1-H), 4.82 (1 H, m, 3-H), 6.11 (1 H, s, 6-H), and 7.00 (0.5 H, s, OH); $\delta_C(CDCl_3)$ 178.4 (C-7), 169.4 and 169.3 (Me*C*OO), 101.7 (C-6), 87.8 (C-15), 78.3 (C-16), 76.9 (d), 74.3 (C-20), 71.5 (d), 50.4 (C-5), 49.8 (C-8), 48.9 (C-10), 47.6 (d), 43.7 (d), 34.9 (C-4), 34.8 (t), 27.4 (C-18), 27.1 (t), 25.5 (q), 22.8 (q), 21.9 (q), 21.3 (t), 20.9 (q), and 18.1 (t) (Found: $M^+$, 466.2203. $C_{24}H_{34}O_9$ requires *M*, 466.2203).

*Oxidation of the* cis-*Glycol* (**23**) *with Dimethyl Sulphoxide–Acetic Anhydride*.—The *cis*-glycol (**23**) (8.4 mg) dissolved in dimethyl sulphoxide (0.1 ml) and acetic anhydride (0.1 ml) was stirred at room temperature for 9 h. The reaction mixture was poured into an ice-cold saturated aqueous sodium hydrogen carbonate and the mixture was extracted with chloroform. The chloroform extract was washed with water, dried, and evaporated to give a residue (10.6 mg) which was purified on a silica gel plate (solvent: diethyl ether) to give trichorabdonin diacetate (**17**) (2.2 mg) [Found: $(M + 1)^+$, 465.2125. $C_{24}H_{33}O_9$ requires *M*, 465.2124]. This compound was identified by comparison (i.r. and $^1H$ n.m.r. spectra) with an authentic sample of trichorabdonin diacetate (**17**).

*Treatment of Dihydroenmein* (**16**) *with Boron Trifluoride–Ether in Acetic Anhydride*.—A mixture of dihydroenmein (**6**) (200 mg), acetic anhydride (12 ml), and boron trifluoride–diethyl ether (2 ml) was stirred at room temperature for 2 days. The reaction mixture was then poured into ice–water and the resulting oily precipitate was extracted with chloroform (3 × 40 ml). The chloroform extract was washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated under reduced pressure to give a residue which was chromatographed on a silica gel (12 g) column with diethyl ether as eluant and then on a silica gel plate (solvent, diethyl ether) to give the enol acetate (**24**) (106 mg), the methyl ketone (**25**) (50 mg), and dihydroenmein diacetate (**9**) (36 mg).

*Enol acetate* (**24**). $\nu_{max.}(CHCl_3)$ 1 735, 1 370, and 1 180 $cm^{-1}$; $\delta_H(CDCl_3)$ 1.04 and 1.06 (each 3 H, s, tert. $Me_2$), 1.57 (3 H, s, 16-Me), 2.06, 2.10, and 2.19 (each 3 H, s, $Ac_3$), 2.35 (1 H, s, 5-H), 3.66 and 4.10 (each 1 H, ABd, *J* 9 Hz, 20-$H_2$), 4.67 (1 H, dd, *J* 6 and 11 Hz, 1-H), 4.90 (1 H, m, 3-H), and 6.11 (1 H, s, 6-H); $\delta_C(CDCl_3)$ 173.2 (C-7), 169.7, 169.4, and 167.5 (Me*C*OO), 145.7 (C-15), 132.7 (C-16), 101.4 (C-6), 77.1 (C-3), 76.3 (C-20), 71.7 (C-1), 53.5 (C-8), 48.8 (C-5), 48.3 (C-10), 41.6 (d), 38.0 (d), 37.3 (t), 34.5 (C-4), 27.3 (C-18), 27.0 (t), 22.8 (C-19), 21.3 (t), 21.3 (t), 21.2, 20.9, and 20.7 (*Me*CO–O–), and 11.7 (C-17) [Found: $(M + 1)^+$, 491.2271. $C_{26}H_{35}O_9$ requires *M*, 491.2278].

*Methyl ketone* (**25**). $\nu_{max.}(CCl_4)$ 1 758, 1 720, and 1 702 $cm^{-1}$; $\delta_H(CDCl_3)$ 1.05 and 1.07 (each 3 H, s, tert. $Me_2$), 1.33 (3 H, s, 16-Me), 2.01 and 2.10 (each 3 H, s, $Ac_2$), 2.23 (1 H, s, 5-H), 2.32 (3 H, s, Ac), 4.08 (2 H, s, 20-$H_2$), 4.59 (1 H, dd, *J* 6 and 11 Hz, 1-H), 4.90 (1 H, m, 3-H), and 6.16 (1 H, s, 6-H); $\delta_C(CDCl_3)$ 211.9 (C-15), 203.7 (CO), 170.9 (C-7), 169.4 and 169.2 (Me*C*OO–), 101.6 (C-6), 76.9 (d), 75.3 (d), 72.3 (C-20), 69.1 (C-16), 57.6 (C-8), 50.2 (C-5), 48.7 (C-10), 46.4 (d), 34.8 (C-4), 34.4 (d), 33.3 (t), 27.4 (q), 27.3 (q), 27.0 (t), 22.7 (q), 21.3 (q), 20.0 (q), 20.1 (t), 18.9 (t), and 18.5 (C-17) [$M^+$, 490.2181. $C_{26}H_{34}O_9$ requires *M*, 490.2201).

*Dihydroenmein diacetate* (**9**). This compound was identified by comparison (i.r., $^1H$- and $^{13}C$-n.m.r. spectra) with an authentic sample.

*Epoxidation of the Enol Acetate* (**24**).—*m*-Chloroperbenzoic acid (50.4 mg) was added to a solution of the enol acetate (**24**) (73.8 mg) dissolved in anhydrous chloroform (1.2 ml), at 0 °C; the mixture was then stirred at 4 °C for 1 day and at room temperature for 5 h. Subsequently, it was diluted with chloroform, washed with saturated aqueous sodium hydrogen carbonate and water, dried, and evaporated to give a residue; this was purified on a silica gel (8 g) column (solvent: chloroform–acetone) to give the epoxide (**26**) (63.8 mg). Recrystallization from chloroform gave colourless needles, m.p. 182—187 °C; $\nu_{max.}(CHCl_3)$ 1 730 and 1 365 $cm^{-1}$; $\delta_H(CDCl_3)$ 1.02 and 1.06 (each 3 H, s, tert. $Me_2$), 1.52 (3 H, s, 16-Me), 2.09, 2.12, and 2.15 (each 3 H, s, $Ac_3$), 2.02 (1 H, s, 5-H), 2.86 (1 H, dd, *J* 5 and 11 Hz, 9-H), 3.66 and 4.08 (each 1 H, ABd, *J* 11 Hz, 20-$H_2$), 4.62 (1 H, dd, *J* 6 and 12 Hz, 1-H), 4.89 (1 H, m, 3-H), and 6.10 (1 H, s, 6-H); $\delta_C(CDCl_3)$ 171.7 (s), 169.9 (s), 169.4 (s), 168.3 (s), 101.2 (C-6), 91.3 (C-15), 77.2 (d), 75.3 (C-20), 71.8 (d), 68.9 (C-16), 52.8 (C-8), 49.5 (C-5), 48.5 (C-10), 39.8 (d), 36.4 (d), 34.6 (C-4), 30.2 (t), 27.4 (q), 27.1 (t), 22.8 (q), 21.1 (q), 21.1 (q), 20.9 (q), 20.6 (t), 19.4 (t), and 14.3 (C-16) (Found: $M^+$, 506.2155. $C_{26}H_{34}O_{10}$ requires *M*, 506.2152).

*Alkaline Hydrolysis of the Epoxide* (**26**).—Potassium carbonate (20 mg) and a few drops of water were added to a solution of the epoxide (**26**) (25.8 mg) dissolved in methanol (1 ml), and the mixture was stirred at room temperature for 1 h. After dilution with an excess of water, the reaction mixture was neutralized with 5% acetic acid and the solvent was removed under reduced pressure. The residue was partitioned between ethyl acetate and water. The ethyl acetate extract was dried and evaporated under reduced pressure to give a residue (10.9 mg) which was recrystallized from methanol to give colourless needles, m.p. > 300 °C (Found: C, 62.9; H, 7.5. $C_{20}H_{28}O_7$ requires C, 63.14; H, 7.42%). This compound was identified with naturally occurring trichorabdonin (**16**) by comparison of mixed m.p.s and i.r. and $^1H$ n.m.r. spectra.

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