Phytochemistry, 1973, Vol. 12, pp. 863 to 869. Pergamon Press. Printed in England.

RUPICOLIN-*A* AND -*B*, RUPIN-*A* AND -*B*, AND CUMAMBRIN-*B* OXIDE FROM *ARTEMISIA TRIPARTITA* SSP. *RUPICOLA**

M. A. IRWIN and T. A. GEISSMAN

Department of Chemistry, University of California, Los Angeles, CA 90024, U.S.A.

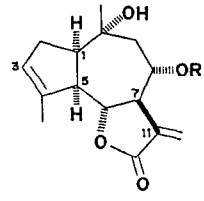
(*Received* 10 *October* 1972. *Accepted* 21 *October* 1972)

Key Word Index—*Artemisia tripartita*; Compositae; sesquiterpene lactone; guaianolide; stereochemistry; confirmation; mass spectral fragmentation; biosynthesis.

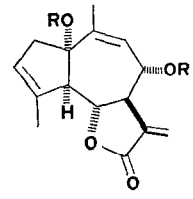
Abstract—Five new sesquiterpene lactones have been isolated from *Artemisia tripartita* Rydb. ssp. *rupicola* Beetle. The compounds, all guaianolides, are structurally related in what appears to be a sequence in which epoxidation plays the principal role.

INTRODUCTION

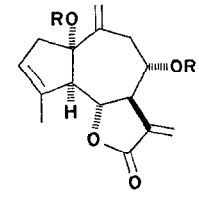
THE PRESENCE of cumambrin-*B* (I) and -*A* (II) in *Artemisia tripartita* Rydb. ssp. *rupicola* Beetle, and in *A. nova* Nels. has been described.[1] Further study of several collections of *A. tripartita* ssp *rupicola*,[2] identical by TLC comparison, has led to the isolation of a number of more highly oxygenated guaianolides. Extensive chromatographic separation resulted in a large number of discrete fractions, from which the new compounds described here were obtained. The structures of the cumambrins, the rupicolins, and the rupins suggest that these compounds represent the members of a series in which successive epoxidations lead to the introduction of oxygen in hydroxyl and epoxy groupings.



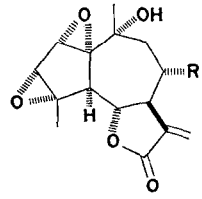
(I) R = H Cumambrin-*B*
(II) R = Ac Cumambrin-*A*



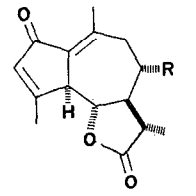
(III) R = H Rupicolin-*A*
(V) R = CHO



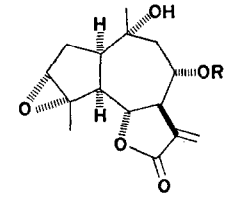
(IV) R = H Rupicolin-*B*
(VII) R = CHO



(IX) R = H Canin
(X) R = OH Rupin-*A*
(XI) R = OAc Rupin-*B*



(XII) R = H Deacetoxymatricarin
(XIII) R = OH Deacetylmatricarin
(XIV) R = OAc Matricarin



(XVI) R = H Cumambrin-*B*-oxide
(XVII) R = Si $(Me)_3$

* Contribution No. 2951 from the Department of Chemistry, U.C.L.A.

[1] IRWIN, M. A. and GEISSMAN, T. A. (1969) *Phytochem.* **8**, 305.

[2] We are indebted to Dr. A. A. BEETLE and Dr. R. O. ASPLUND, University of Wyoming, and to Dr. G. H. WARD, Knox College, for the collection and identification of the plants used.

RESULTS AND DISCUSSION

Rupicolin-*A* (III) and -*B* (IV) were first obtained as a mixture which was barely resolved on TLC, but which was separated by chromatography over silica gel into the two compounds.

Rupicolin-A (III), $C_{15}H_{18}O_4$, had m.p. 155–156° with solidification and remelting at 167–168·5°. Its IR spectrum revealed absorption for hydroxyl groups (3555 and 3370 cm^{-1}), a γ-lactone (1760 cm^{-1}) and carbon–carbon unsaturation (1645 cm^{-1}). That the lactone is a dihydroxy compound was shown by the MS, in which there appeared ion peaks at *m/e* 262 (M^+), M−18, M−15–18, M−18–18, and M−15–18–18, and that it is an α-methylene-γ-lactone was indicated by intense and absorption in the UV spectrum. It showed a negative Cotton effect at 260 nm, characteristic of the *trans*-fused lactone at C-6/C-7.[3]

The NMR spectrum (pyridine-d_5) of rupicolin-*A* is clearly interpretable in terms of the structure III. The C-10 methyl group, coupled with H-9 (0·9 Hz) and H-8 (0·9 Hz), was seen as a 3-proton triplet at δ 2·07. The C-9 proton, coupled with the C-10 methyl group and H-8, gave a narrow multiplet at δ 5·28. The C-8 proton, coupled (10 Hz) with H-7, gave a doublet at δ 4·45, broadened by coupling with H-9 and the C-10 methyl group. This signal was shifted downfield on formylation. The proton at C-7, coupled with H-8 (10 Hz), H-6 (9 Hz) and the C-11 methylene group (3 and 3 Hz), was seen as a multiplet at δ 3·45. The 2 protons of the C-11 methylene group gave a pair of quartets, coupled with H-7 (3 Hz) and geminally coupled (1·7 Hz), at δ 6·44 and 6·55. The pronounced geminal coupling and the unusually low field position of the proton that is *trans* to the lactonic carbonyl group are perturbations clearly indicative of the presence of an α-disposed hydroxyl group at C-8.[4] On formylation the geminal coupling effectively vanishes and the signals of the methylene group appear as a pair of doublets (3 Hz) at δ 5·73 and 6·30. The methine proton of the lactone grouping, H-6, was seen as a quartet at δ 4·10, with coupling to H-7 (9 Hz) and H-5 (11 Hz). In accord with this, the proton at C-5 appeared as a doublet at δ 3·07, coupled with H-6 (11 Hz) and broadened slightly by small couplings with H-3 and the C-2 protons. The annular methylene group at C-2 gave a closely spaced *AB* quartet centered at δ 2·7, with geminal coupling of 16 Hz and broadening due to smaller couplings. The large couplings (9–11 Hz) among the protons at C-5, C-6, C-7 and C-8 are essentially identical with those of cumambrin-B (I) and its derivatives, the structures of which have been established.[1]

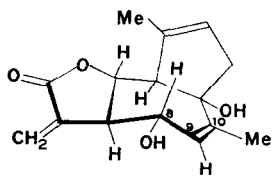
That the configuration of the hydroxyl group at C-1 is α, as shown in III, is clear from these observations. The signal of H-6 is located at the usual position (near δ 4·0) for this type of proton. A model shows that a β-disposed hydroxyl group at C-1 would be in close proximity to H-6 causing it to appear at an unusually low field.[5] Moreover, there is no significant change in the H-6 signal on diformylation of rupicolin-*A*. The effect of formylation of a β-disposed hydroxyl group would be a substantial upfield shift in H-6.

The NMR spectrum of rupicolin-*A* (III) is best interpreted in terms of conformation VI. The magnitude of the coupling between H-8 and H-9 (1–2 Hz) and between H-8 and the C-10 methyl group (0·9 Hz) shows that H-8 lies out of the plane of the 9,10-double bond. The equatorial disposition of the C-8 hydroxyl group is revealed by the pattern (deshielding and geminal coupling[4]) of the C-11 methylene group. Although another configuration, and

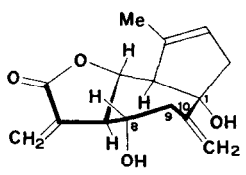
[3] STÖCKLIN, W., WADDELL, T. G. and GEISSMAN, T. A. (1970) *Tetrahedron* **26**, 2397.
[4] YOSHIOKA, H., MABRY, T. J., IRWIN, M. A., GEISSMAN, T. A. and SAMEK, Z. (1971) *Tetrahedron* **27**, 3317.
[5] JACKMAN, L. M. and STERNHELL, S. (1969) *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, p. 71, Pergamon, New York; BHACCA, M. and WILLIAMS, D. H. (1964) *Applications of NMR Spectroscopy in Organic Chemistry*, p. 183, Holden-Day, San Francisco.

conformation, containing a β-disposed hydroxyl group at C-8 could be accommodated to these signals, the co-occurrence and close structural relationship of the rupicolins and cumambrin-*B*, for which the α-configuration has been established, make this alternative an unlikely one.

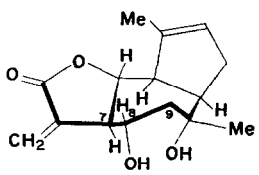
Rupicolin-B (IV), $C_{15}H_{18}O_4$, m.p. 142–144°, showed IR absorption characteristic of hydroxyl (3560 and 3410 cm^{-1}), γ-lactone (1760 cm^{-1}) and double bond (1660 and 1635 cm^{-1}) groupings. Prominent MS ions at *m/e* 262 (M^+), M−15, M−18, M−15–18 and M−18–18, combined with elemental analysis, establish its constitution and the presence of two hydroxyl groups. The NMR spectrum (pyridine-d_5) is in accord with structure IV and accommodates the difference between rupicolin-*A* and -*B*. Thus, the signals for the protons at C-2, C-3, C-4 (Me), C-5, C-6 and C-11 (CH_2) are very similar in the two compounds. The C-10 exocyclic methylene group in rupicolin-*B* (IV) displays a pair of doublets at δ 5·24 and 5·49, with a small geminal coupling (1·8 Hz). The protons of the annular methylene group at C-9, geminally coupled (13 Hz) and coupled with H-8 (7 and 5 Hz), appeared as a pair of quartets at δ 3·22 and 2·75, which, though partially obscured, were clearly identified by comparison of 60 and 100 MHz spectra as the *AB* part of an *ABX* pattern. The proton at C-8 gave a diffuse signal at δ 4·05. The signal of H-8 in rupicolin-*B* diformate (VII, $CDCl_3$) lacks the broadening shown by this signal in rupicolin-*B*; it is a sharply defined multiplet at δ 5·05, with reciprocity of the splitting (9 and 6 Hz) seen in the protons at C-9 and splitting due to H-7 (10 Hz) and the formyl proton (1 Hz).



(VI)



(VIII)



(XV)

The most probable conformation of rupicolin-*B*, deduced from these data, is that shown in VIII, which is in accord with the equatorial position of the C-8 hydroxyl group (as defined by the deshielding and geminal coupling of the C-11 methylene group[4]), and the magnitudes of the H-8/H-9 coupling constants (7 and 5 Hz), which appear to exclude a conformation in which H-8 and H-9 α are *trans*-diaxially disposed. The C-10 exomethylene protons produced singlets at δ 5·21 and 5·27 in rupicolin-*B* diformate (VII, $CDCl_3$). The loss of geminal coupling between these protons and the upfield shift of one of them on diformylation are consistent with an interaction between the C-1 hydroxyl group and the exomethylene proton *cis* to it.

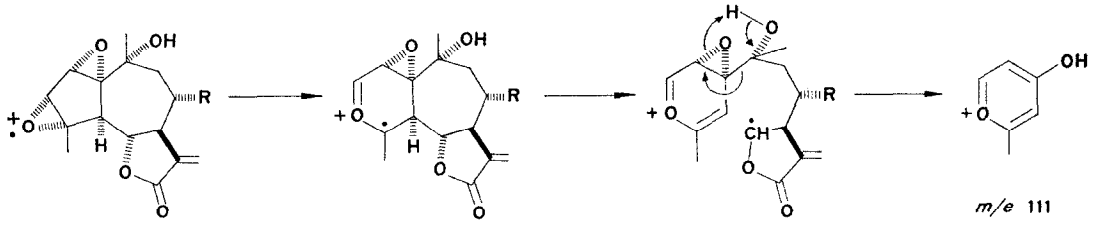
Rupin-*A* (X) and -*B* (XI) were isolated from the same plant sample that afforded cumambrin-*B* and the rupicolins. It will be noted that the rupins bear the same relationship to canin (IX)[6] that is found in cumambrin-*A* and -*B* and 8-deoxycumambrin-*B*, and in deacetoxymatricarin (XII), deacetylmatricarin (XIII) and matricarin (XIV).

Rupin-A (X), $C_{15}H_{18}O_6$, which decomposed above 260°, formed an acetate that was identical with rupin-*B* (XI), $C_{17}H_{20}O_7$, m.p. 235–245° dec. Rupin-*A* showed IR absorption (Nujol) for hydroxyl (3460 and 3415 cm^{-1}), γ-lactone (1740 cm^{-1}) and carbon–carbon double bond (1655 cm^{-1}) groupings. Although the carbonyl stretching frequency of the

[6] LEE, K. H., SIMPSON, R. F. and GEISSMAN, T. A. (1969) *Phytochem.* **8**, 1515.

lactone group of rupin-*A* is lower than is usually observed for an α-methylene-γ-lactone, those (measured in $CHCl_3$) of rupin-*B* (1765 cm^{-1}) and canin (1770 cm^{-1}) are normal. The MS of IX, X and XI showed no molecular ions (at *m/e* 278, 294 and 336, respectively), but the presence in the MS of rupin-*A* of ion peaks at M+1 and M−18; and in that of rupin-*B* of ions M−15, M−15–42, M−60 and M−18–60, coupled with elemental analyses, establish the compositions of X and XI and the presence of two hydroxyl groups (one of them acetylated in XI).

The MS of IX, X and XI are all characterized by the appearance of an especially abundant ion (base peak) at *m/e* 111,[7] a clear indication that the three compounds have a structural feature in common, and, since they differ in having H, OH and OAc at C-8, it would appear that the remainder of their structures is the same. Scheme 1 accounts for the formation of the ion fragment *m/e* 111 and accommodates the structures given for canin and the two rupins.



SCHEME 1. MS FRAGMENTATION OF CANIN AND THE RUPINS.

The principal basis for the assignment of structure and stereochemistry of rupin-*A* (X) and -*B* (XI) lies in the close correspondence of their NMR spectra with that of canin (IX), except for the features associated with the hydroxyl and acetoxyl group at C-8 in X and XI. The NMR spectrum (pyridine-d_5) of rupin-*A* is interpreted as follows. The methyl groups at C-4 and C-10 were seen as singlets at δ 1·51 and 1·25, respectively. The protons at C-2 and C-3, coupled (1·3 Hz) only with each other, gave a pair of narrow doublets at δ 3·22 and 3·75. The C-5 proton, coupled (10 Hz) with H-6, gave a doublet at δ 3·21. The C-6 proton, coupled almost equally (10 Hz) with H-5 and H-7, gave an approximate triplet at δ 4·53. The C-7 proton, coupled with H-6 (10 Hz), H-8 (9 Hz) and the protons of the C-11 methylene group (3 and 3 Hz), gave a multiplet at δ 3·94. The large couplings among the C-5, C-6, C-7 and C-8 protons are in accord with their all-*trans*-pseudoaxial disposition. The protons of the C-11 methylene group showed signals characteristic of the presence of an α-disposed hydroxyl group at C-8:[4] two closely spaced quartets at δ 6·36 and 6·42, coupled with H-7 (3·5 and 3·0 Hz, respectively) and geminally coupled (1·6 Hz). On acetylation to rupin-*B* (XI), these signals shift to δ 5·69 and 6·28 and exhibit coupling with H-7 of 3·1 and 3·3 Hz, respectively; geminal coupling is barely resolved at 0·6 Hz. The C-8 proton in rupin-*A* (8-OH) appeared as a multiplet obscured by other signals at δ 4·3, and in rupin-*B* (8-OAc) as a multiplet (couplings of 9, 7 and 4 Hz) at δ 5·53. The C-9 protons gave a pair of quartets as the *AB* part of an *ABX* pattern, appearing at δ 2·22 and 2·54, geminally coupled (15 Hz) and coupled (4 and 6 Hz, respectively) with H-8.

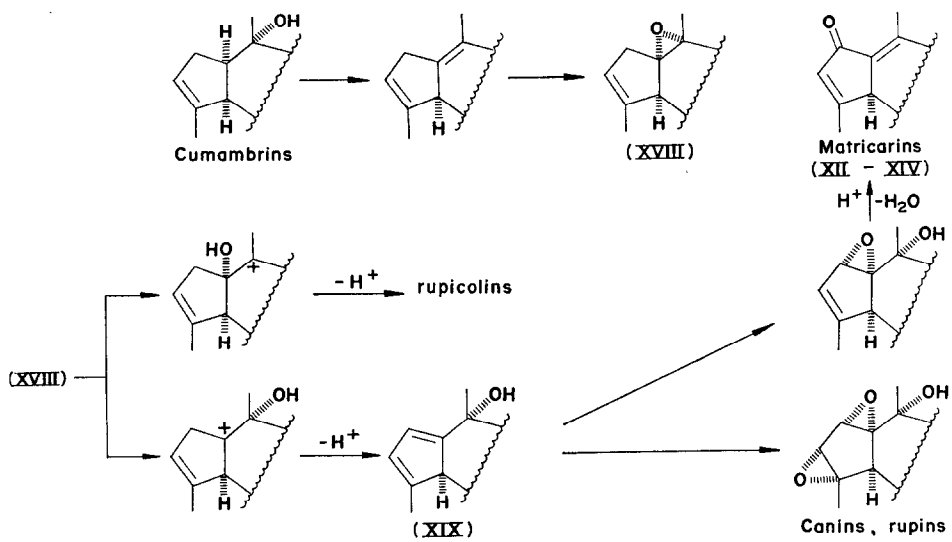
Structural and spectral similarity suggest that cumambrin-*B* (I), its oxide (XVI), the rupins (X and XI) and canin (IX) have analogous conformations. The following observations support conformation XV for cumambrin-*B*. The unusually low field of H-7 (δ 3·7, $CDCl_3$)

[7] This was erroneously reported as *m/e* 112 in Ref. 6.

and the upfield shift of this proton in passing from the acetate (δ 3·9) and formate (δ 4·0) of the C-8 hydroxyl group to the diacetate (δ 3·5) and diformate (δ 3·6) indicate that H-7 is in close proximity with the tertiary hydroxyl group. The couplings of 2–6 Hz between H-8 and the two H-9, exhibited by cumambrin-*B* and its analogs, eliminate a *trans*-diaxial disposition of H-8 and H-9α.

Cumambrin-B 3,4-*oxide* (XVI) was isolated as the trimethylsilyl derivative from the extract of *A. tripartita* ssp *rupicola*. After separation of rupin-*B* by crystallization from the appropriate column fractions, the non-crystalline residues were treated with trimethylchlorosilane and pyridine and chromatographed over silica gel. The crystalline TMS-derivative of XVI was obtained in very small amount (11 mg), and was identified by comparison with the compound (XVII) prepared by epoxidation and trimethylsilylation of cumambrin-*B* (I).

The NMR spectrum of the TMS-derivative (XVII) of XVI was in complete accord with the structure shown; it was strikingly similar to that of the TMS-derivative of cumambrin-*B* itself, differing from the latter chiefly in the appearance of a singlet (at δ 3·29, $CDCl_3$), broadened slightly by coupling with the C-2 protons, for the proton at C-3 on the C-3/C-4 oxide grouping. The signals for the protons of the C-11 methylene group appeared as a pair of quartets at δ 5·82 and 6·20, showing allylic coupling (3 Hz) with H-7 and geminal coupling (1 Hz). The α-disposition of the oxide is assumed, but is most probable, arising by attack at the least hindered face of the 5-membered ring.



SCHEME 2. POSSIBLE BIOSYNTHESIS OF *Artemisia tripartita* GUAIANOLIDES.

The intimate relationships between the structures of the cumambrins, cumambrin-*B* oxide, the rupicolins, and the rupins suggests a biosynthetic sequence, outlined in Scheme 2, in which epoxidation plays the principal role. It is noteworthy that the matricarins (XII–XIV), common constituents of a number of species of the section *Tridentatae*[8] closely allied with *A. tripartita* ssp *rupicola* and *A. nova*, are simply and directly derivable from an 11,13-

[8] BEETLE, A. A. (1960) *Univ. Wyom. Agric. Exptl. Sta. Bull.* No. 368.

dihydro form of the presumed precursor (XVIII) of the rupicolins. It is further to be noted that XVIII represents globicin and arborescin, and XIX is a double-bond isomer of artabsin.[9]

EXPERIMENTAL

M.ps were taken in capillaries and are corrected. TLC was carried out with the use of silica gel G-coated plates (0·25 mm) developed in $CHCl_3$–Me_2CO. Spectra were measured on: NMR, Varian A-60D and HA-100; MS (70 eV, direct insertion), AEI-MS9; IR ($CHCl_3$, except as noted), Perkin–Elmer 237.

Isolation of compounds. Three collections of *A. tripartita* ssp *rupicola*,[10] having a combined weight of 4·9 kg, comprize the material from which the compounds were isolated. The principal collection (3·2 kg) was processed as follows. The dried and ground aerial part of the plant was extracted exhaustively with $CHCl_3$ at ordinary temperature. The residue left after removal of the solvent was extracted 3× with hot 30% aq. EtOH (steam was passed through the mixture during the first extraction to remove the last of the $CHCl_3$). The combined aqueous phases and the tar were treated separately. The tarry material was chromatographed over silica gel and yielded cumambrin-*B*. The aqueous phase was extracted with $CHCl_3$ and the residual oily material obtained by evaporation of the solvent was chromatographed over silica gel using chloroform with gradually increasing proportions of acetone as eluant, yielding additional cumambrin-*B*[11] and a number of varied fractions. At this point, monitoring by TLC permitted the selection and combination of fractions with similar ones from the separately processed other two collections. Although the source of the following compounds cannot be attributed to an individual collection, the 3·2-kg collection contributed by far the bulk of the crude material from which the compounds were isolated. A mixture (4·6 g) of rupicolin-*A* and -*B*, 0·5 g of artecalin, and 0·07 g of rupin-*B* were obtained by repeated chromatography and crystallization of less polar fractions. The mother liquor obtained after crystallization of rupin-*B* was treated with trimethylchlorosilane and pyridine, the solvent was removed *in vacuo*, and the product was chromatographed to give 11 mg of the crystalline trimethylsilyl ether of cumambrin-*B* 3,4-oxide. The various mother liquors were combined and washed with Na_2CO_3 solution. Acidification of the alkaline extract followed by $CHCl_3$ extraction gave a mixture of phenolic compounds from which 6-hydroxy-7-methoxycoumarin (4·0 g) was isolated by chromatography followed by crystallization and sublimation. Extensive rechromatography of polar fractions, obtained after the above compounds had been eluted from the column, yielded 1 g of ridentin, 0·5 g of a mixture of ridentin and ridentin-*B*, and 0·5 g of rupin-*A*.

Rupicolin-A (III) *and* -B (IV). The mixture of rupicolin-*A* and -*B* crystallized from EtOAc as granules having m.p. 152–153° and $[\alpha]_D^{28}$ +98° (*c* 1·10, MeOH). It was barely resolved on TLC, but careful chromatography of 0·2 g over a 2·8 × 53 cm column of silica gel, using acetone–$CHCl_3$–benzene (1:5:4 and 3:10:7) afforded 66 mg of rupicolin-*A* and 43 mg of rupicolin-*B*.

Rupicolin-A, crystallized from ethyl acetate–EtOH–Et_2O as colorless platelets, had m.p. 155–156° followed by solidification and remelting at 167–168·5°. Its IR spectrum showed peaks at 3555, 3370, 1760 and 1645 cm^{-1}. Its NMR spectrum has been discussed above. The circular dichroism curve showed a maximum $[\theta]_{245}$ −1412°. The MS showed principal ion peaks at *m/e* (rel. int.) 262 (0·5, M^+), 244 (2·1), 229 (1·4), 226 (1·8), 211 (2·1) and others including 41 (100) (*Anal.* Calc. for $C_{15}H_{18}O_4$: C, 68·68; H, 6·92. Found: C, 68·52; H, 6·94%).

Rupicolin-B crystallized from ethyl acetate–EtO_2 as colorless granules, m.p. 142–144°. Its IR spectrum had peaks at 3560, 3410, 1760, 1660 and 1635 cm^{-1}. The NMR spectrum has been described in the Discussion. The MS showed principal ion peaks at *m/e* (rel. int.) 262 (8·3, M^+), 247 (5·6), 244 (22), 233 (8·3), 229 (7·7), 226 (9·7), 219 (18), 216 (12), 215 (7·4), 211 (6·4) and others including 41 (100) (*Anal.* Calc. for $C_{15}H_{18}O_4$: C, 68·68; H, 6·92. Found: C, 68·87; H, 6·91%).

Rupicolin-A *diformate* (V) *and rupicolin*-B *diformate* (VI). A solution of the mixture of rupicolin-*A* and -*B* in an equilibrated mixture of formic acid and Ac_2O was allowed to stand for 4 days. $CHCl_3$ was added, and the solution was washed with aq. sodium carbonate, dried, and chromatographed. The diformates were located by TLC, separated and recrystallized.

Rupicolin-A *diformate* crystallized from EtOAc–Et_2O as needles, m.p. 180–181°. Its IR spectrum showed peaks at 1765 and 1720 cm^{-1}. The relevant features of the NMR spectrum have been described above. The MS showed principal ions at *m/e* (rel. int.) 318 (0·24, M^+), 272 (11), 226 (82), 211 (71) and others including 43 (100) (*Anal.* Calc. for $C_{17}H_{18}O_6$: C, 64·14; H, 5·70. Found: C, 64·23; H, 5·95%).

[9] See GEISSMAN, T. A. (1972) *Biosynthesis of Sesquiterpene Lactones of Compositae, Proc. XI Annual Symposium Phytochem. Soc. No. Amer., Monterrey, Mexico, October* 1971, Academic Press, New York.

[10] The plants used are identified by the Voucher Nos. GHW-966-ATR (0·36 kg, G. H. Ward), AAB-81366-ATR (1·35 kg, A. A. Beetle) and ROA-8767-ATR (3·2 kg, R. O. Asplund), and were essentially identical except for the presence in the 0·36-kg collection of the eudesmanolide colartin (IRWIN, M. A. and GEISSMAN T. A. (1969) *Phytochem.* **8**, 2411).

[11] The yield of cumambrin-*B* from plants of this group is often high: 3·2 kg of *A. tripartita* ssp *rupicola* yielded 30 g; 0·36 kg yielded 1·6 g; 1·36 kg yielded 3·6 g; 0·37 kg of *A. nova* yielded 1·3 g; and 5 kg of *A. nova* yielded 40 g.

Rupicolin-B *diformate* crystallized from EtOAc–Et_2O as needles, m.p. 137–138°. Its IR spectrum showed peaks at 1765 and 1725 cm^{-1}. Its NMR spectrum was in accord with the structure VII, and the relevant features have been described above.

Rupin-A (X). Rupin-*A* crystallized from EtOH as granules, dec. 260–300°, homogeneous on TLC. Its IR spectrum (Nujol) showed absorption at 3460, 3415, 1740 and 1655 cm^{-1}. The circular dichroism curve showed a maximum $[\theta]_{250}$ −2660°. The MS showed no molecular ion peak (*m/e* 294), but a prominent ion at *m/e* 111 (base peak), the interpretation of which has been given above, and a series of very weak higher mass ions ending with *m/e* 295 (M+1). The NMR spectrum has been described in the Discussion (*Anal.* Calc. for $C_{15}H_{18}O_6$: C, 61·22; H, 6·16. Found: C, 61·40; H, 6·21%).

Rupin-B (XI). Rupin-*B* was found to be identical (m.p., IR, NMR, MS, TLC) with rupin-*A* acetate. Acetylation of rupin-*A* with Ac_2O–pyridine yielded XI as needles (from EtOAc), m.p. 235–245° dec. Its MS showed no molecular ion (*m/e* 336), but contained peaks at *m/e* (rel. int.) 321 (0·04), 279 (0·4), 261 (0·2), 258 (0·3) and others including 111 (100). The relevant features of the NMR spectrum have been discussed above (*Anal.* Calc. for $C_{17}H_{20}O_7$; C, 60·71; H, 5·99. Found: C, 60·72; H, 6·14%).

Cumambrin-B 3,4-*oxide* (XVI). Cumambrin-*B* oxide was isolated as its trimethylsilyl ether as described above. It was present in too small an amount to permit extensive study, but was found to be identical with the TMS ether of the oxide prepared from cumambrin-*B*. A solution of 440 mg of cumambrin-*B* and 530 mg of *m*-chloroperbenzoic acid in 20 ml of $CHCl_3$ was allowed to stand for 3 hr, then washed with aq. sodium sulfite and sodium carbonate. Evaporation of the $CHCl_3$ solution gave cumambrin-*B* oxide (XVI) which was crystallized from EtOAc–Et_2O as granules (120 mg), m.p. 189–190·5° (*Anal.* Calc. for $C_{15}H_{20}O_5$: C, 64·27; H, 7·19. Found: C, 64·32; H, 7·06%). The mother liquor from which the oxide had crystallized was concentrated and treated with trimethylchlorosilane–pyridine. After 2 hr the solvents were removed *in vacuo* and the residue dissolved in Et_2O. The solution, which contained both the mono- and bis-TMS ethers (by TLC) was concentrated, giving crystalline cumambrin-*B* oxide TMS ether (XVII), which was recrystallized from EtOAc–Et_2O. The compound was identical (m.p., m.m.p., TLC) with the material isolated from the plant. It had m.p. 178·5–179·5°, and an IR spectrum that showed absorption at 3500, 1760 and 1660 cm^{-1}. Its NMR spectrum is described in the Discussion. Its MS showed principal ions at *m/e* (rel. int.) 352 (0·2 M^+), 337 (0·9), 334 (2), 319 (0·6) and others including 43 (100).

Acknowledgements—This study was supported by a research grant from the U.S. Public Health Service, GM-14240. Dr. G. Chmurny assisted in the NMR measurements, and analyses are by Miss Heather King, U.C.L.A.