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NATURALLY OCCURRING FULVENE HYDROCARBONS

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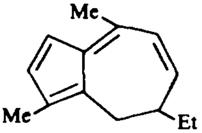
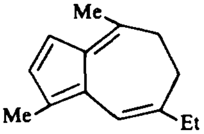
Abstract— Two dihydrochamazulene hydrocarbons have been isolated from *Artemisia absinthium L.* and are assigned the structures of 3,6-dihydrochamazulene and 5,6-dihydrochamazulene from spectral evidence. A hydrocarbon (*lactarofulvene*) isolated from *Lactarius deliciosus L.* is assigned the structure of 1-methylene-1,6-dihydrolactarazulene from spectral data.

There have appeared in the chemical literature[1,2] two instances of sesquiterpene hydrocarbons which were proposed to contain a fulvene π-system.

Sórm, *et al.*[1] first isolated chamazulenogen from the oil of *Artemisia absinthium L.*, and assumed it to be a single hydrocarbon having structure I, II or III based on preliminary evidence. These same workers, following up some earlier work of Willstaedt,[2b] also made a preliminary study of a sesquiterpene hydrocarbon from *Lactarius deliciosus L.* which they surmised might be related to chamazulenogen. The data presented below establishes the structures of the compounds mentioned above.



I



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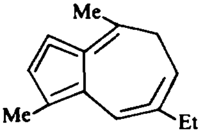
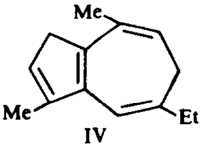
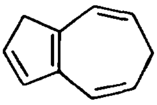


III

Chamazulenogen can be derived from the oil of *Artemisia absinthium L.* or by the dehydration–decarboxylation of artabsin.[1b] By dehydrogenation it was established that chamazulenogen had the chamazulene skeleton leaving only the placement of the double bonds to establish the structure. Using the procedure previously described we have isolated an orange hydrocarbon fraction from *Artemisia absinthium L.* (American), which exhibited the ultraviolet spectrum and chemical characteristics attributed to chamazulenogen. The NMR spectrum of this hydrocarbon fraction indicated that it was a mixture of two components, one of which predominated. However, these two isomeric components were separated by chromatography on an



IV



V

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aluminum oxide–silver nitrate column. The NMR spectra of the two components IV and II (Figs 1 and 2) allowed the structural assignments indicated.

In order to facilitate the structural assignment of the components of chamazulenogen, the NMR spectra of chamazulene[3] and 1,6-dihydroazulene (V) were also determined. 1,6-Dihydroazulene has been reported to be the product resulting from the sodium–liquid ammonia reduction of azulene,[4] although no details are presently available in the literature. However, a synthesis of 5,6-dihydroazulene[5] from the condensation of cyclopentadiene and glutaric dialdehyde has been reported. Since we initially expected that chamazulenogen was a derivative of the 5,6-dihydroazulene system we repeated the reported synthesis of 5,6-dihydroazulene. However, the NMR spectrum of the compound resulting from the condensation of cyclopentadiene with glutaric dialdehyde excludes the 5,6-dihydroazulene structure and establishes that the hydrocarbon has the 1,6-dihydroazulene structure (V).

The lowest field multiplet ($\sim 3{\cdot}8\ \tau$) in the NMR spectrum of 1,6-dihydroazulene (Fig. 1) contains the AB (H_2H_3) part of an ABX_2 system (the X hydrogens occur at $7{\cdot}05\ \tau$) for the 5-membered ring in which J_{AX} and J_{BX} are approximately equal and small consistent with the corresponding structural features of indene[6] and 1-azulenium ion.[7] This relationship was verified by decoupling experiments whereby irradiation at $7{\cdot}05\ \tau$ caused the AB part of the ABX_2 system to become a simple AB quartet. Also contained in this lowest field multiplet are the four and eight hydrogens which make up the AA′ part of an $AA'BB'X_2$ system for the 7-membered ring. The chemical shifts of the 4 and 8 hydrogens are not identical due to the asymmetry caused by the 5-membered ring. The next multiplet at $5{\cdot}1\ \tau$ consists of the two overlapping BB′(H_5,H_7) signals which again do not have the same chemical shifts because of the molecular asymmetry. Irradiation of the triplet at $7{\cdot}95\ \tau$ causes collapse of this multiplet at $5{\cdot}1\ \tau$ to a double doublet, consistent with the assigned structure. This same decoupling experiment also verified the assignment of the triplet at $7{\cdot}95\ \tau$ as the hydrogens of the 6 position.

Comparison of the NMR spectrum of 1,6-dihydroazulene with the NMR spectrum of the major hydrocarbon product isolated from chamazulenogen readily demonstrates that this latter compound has the 3,6-dihydrochamazulene structure IV (Fig. 1). The hydrogens for the 8 and 2 positions appear at lowest field and exhibit both the chemical shift and coupling constants expected for the assigned structure. The triplet at $5{\cdot}12\ \tau$ was assigned to the 5 hydrogen and exhibited the expected chemical shift and coupling constants. Furthermore, irradiation of this triplet caused the doublet for hydrogen 6 at $7{\cdot}8\ \tau$ to collapse to a singlet. The remaining hydrogens can also be readily assigned as indicated in Fig. 1 by the observed chemical shifts and coupling constants as well as by decoupling experiments.

The NMR spectrum of the minor component isolated from chamazulenogen establishes the structure II (Fig. 2). Since we were unable to isolate pure 5,6-dihydroazulene as a model compound for the expected NMR spectrum of 5,6-dihydrochamazulene (II), the NMR spectrum of chamazulene was investigated. The doublet at $2{\cdot}05\ \tau$ in the NMR spectrum of chamazulene (Fig. 2) is assigned to the 8 hydrogen which is coupled to the 6 hydrogen by 2·0 c/s. This serves to identify the 5 hydrogen at $3{\cdot}23\ \tau$ ($J_{5,6} = 10{\cdot}5$ c/s) and the 6 hydrogen at $2{\cdot}83\ \tau$ ($J_{6,5} = 10{\cdot}5$ c/s, $J_{6,8} = 2{\cdot}0$ c/s) which are the AB part of the ABX system of the 7-membered ring. The remaining AB system ($J = 3{\cdot}8$) at 2·93 and $2{\cdot}55\ \tau$ is due to the 2 and 3 hydrogens. Comparison

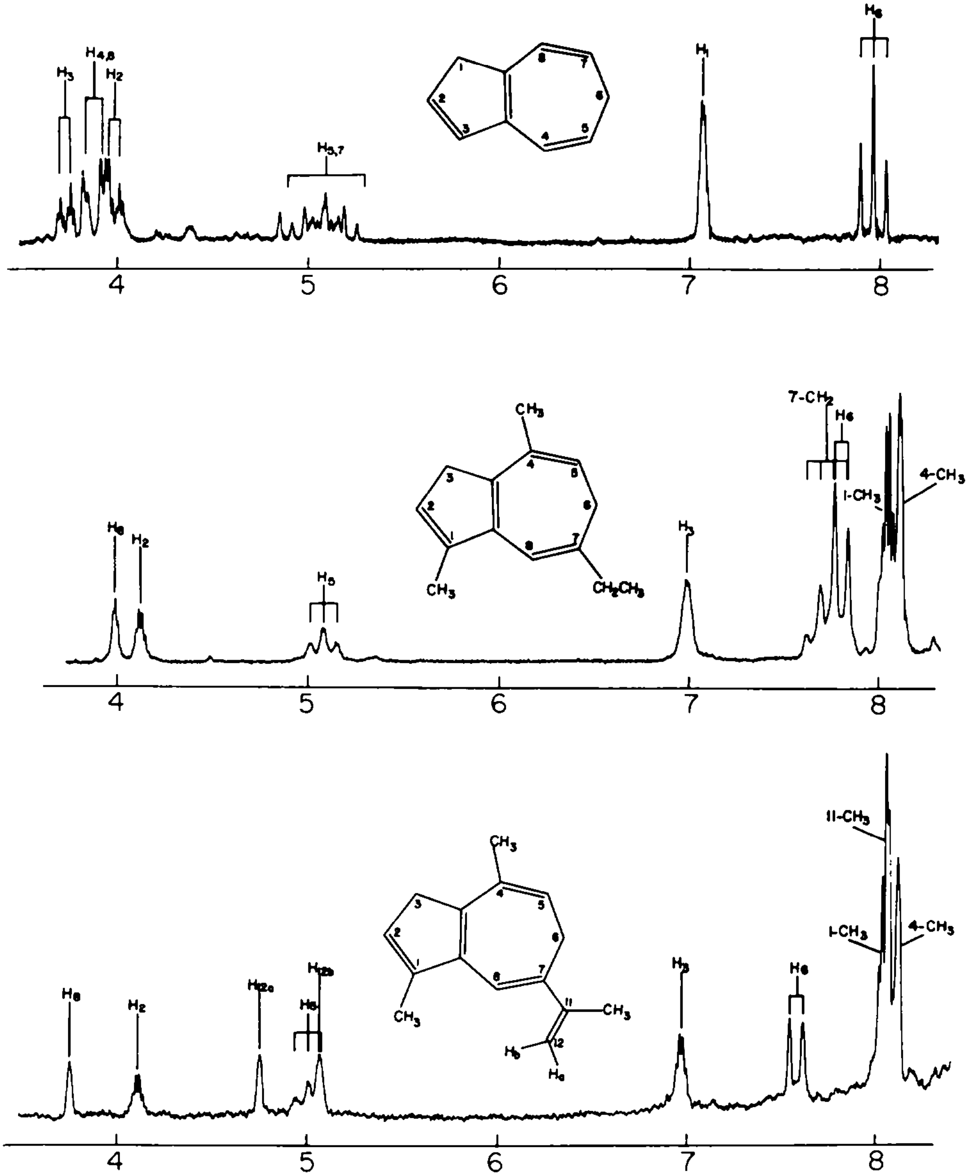


FIG. 1. NMR spectra of 1,6-dihydroazulene, 3,6-dihydrochamazulene (methyl group of the ethyl not shown) and 3,6-dihydrolactarazulene in CCl_4 with TMS as an internal standard.

of this NMR spectrum of chamazulene with that of the minor component from chamazulenogen verifies the 5-membered ring assignment of structure II by the AB doublet (partially obscured by the 8 hydrogen) with a characteristic coupling constant (5·2 c/s) for an unsaturated nonaromatic 5-membered ring.[8] The 8 hydrogen appears as a broad singlet due to the small coupling constant $J_{6,8}$. The remaining hydrogens can be assigned as indicated in Fig. 1. Any other arrangement of the double bonds in the 7-membered ring would require either another vinyl hydrogen (7,8-dihydrochamazulene) or a vinyl hydrogen occurring as a triplet with a coupling constant of ca. 7 c/s (5,8-dihydrochamazulene) inconsistent with the observed spectrum.

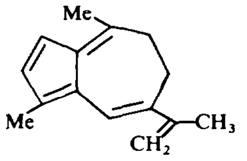
The UV spectra of the two components of chamazulenogen are shown in Fig. 4 and support the structural assignments derived from the NMR spectra. Several 6-vinyl fulvenes have been reported[9] and all exhibit a long wavelength absorption at approximately 395 mμ which appears at shorter wavelength than that of 5,6-dihydrochamazulene (428 mμ), further establishing the assignment of the 7-membered ring double bonds. The UV spectrum of the crude product from the condensation of cyclopentadiene with glutaric dialdehyde exhibits a low intensity long wavelength band at 418 mμ consistent with the presence of some 5,6-dihydroazulene, but of insufficient concentration to be observed by NMR spectroscopy.

Attempts to separate the 5,6-dihydroazulene from the 1,6-isomer by chromatography using the same conditions underwhich 3,6-dihydrochamazulenewas successfully separated from 5,6-dihydrochamazulene led only to oxidation of the mixture to azulene. During the separation of 3,6-dihydrochamazulene from 5,6-dihydrochamazulene by chromatography on aluminum oxide–silver nitrate, concurrent oxidation to chamazulene was also apparent. The order of elution was 3,6-dihydrochamazulene, chamazulene and 5,6-dihydrochamazulene. This indicates that under these conditions only 3,6-dihydrochamazulene is oxidized at a significant rate.

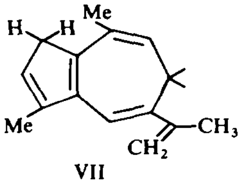
The observation that these dihydroazulene or dihydrochamazulene derivatives are primarily the 1,6- or 3,6-isomers rather than the 5,6-isomers was not expected. Mechanistically it would be anticipated that the kinetic products from the condensation of cyclopentadiene with glutaric dialdehyde or the dehydration–decarboxylation of artabsin should be the 5,6-dihydroazulene systems. Therefore, the observed component mixtures may be due to equilibration under the reaction conditions for their formation. Recent data indicates that fulvenes do not possess appreciable characteristics of resonance stabilized species.[9] The experimental resonance energies of dimethyl fulvene (12 Kcal)[10] and cycloheptatriene (9 Kcal)[11] are comparable, and because of the inherent experimental error in such measurements could not be used to predict the expected equilibrium content of the dihydroazulenes with any certainty.

Extraction of fresh samples of *Lactarius deliciosus L.* with hexane, and chromatography on alumina yielded a bright red–orange hydrocarbon which polymerized with extreme facility. Since previous descriptions of the orange hydrocarbon from this source presented insufficient physical data upon which to make a sound comparison, we can only assume at this time that we are dealing with the same material. The ultraviolet spectrum of this compound (Fig. 5) exhibits a strong similarity to that of 5,6-dihydrochamazulene (II) indicating that they are closely related. Additionally, the previous data on this compound indicated that it was probably a dihydrolactarazulene.[2a]

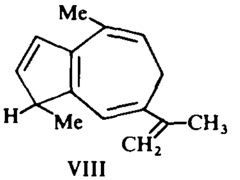
The NMR spectrum (Fig. 3) of this hydrocarbon lactarofulvene, exhibited significant differences from that of 5,6-dihydrochamazulene. The absence of a characteristic 5-membered ring methylene absorption at ca. 7τ eliminated the 3,6-dihydrolactarazulene (VII) structure for this compound. The appearance of only a two hydrogen doublet in the allylic region of the NMR spectrum, and only two vinyl Me groups (by integration) eliminated the 5,6-dihydrolactarazulene structure (VI). The 1,6-dihydrolactarazulene structure (VIII), was eliminated by the lack of an upfield Me doublet and no detectable quartet for the 1-hydrogen. In fact the ratio of vinyl to non-vinyl hydrogens indicated that the molecule was not a dihydrolactarazulene but an isomer of lactarazulene. The fact that the NMR spectrum exhibited only a two hydrogen doublet and two vinyl Me absorptions above 6 τ suggested that lactarofulvene possessed the 1-methylene-1,6-dihydrolactarazulene structure (IX). The remaining vinyl portion of the NMR spectrum was consistent with this assignment but could not provide conclusive evidence in support of it. However, consistent with this structure, decoupling experiments indicated that irradiation of the doublet at 7·33 τ caused the partially obscured single hydrogen triplet at 4·75 τ to collapse to a singlet. Similar irradiation at the center of this partially obscured triplet caused the doublet at 7·33 τ to collapse to a singlet, thus establishing the relationship of these three hydrogens.



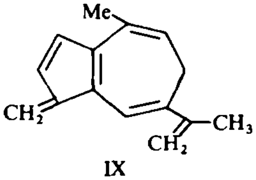
VI



VII

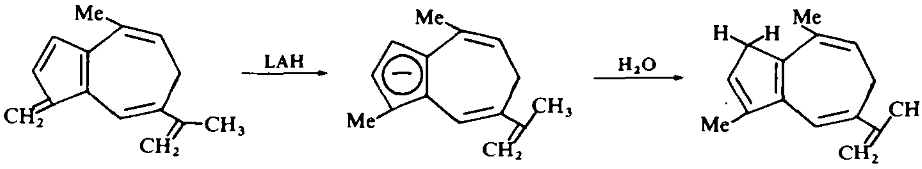


VIII



IX

Treatment of this hydrocarbon with LAH in ether caused reduction characteristic of fulvene hydrocarbons, giving a new hydrocarbon product which exhibited a NMR spectrum (Fig. 2) consistent with an assigned structure of 3,6-dihydrolactarazulene (X). This product would be expected in light of the above results with chamazulenogen. The NMR spectrum (Fig. 1) of this latter hydrocarbon now exhibited an absorption at 6·95 τ with the expected coupling constants characteristic of a 5-membered ring methylene of a dihydroazulene skeleton. In addition, by



(X)

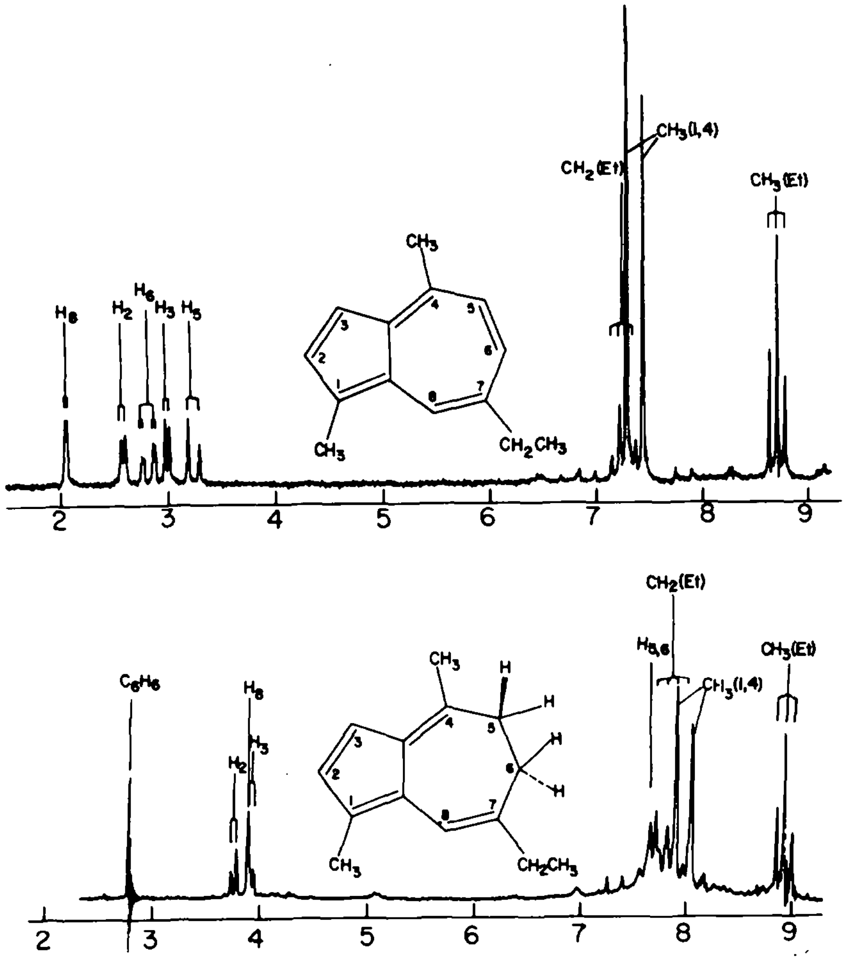


FIG. 2. NMR spectra of chamazulene and 5,6-dihydrochamazulene (the benzene absorption resulted from a portion of this solvent remaining from chromatography) in CCl_4 with TMS as an internal standard.

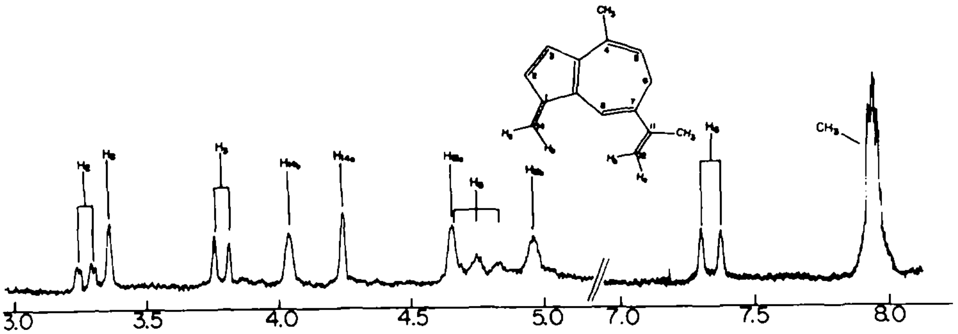
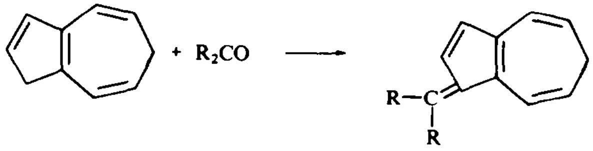


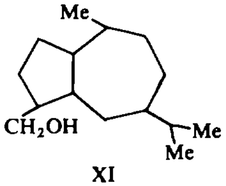
FIG. 3. NMR spectrum of lactarofulvene in CCl_4 with TMS as an internal standard.

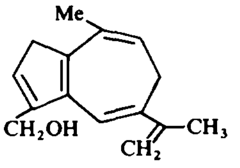
analogy to the NMR spectrum of 3,6-dihydrochamazulene and by decoupling experiments verifying the relationship of H_5 and H_6, the structure of X can be established as indicated in Fig. 2. The assignments of H_{12a} and H_{12b} were made on the basis of broadening due to *cis* or *trans* coupling with the Me group. The observed downfield shift of the 8 hydrogen can be accounted for by the anisotropy of the isopropenyl group present in 3,6-dihydrolactarazulene.

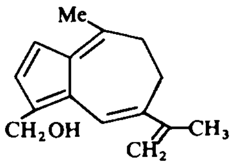
With this data the complete assignment of the NMR spectrum of lactarofulvene could be made. The 2 and 3 hydrogens were assignable as the AB quartet ($J = 5{\cdot}5$) at 3·27 τ and 3·7 τ. The second order coupling observed for the portion of this quartet occurring at 3·27 τ is consistent with a small coupling with the exocyclic methylene hydrogens at C_{14} and identifies this absorption as due to hydrogen two. The hydrogen at C_8 is assigned by analogy to the other compounds in the series. The distinction between the hydrogens occurring at C_{14} or C_{12} was made on the basis that the hydrogens at C_{12} should exhibit broader lines because of coupling with the three hydrogens of the Me group, while the hydrogens at C_{14} are coupled only to the hydrogen at C_2. The C_{12} and C_{14} Ha and Hb assignments are based on an expected greater *trans* coupling constant to either the Me or hydrogen two. The assignments of H_5 and H_6 were made by analogy to the remaining compounds in the series and by the decoupling experiments described above.

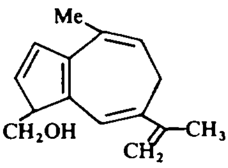
The unusual structure of lactarofulvene is not without precedent. The condensation of 1,6-dihydroazulene with carbonyl compounds has been reported to give this same type of cycloheptatrienylfulvene π-system,[4] although no experimental details or physical constants have been reported. Benešova *et al.* in their preliminary work with extractives of *Lactarius deliciosus L.* established that an alcohol component, upon hydrogenation, gave the saturated alcohol (XI), which was identical to the alcohol resulting from the complete hydrogenation of Lactaroviolin.[2a] Assuming that this alcohol had either the structure XII or XIII, a vinylogous elimination of water would give 1-methylene-1,6-dihydrolactarazulene (IX). The remaining structure XIV which would have the hydroxymethylene at a saturated carbon appears less likely from the fact that the Me group of II, IV and X are at vinyl positions.




XI


XII


XIII


XIV

Work is presently in progress to elucidate the structure of the remaining constituents of *Lactarius deliciosus L.*

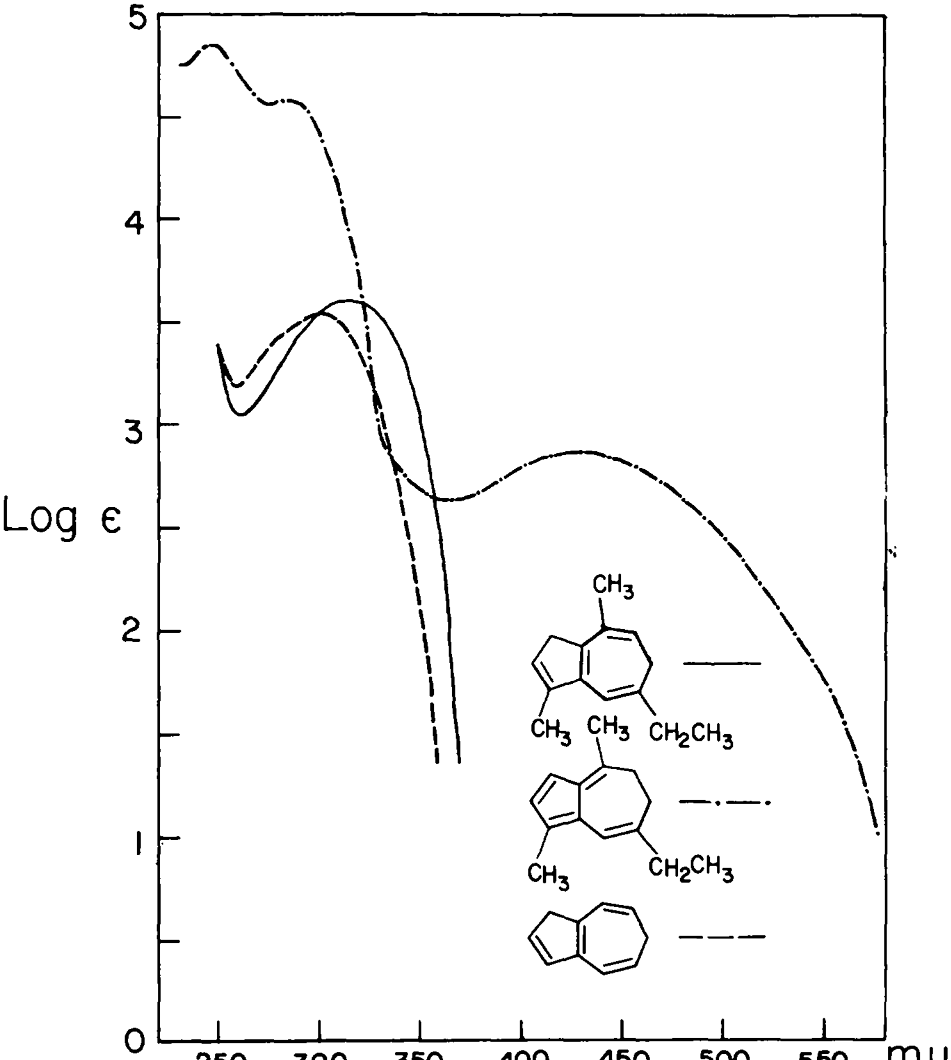


FIG. 4. UV spectra of 3,6-dihydrochomazulene, 5,6-dihydrochamazulene and 1,6-dihydroazulene in cyclohexane.

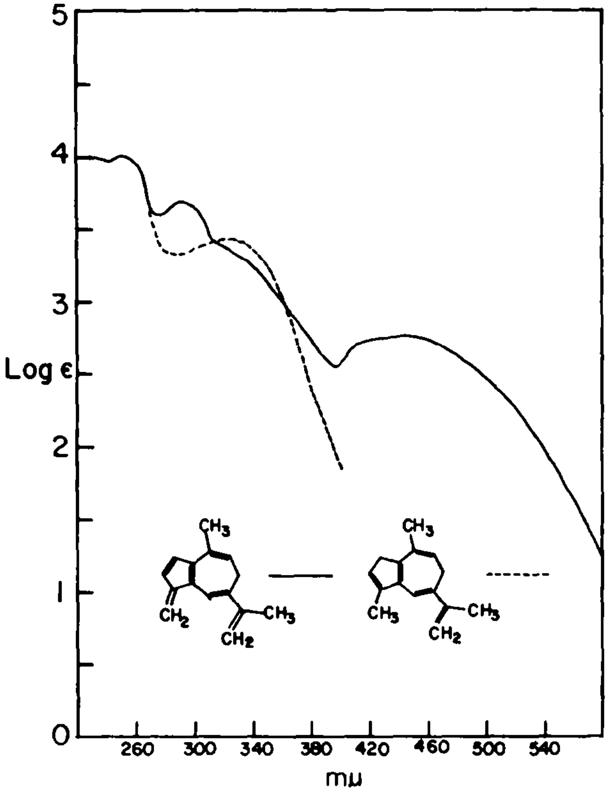


FIG. 5. UV spectra of lactarofulvene (1-methylene-1,6-dihydrolactarazulene) and 3,6-dihydrolactarazulene in cyclohexane.

EXPERIMENTAL

All m.ps are corrected. The NMR spectra were obtained using a Varian HA-100 high resolution spectrometer. UV spectra were recorded on a Cary model 14 spectrometer.

Chamazulenogen. Wormwood Oil (American), S. B. Penick and Co., (100 g) was distilled under reduced press. The fraction b.p. 95–120°/0·3 mm was collected (15 g) and then chromatographed on alumina (5 × 25 cm). The orange chamazulenogen was eluted with pentane immediately before the blue chamazulene band. Evaporation of the chamazulenogen fraction with N_2 yielded 5 g of an intense orange oil. A NMR spectrum showed it to be predominantly IV. On exposure to air a pentane soln of chamazulenogen readily turned blue and deposited a flocculent white ppt.

Isolation of the two components of chamazulenogen. 5% $AgNO_3$ aq on alumina was prepared by stirring 35 g $AgNO_3$ in 200 ml water with 610 g Al_2O_3 (Merck). The water was evaporated in a large evaporating dish with constant stirring. The dried material was then heated until evolution of nitrogen dioxide began. The material was placed in a vacuum desiccator and allowed to cool at 0·1 mm. Chamazulenogen (5·0 g) was chromatographed on alumina (3·5 × 15 cm) prepared in this manner. Upon elution with pentane a pale yellow band was removed from the column. The yellow soln was concentrated under N_2 to ca. 10 ml and diluted to ca. 20 ml with CCl_4. This process was repeated until all the pentane was removed. Final concentration to ca. 1 ml gave a 3,6-dihydrochamazulene soln in CCl_4 suitable for NMR studies. Evaporation of the solvent yielded a pale yellow oil, which slowly polymerized at room temp under N_2. By progressively eluting the column with 5%benzene–pentane (50 ml), a blue chamazulene containing band was removed. After workup as above, NMR analysis showed the material to be mostly 3,6-dihydrochamazulene. Elution of the column with benzene (575 ml) afforded an intense orange oil. The benzene fractions were combined and once more chromatographed on 5% $AgNO_3$ on alumina. After elution of the blue band containing chamazulene and 3,6-dihydrochamazulene with 25% benzene–pentane, an orange band was eluted from the column with 50% benzene–pentane. After workup as above, a soln of 5,6-dihydrochamazulene in CCl_4 was obtained, suitable for NMR analysis. Evaporation of the solvent yielded a black–orange oil which slowly polymerized on standing at room temp under N_2. Solns of 3,6- or 5,6-dihydrochamazulene in pentane were evaporated in the cold with N_2, in weighed volumetric flasks. The residual oil was rapidly weighed and diluted with cyclohexane for the purpose of taking UV spectra. Using the epsilon values determined in this manner, the original mixture was found to consist of 94% 3,6-dihydrochamazulene and 6% 5,6-dihydrochamazulene. UV spectra (cyclohexane) 3,6-dihydrochamazulene, 313 mμ (3·60); 5,6-dihydrochamazulene, 428 mμ (2·86), 284 mμ (4·58) and 247 mμ (4·85).

1,6-Dihydroazulene. 1,6-Dihydroazulene was synthesized according to the method of Fenton and Hurmitz[6] for the reported synthesis of 5,6-dihydroazulene. A bright red fraction (b.p./04 mm, 37°–38°) was collected which did not solidify on cooling. The sample was diluted under N_2 with CCl_4. The NMR spectrum showed it to be almost completely 1,6-dihydroazulene. UV spectrum (cyclohexane), 303 mμ (3·53).

Chamazulene. The crude chamazulene isolated during the chromatography of the chamazulenogen containing fraction of wormwood oil was converted to the trinitrobenzene complex in the usual manner (m.p. 132·5°, reported m.p. 132°).[4] The complex was decomposed on alumina in the usual way and the resulting chamazulene was further chromatographed on alumina 3 times. This sample was used to determine the NMR spectrum (Fig. 1).

Lactarofulvene (1-methylene-1,6-dihydrolactarazulene) (IX). Fresh carpophores of *Lactarius deliciosus L.* (5 Kg collected in northern California in December) were thinly sliced and immersed in a mixture of 2 l. of EtOH and 1 l. of pentane and stirred occasionally. After 24 hr the bright orange pentane layer was passed directly through a neutral Merck alumina column (15 × 3½ cm) which left the colored material at the top. The orange lactarofulvene was eluted from the column with 10% benzene–pentane (250 ml). After evaporation of the solvent with a N_2 stream, the residual intensely orange oil was dissolved in ca. 5 ml pentane and again chromatographed on alumina (15 × 3½ cm). After elution with 10% benzene–pentane (250 ml), and removal of the solvent with a N_2 stream, the lactarofulvene (128 mg) was taken up in CCl_4 for the purpose of obtaining an NMR spectrum. UV spectrum (cyclohexane) 440 mμ (2·76), 290 mμ (3·67), 252 mμ (3·98).

3,6-Dihydrolactarozulene (V)-*Lactarofulvene* (128 mg, 0·65 mmole) was dissolved in ca. 100 ml anhyd ether in a flask equipped with a magnetic stirrer and N_2 inlet. LAH (25 mg, 0·65 mmole) was added to the mixture. After ca. 5 min an additional 15 mg LAH was added. The mixture became cloudy white. A saturated soln of sodium tartrate was then added dropwise until gas evolution ceased. The ether layer was removed with a dropper and the aqueous phase was washed twice with ether. The combined ether layers were evaporated with a N_2 stream. The residue was taken up in a little pentane and chromatographed twice on alumina (1 × 5 cm). After evaporation of the solvent, 3,6-dihydrolactarazulene (30 mg, 23%) was obtained suitable for determination of the NMR spectrum. UV spectrum (cyclohexane) 323 mμ (3·42). The 3,6-dihydrolactarazulene could be dehydrogenated with 10% Pd–C in refluxing benzene to give a blue material. UV spectrum (cyclohexane) 732 mμ, 695 mμ (sh), 659 mμ, 630 mμ, 605 mμ, 581 mμ (sh), 556 mμ (sh), 380 mμ (sh), 290 mμ, 260 mμ (sh), 254 mμ, 245 mμ, 238 mμ (13). A partial UV spectrum lactarazulene in ether has been reported: 662 mμ, 632 mμ, 603 mμ, 581 mμ, 556 mμ.[12]

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