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(40) We may note the striking similarity between cyclopentanone and the thujones, analogous to that between the methylcyclopentanols and thujanols.
(41) Our conclusion is in contrast with that of Tori[11] who proposed a boat form in both ketones with a dihedral angle of 30–40° between C2–C3 and C3–C4. Norin et al.[6] indicated a similar conformation.
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(51) The possibility that the cyclopropane methylene bridge as an additional substituent in position 3 (relative to OH) could contribute to the rate enhancement cannot be excluded. Rates of oxidation of the trans–cis pairs of alcohols **13–14**, **15–16**, and **17–18** are very similar within each pair. However, the question of an additive effect is open.
(52) We may use the same approach that we applied in estimating the effect of the *i*-Pr group in thujanol (**5**) and view the $-CH_2-$ bridge as remotely comparable to $-CH_3$. Then, *cis*-3-methylcyclopentanol (**14**) is oxidized 3.42 times faster than cyclopentanol.[50] This comes very close to the observed rate (5.31) for isothujanol (**4**), in which an additional effect of the neighboring methyl group will be present.
(53) An –OH group located at a conformationally mobile section of a five-membered ring, which itself is a part of a bicyclic system, can escape severe steric interactions through slight torsional adjustments when compared to an –OH group located at a rigid position of such a bicyclic system. A good example is the pair of alcohols **19** and **20**. The size of the molecule itself appears unimportant as shown by the rate of oxidation of alcohol **21**. Displacement of an OH group by only 0.3 Å is sufficient to reduce ground state interactions to ⅓ of their original magnitude.[43,44,54] This corresponds to about 12° in angular rotation, a value close to the 14° indicated for the torsional angle between C2–C3 (and C3–C4) by our LSR study.
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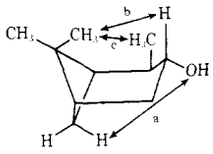
(55) Sen and Jones[56] proposed on the basis of a H^1 NMR study that in the analogous aminopinane the NH_2 group is pseudoequatorial. We assume an analogous conformation in isopinocampheol:



Dreiding models reveal strong steric interaction along b and c. Extent of the boatlike conformation is given by the balance of these two interactions. Oxidation will relieve b and (depending on the conformation of the resulting ketone) possibly c. Relief of the latter type is, to a degree, illustrated by comparing alcohols **22** and **23.**
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(61) Actually, a slight rate enhancement effect is present. Such effects, caused by remote alkyl groups, were observed in the cyclohexane series, e.g., **28** and **29** of Table IV. Effects of alkyl groups were discussed by Eliel.[57,58] Interpretation of results on the basis of axial and equatorial characteristics comparable to the cyclohexane series is not quite applicable. Rates of acetylation and their ratios in alcohols **9** and **10** in comparison to **24** and **25** are an example. Rates of acetylation of the two methylcyclopentanols **9** and **10** are very similar to the rates of the two methoxycyclopentanols **26** and **27**, Table IV.
(62) Actually, it would support the conformation of isopinocampheol as indicated in ref 55. There, the approach of Ac_2O along a would encounter little hindrance. However, the acetylation rate of **12** still remains obscure when it is compared with, e.g., *p*-*tert*-butylcyclohexanol (**30**).
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Synthetic Studies on Terpenoids. 5.[1] Syntheses of γ- and δ-Lactones from β-(2,7-Dimethyl-1,2-dihydroxycycloheptyl)propionic Acid[2]

Opinder Singh Bhanot, Tushar Kanti Das, Indranil Gupta, Harcharan Singh Suri, and Phanindra Chandra Dutta*

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta 700032, India

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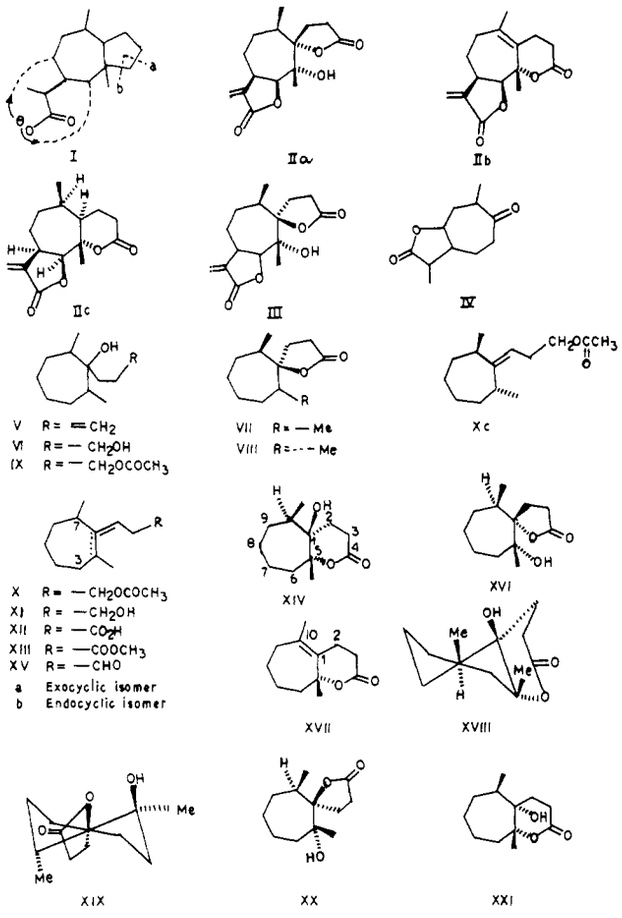
Starting from 2,7-dimethylcycloheptanone, the lactones VII, VIII, XIV, XVI, XX, and XXI have been synthesized and their conformation and stereochemistry studied. XVI represents the partial structure of IIa. VII and XXI represent the partial structures of III and IIc, respectively. Isomerization of δ-lactone to γ-lactone in the presence of acid has been discussed.

The γ-lactone moiety associated with sesquiterpene monolactones involves the isopropyl group. The other lactonic moiety in the recently discovered sesquiterpene dilactones,[3] which are again related to pseudoguaianolides (I), is formed through fission of the cyclopentane ring at a, viz., vermecrin[4] and greenein,[5] or at b, viz., psilostachyins[6] (IIa–c) and canambrin[7] (III). Experiments have been initiated in this laboratory and reported earlier[2] with a view to developing methods for building up stereospecifically different types of the lactonic functions associated with the cycloheptane ring. The compounds so formed may represent partial structures of IIa–c and III with defined stereochemical assignments at each of the three asymmetric centers present in some of these model compounds. Another aspect of interest is to study the relative rate of formation of different types of lactones, γ- and/or δ-, consistent with conformational stability of the highly mobile cycloheptane ring.

In a previous publication,[8] the lactone IV has been synthesized, its identity with one of the degradation products from xanthumin has been established, and its conformation has been discussed.

2,7-Dimethylcycloheptanone required for these studies was synthesized by two different methods. The condensation product from ethyl 6-bromohexanoate[9] and diethyl methylmalonate on hydrolysis and subsequent esterification afforded diethyl α-methylsuberate. This was also prepared through the fission of ethyl 2-methylcycloheptanone-2-carboxylate in the presence of a catalytic amount of sodium ethoxide.[10] The diester was subjected to cyclization according to modified high-dilution technique.[11] The cyclized product was methylated in situ to afford 2-ethoxycarbonyl-2-7-dimethylcycloheptanone and this on hydrolysis gave 2,7-dimethylcycloheptanone. The ketone was found by GC analysis to be a mixture (4:1) of two components. These were separated by



preparative GC (see Experimental Section). The NMR and mass spectra of both the components are superimposable, but their IR spectra show some distinct difference in the 920–1060-cm^{-1} region. The major component is the *cis*-2,7-dimethylcycloheptanone because, the two methyl groups being situated α to the carbonyl function, it will readily epimerize and assume mainly the equatorial conformation representing the cis stereochemistry. This is further supported by the behavior[12] of 2,6-dimethylcyclohexanone, which is present (85:15, cis:trans).

The ketones were treated with allylmagnesium bromide to afford V in an excellent yield. The crude product obtained by passing diborane gas through V was oxidized[13] with chromic acid to afford the spirolactones VII and VIII. Again, hydroboration of V followed by treatment with alkaline hydrogen peroxide[14] furnished the diols VI. Oxidation of VI with alkaline potassium permanganate solution afforded the same mixture of spirolactones as evident from comparative IR and GC studies. Analytical GC of the lactonic mixture showed two peaks with retention times of 12 and 13 min, and the ratio of peak heights was ca. 15:78 with minor components (~6%). The lactonic mixture was separated into two components by preparative GC (see Experimental Section). One component (A) is a colorless oil (15%), and another (B), colorless prisms (78%). However, it was very difficult to separate the mixture into pure components by preparative GC because retention times of two components were close to each other. Therefore, two components were not obtained in a pure state, and their purities were shown to be 95% by analytical GC. The major component B should possess the stereoformula VII because allylmagnesium bromide attacked mainly from the opposite side of the two cis-oriented methyl groups in dimethylcycloheptanone. The minor component A should be depicted by VIII as it has arisen from the minor constituent of dimethylcycloheptanone. Both the components absorbed in the IR at 1760 cm^{-1} in the carbonyl region, but showed some significant difference in the 800–1300-cm^{-1} region. The NMR spectra of VII showed two distinct doublet of the two secondary methyl groups centered at δ 1.0 (J = 6 Hz) and 0.904 (J = 7 Hz). The two secondary methyl groups of compound VIII appeared as two distinct doublets centered at δ 1.0 (J = 6 Hz) and 0.89 (J = 7 Hz).

The diols VI were treated with acetic anhydride and pyridine to give the hydroxyacetates IX, which on dehydration with phosphorus oxychloride and pyridine afforded the unsaturated acetates Xa,b. Analytical GC showed it to be a mixture of two components (80:15) with a minor constituent (~5%). The NMR spectra of the unsaturated acetates confirm the structure Xa for the major constituent. The presence of a low-intensity singlet at δ 1.75 can be assigned to the vinylic methyl group, suggesting thereby that the isomeric acetate Xb is also present in a lesser amount. The minor constituent mentioned above may be Xc, which is the only other possibility in the acetate mixture and may arise from the minor constituent (~20%) originally present in dimethylcycloheptanone. However, its presence could not be detected through NMR studies. For further confirmation, the isomeric acetates were separated into pure constituents Xa and Xb through preparative GC and their structures confirmed by NMR studies (see Experimental Section). The IR and mass spectra of Xa and Xb showed slight but significant differences. The same mixture of unsaturated acetates (Xa,b) was also prepared by treatment of VI with acetic anhydride in the presence of anhydrous acetate. Their identity was established through comparative IR, NMR, and GC studies.

Xa,b were saponified to XIa,b, which on oxidation with Jones reagent furnished XIIa,b, and the pure crystalline acid XIIa was isolated as the major fraction (vide infra). The corresponding methyl ester mixtures (XIIIa,b) could not be separated into pure components by using different columns in preparative GC. The mixture was treated with an excess of an ethereal solution of monoperphthalic acid. The crude epoxide, arising mainly from attack of the oxidizing agent from the opposite side of the secondary methyl group due to steric reasons, was boiled with aqueous sodium hydroxide solution to effect opening of the epoxide ring through the carboxylate ion. The products were separated into a neutral and an acidic fraction and the latter corresponds to about 80% of the mixture. The neutral material was chromatographed and a solid compound having a δ-lactone moiety was isolated from the benzene–ether fraction (50:1) and it showed a single peak it GC. The diaxial opening[15] of the epoxide, irrespective of the stereochemistry of the oxide ring, should give rise to the cis lactone. The methyl group at C-5 is already in the equatorial position and hence β oriented. Therefore, the hydroxylactone may be given the stereochemical assignment as depicted in XIV. Elution with benzene–ether (1:1) afforded a hydroxylactone as a liquid with a γ-lactonic moiety as revealed in the IR. Its purity was tested through TLC in different solvent systems. Elemental analyses, various spectral data, and the well-appreciated diaxial opening of the epoxide ring again suggested that XX should be the stereoformula of the hydroxy-γ-lactone. XIV with C-1 hydroxyl and C-10 hydrogen in trans disposition was anticipated to be easily dehydrated to XVII. When subjected to dehydration with phosphorus oxychloride and pyridine or thionyl chloride and pyridine at low temperature it yielded a complex mixture[16] of unsaturated compounds, as revealed in the NMR. The presence of XVII, the partial structure of IIb, in the product is indicated by an ill-defined triplet at δ 1.72.

The crystalline acidic fraction was found to be XIIa and is characterized by one olefinic proton at δ 5.45, coupled to two protons at δ 3.15 (J = 7.5 Hz). A decoupling experiment confirmed this. There is a hydroxyl proton appearing at δ 11.47 arising from the carboxylic acid function. Both the methyl

groups are split into doublets at δ 0.94 and 1.04 (J = 7.5 Hz). It is interesting to note that the β,γ-unsaturated acid (XIIa) resisted epoxidation with monoperphthalic acid under these conditions and epoxidation is most likely stereospecific.

With a view to studying the possibility of the formation of a γ- and/or δ-lactone from a vicinally situated cis-hydroxylated acid from XIIIb, experiments had been designed accordingly. As the desired unsaturated acid is present as a minor constituent, attempts have been made to force the double bond to migrate inside the ring leading to the formation of the tetrasubstituted double bond as is found in XIIb. Xa,b was treated with *N*-lithioethylenediamine[17] and the product did not exhibit any IR absorption for the acetate group, indicating thereby that this had been knocked off. The material was reacetylated and from the NMR it was found that about 50% of conversion to the endocyclic isomer had taken place. Estimation was possible through comparison with the methylene protons of the acetate function and the vinyl proton of the exocyclic isomer. This types of isomerization was next studied with XIa,b. In this case also only 50% of conversion had taken place. Increase of the reaction period had virtually no effect on the extent of isomerization (beyond 50%) and this was evidently an equilibrium mixture. This arises due to severe 3,7-interaction, present in the endocyclic bond isomer, and this is a characteristic property of cycloheptene derivatives.[18] Next it was decided to oxidize the isomerized XIIa,b. Oxidation with Jones reagent having been found unsatisfactory, oxidation with ruthenium tetroxide was next attempted. The oxidation product in this case was found to be a mixture of neutral and acidic parts and from the nature of the products it was evident that ruthenium tetroxide had affected the double bond. The isomerized XIa,b were next oxidized with chromium trioxide and pyridine to the corresponding aldehydes (XVa,b). These were again oxidized with silver oxide to afford the unsaturated acids (XIIa,b). The corresponding methyl esters (XIIIa,b) were oxidized with osmium tetroxide giving rise to cis disposition of the two vicinal groups. The resulting product was characterized in the IR by two distinct bands corresponding to a broad band in the hydroxyl region and a single band at 1735 cm^{-1} characteristic of the ester function. This was hydrolyzed under mild alkaline conditions and the free hydroxy acid was subjected to lactonization under mild acidic conditions. The acidic material was removed and the neutral material thus obtained exhibited two distinct bands at 1760 and 1740 cm^{-1} in the IR indicating the presence of a γ-lactone and a δ-lactone. On chromatography over neutral alumina, hydroxy-γ-lactone XVI was isolated as a liquid on elution with benzene–ether (1:1). Its purity was tested through TLC in different solvent systems and sharp NMR signals. The molecular ion peak in the mass spectrum appears at m/e 212 and the base peak is at m/e 194, indicating removal of the elements of water. The presence of tertiary Me at δ 1.3 as a sharp singlet in the NMR of XVI completely ruled out the possibility of the formation of an isomeric hydroxy-γ-lactone from XIIa. XVI represents the partial structure of psilostachyin (IIa). Elution with benzene–ether (50:1) afforded a crystalline material (mp 150 °C). It exhibited a sharp band at 1740 cm^{-1} in the IR indicating the presence of a δ-lactonic moiety. The elemental analyses and other spectral data suggest that XXI is the structure for the δ-lactone. It is likely that the oxidation to the endocyclic double bond has again taken place[19] mostly from the back side of the secondary methyl group in XIIIb because two products could only be isolated. Evidently the trans-lactone ring has been formed and this is present in IIc.

From the conformational analysis of the seven-membered ring, the δ-lactone XIV is represented by the stereoformula XVIII and the spirolactone XVI by XIX on the basis of calculations previously detailed out from this laboratory.[8]

One interesting point should be mentioned here: opening of the epoxide through the carboxylate ion leading to the formation of the δ-lactone XIV is kinetically controlled. Isomerization takes place on treatment with acids resulting in a mixture of γ- and δ-lactones. If the lactonic mixture is warmed (60–70 °C) on a water bath for a prolonged period (4–6 h), the product isolated is the γ-lactone XX; evidently the equilibrium of δ- and γ-lactones shifts to the γ-lactone, thereby affording the thermodynamically more stable γ-lactone XX as the major, if not the only, product. Similar experiments with the mixture of XXI and XVI lead to the same conclusion that the thermodynamically stable γ-lactone XVI is formed as a major product. These results are quite comparable to those with lactonic functions attached to cyclohexane rings.

Experimental Section

Boiling and melting points are uncorrected. The IR spectra were taken on a Perkin-Elmer Model 21 double beam recording spectrophotometer in chloroform solution. UV absorption spectra were measured for 95% ethanol solution with a Beckman DU 2 spectrophotometer (manually operated). The NMR spectra were determined with a Varian A-60 spectrometer for solutions in CCl_4 and peak positions are reported in parts per million from Me_4Si serving as internal reference. Light petroleum refers to the fraction of bp 60–80 °C. All solvent extracts were dried over Na_2SO_4.

2,7-Dimethylcycloheptanone. 2-Methyl-2-ethoxycarbonylcycloheptanone (120 g) was subjected to cleavage in presence of Na (1 g) in EtOH (60 mL) by heating on a water bath for 6 h. The product was worked up to afford diethyl α-methylsuberate (105 g), bp 140 °C (7 mmHg). This was subjected to cyclization according to high-dilution technique and methylated in situ with methyl iodide to afford **2-ethoxycarbonyl-2-7-dimethylcycloheptanone.** The crude keto ester (50 g) was heated under reflux with concentrated HCl (300 mL) for 30 h to afford **2,7-dimethylcycloheptanone** (25 g), bp 105 °C (40 mmHg). Anal. Calcd for $C_9H_{16}O$: C, 77.1; H, 11.5. Found: C, 76.9; H, 11.4. It yielded an orange 2,4-dinitrophenylhydrazone. 99 °C (ethanol). Anal. Calcd for $C_{15}H_{20}O_4N_4$: C, 56.2; H, 6.2. Found: C, 56.1; H, 6.2. The ketones were separated into two components a and b by using a column 6 m in length with 15 mm i.d., and consisting of 5% Carbowax 20M. It was operated at 100 °C with a flow rate of 200 mL/min of He. Compound a and b had retention times of 31.4 and 35.4 min, respectively.

1-Allyl-2,7-dimethyl-1-hydroxycycloheptanes (V). A solution of 2,7-dimethylcycloheptanone (7.5 g) in ether (30 mL) was added under N_2 during 1 h with stirring to a cold (0 °C) slurry of allylmagnesium bromide from allyl bromide (22.5 g) and Mg (12 g) in ether (100 mL). The reaction mixture was left overnight and the excess Grignard reagent decomposed with dilute aqueous NH_4Cl. The organic phase was worked up and distilled to afford V (9 g), bp 98–100 °C (7 mmHg). Anal. Calcd for $C_{12}H_{22}O$: C, 79.0; H, 12.1. Found: C, 79.1; H, 12.1.

2,7-Dimethyl-1-hydroxy-1-(3′-hydroxypropyl)cycloheptane (VI). B_2H_6 generated from the addition of $NaBH_4$ (1 g) in diglyme (25 mL) to boron trifluoride etherate (10 mL) in diglyme (8 mL) was passed through a solution of the unsaturated alcohol V (4 g) in dry THF (50 mL) below 30 °C. After 2 h the solution was flushed with dry N_2 for 20 min and finally with dry air for 6 h. The residual thick mass was diluted with acetone (40 mL) and stirred overnight with a mixture of NaOH solution (10 mL, 10%) and H_2O_2 (16 mL, 30%) at room temperature and next day with an additional amount of H_2O_2 (8 mL) for 2 h. The reaction mixture was partitioned between ether and brine and the organic layer afforded the diols VI (4 g), bp 136 °C (0.8 mmHg), ν_{max} 3500 cm^{-1}. Anal. Calcd for $C_{12}H_{24}O_2$: C, 71.9; H, 12.1. Found: C, 71.6; H, 11.9.

Lactones of 3-(2′,7′-Dimethylhydroxycycloheptyl)propionic Acid (VII, VIII). A. The diol VI (1 g) in H_2O (60 mL), containing KOH (0.3 g), was oxidized by gradual addition of $KMnO_4$ (3 g) during 4 h with stirring at room temperature. The reaction mixture was filtered and the filtrate extracted with ether to remove the neutral material. The alkaline aqueous layer was acidified and extracted with ether. The ethereal extract was washed with aqueous Na_2CO_3 solution (2%) and H_2O and dried. On distillation it afforded VII and VIII (0.6 g), bp 140–142 °C (5 mmHg), ν_{max} 1765 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.4; H, 10.3. Found: C, 73.3; H, 10.2.

B. A solution of the unsaturated alcohol V (4.5 g) in THF (50 mL) was saturated with excess B_2H_6 at a temperature below 30 °C. The

excess reagent was decomposed as described earlier. The residual thick mass was diluted with acetone (40 mL) and Jones reagent (120 mL) added dropwise at 15 °C with stirring over a period of 8 h. After usual workup the concentrated extract (ca. 4 g) was mixed with methanolic NaOH solution (30 mL, 15%) and heated on a steam bath for 30 min. The cooled reaction mixture was diluted with NaOH solution (50 mL, 5%) and the neutral material taken up with ether. The alkaline solution was acidified with dilute HCl and extracted with ether. The ethereal solution was washed with H_2O, dried, and distilled to afford VII and VIII (3 g), bp 140–142 °C (5 mmHg). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.4; H, 10.3. Found: C, 73.2; H, 10.2. The IR and GC spectra of the lactones obtained through different methods were superimposable.

Separation of the Lactonic Mixture (VII and VIII). Before preparative GC the sample was examined in various columns [5% Carbowax 20M, 5% CHDMS, 5% OV-101 (SE-30), 5% XE-60, 2% polyphenyl ether, 5% QF-1]. Of the various columns, 5% XE-60 and 5% QF-1 were found to be suitable and for the present purposes. 5% XE-60 was employed for separation of the lactonic mixture. For analytical GC a glass column 3 mm × 3.0 m consisting of 5% XE-60 on Chromosorb W (80–100 mesh) was operated at 200 °C with a flow rate of 50 ml/min of nitrogen. For preparative GC a column 15 mm × 1.5 m consisting of 5% XE-60 on Chromosorb W (80–100 mesh) was operated at 170 °C with a flow rate of 300 ml/min of He. As the GC of the sample showed a broad peak, it was separated into different fractions. By repeated preparative GC of each fraction the lactone VII was obtained as colorless prisms, mp 34–36 °C, and VIII as a colorless oil.

2,7-Dimethyl-1-hydroxy-1-(3′-acetoxypropyl)cycloheptanes (IX). Ac_2O (15 mL) was added to a solution of the diols VI (3 g) in pyridine (15 mL). After 18 h at room temperature the mixture was poured into H_2O and worked up to afford IX (3.0 g): bp 132 °C (2 mmHg); ν_{max} 3500 and 1730 cm^{-1}. Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.4; H, 10.8. Found: C, 69.3; H, 10.9.

2,7-Dimethyl-1-(3′-acetoxypropyl)cycloheptene (Xb) and Bond Isomer (Xa). A. $POCl_3$ (5 mL) was added to a solution of the monoacetate IX (3 g) in pyridine (12 mL) and allowed to stand overnight. The contents were heated on a steam bath for 1 h and after cooling, the dark reaction mixture was cautiously poured into crushed ice (300 g) and the mixture thoroughly stirred. The organic material was distilled to afford the acetates Xa,b (2.3 g), bp 94–95 °C (0.6 mmHg), ν_{max} 1730 cm^{-1}. Anal. Calcd for $C_{14}H_{24}O_2$: C, 75.0; H, 10.8. Found: C, 74.9; H, 10.6. The isomerized acetate mixture was separated by preparative GC using a column 6 m in length with 15 mm i.d. consisting of 5% diethylene glycol succinate polyester at 150 °C with a flow rate of 200 mL/min of He. The exocyclic isomer had a retention time of 17.1 min and the endocyclic isomer had a retention time of 24.0 min. Endocyclic isomer: NMR δ 1.1 (3 H, d, J = 7 Hz), 1.65 (3 H, s), 2.05 (3 H, s), 4.1 (2 H, t, J = 6 Hz); M^+ m/e 224; ν_{max} 1730 cm^{-1}. Exocyclic isomer: NMR two methyls split into two doublets, δ 0.93, 1.03 (J = 7 Hz), 2.05 (3 H, s), 2.45 (2 H, t, J = 8 Hz), 4.1 (2 H, t, J = 6 Hz), and 3.15 (1 H, t); M^+ m/e 224: ν_{max} 1730 cm^{-1}.

B. A mixture of the diols VI (3.2 g), anhydrous NaOAc (4 g), and Ac_2O (20 mL) was refluxed in an oil bath for 5 h. The reaction mixture was cooled and excess of Ac_2O decomposed by adding H_2O and warming it on a water bath for 15 min. The organic material was taken up in ether and the ethereal solution washed with Na_2CO_3 solution (5%) and H_2O and dried. On distillation it afforded the unsaturated acetates (Xa,b, 3.5 g), bp 100–102 °C (1 mmHg). Anal. Calcd for $C_{14}H_{24}O_2$: C, 75.0; H, 10.8. Found: C, 74.8; H, 10.8. The IR spectra of the two samples prepared through different methods were superimposable.

2,7-Dimethyl-1-(3′-hydroxypropyl)cycloheptene (XIb) and Bond Isomer (XIa). The unsaturated acetate mixture (Xa,b, 3 g) was heated under reflux for 3 h with alcoholic KOH solution (40 mL, 2 N). Workup afforded the unsaturated alcohols (XIa,b, 2.2 g), bp 92–93 °C (0.6 mmHg). Anal. Calcd for $C_{12}H_{22}O$: C, 79.0; H, 12.1. Found: C, 79.0; H, 12.0.

3-(2′,7′-Dimethylcycloheptylidene)propionic Acid (XIIa). Jones reagent (5.5 mL) was slowly added to a cooled (0 °C) solution of the unsaturated alcohols (XIa,b, 3 g) in acetone (60 mL) with occasional shaking during 10 min. The reaction mixture was kept at 0 °C for a further 15 min. Usual workup yielded XIIa,b (1 g), bp 135–137 °C (8 mmHg). Fractional crystallization afforded XIIa (700 mg), mp 86 °C (light petroleum), ν_{max} 1715 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.4; H, 10.3. Found: C, 73.3; H, 10.1.

Methyl 3-(2′,7′-Dimethylcycloheptenyl)propionate (XIIIb) and Bond Isomer (XIIIa). Unsaturated acids (XIIa,b, 2 g) were esterified with an ethereal solution of CH_2N_2 and after usual workup and distillation, afforded XIIIa,b (1.8 g), bp 110 °C (0.2 mmHg). Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.2; H, 10.5. Found: C, 74.1; H, 10.3.

δ-Lactone of 3-(2′,7′-Dimethyl-*trans*-1′,2′-dihydroxycycloheptyl)propionic Acid (XIV) and γ-Lactone of 3-(2′,7′-Dimethyl-*trans*-1′,2′-dihydroxycycloheptyl)propionic Acid (XX). An ethereal solution of monoperphthalic acid (90 mL, 4%) was added to the unsaturated esters (XIIIa,b, 1.7 g) in ether (20 mL) at 0 °C and the residue left after removal of the solvent was heated under reflux with NaOH solution (25 mL, 5%). The alkaline aqueous solution, after removing neutral material with ether, was acidified with dilute HCl and warmed on a water bath (50 °C) for 30 min. The organic material was taken up in ether and the ethereal extract washed with Na_2CO_3 solution (2%). The residue obtained after removal of the solvent was chromatographed over neutral alumina. The fraction eluted with benzene and ether (50:1) afforded the solid δ-lactone XIV (60 mg): mp 68 °C (light petroleum); ν_{max} 3620 and 1740 cm^{-1}; NMR δ 1.04 (3 H, d, J = 7 Hz, 2-Me), 1.34 (3 H, s, 7-Me), and 2.0 (1 H, s, exchangeable). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.9; H, 9.5. Found: C, 67.8; H, 9.4. Elution with benzene–ether (1:1) afforded the γ-lactone XX (240 mg) as a liquid which was evaporatively distilled at 120–122 °C (0.1 mmHg): ν_{max} 1760 cm^{-1}; NMR δ 0.9 (3 H, d, J = 7 Hz), 1.4 (3 H, s), and 2.1 (1 H, s, exchangeable). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.9; H, 9.5. Found: C, 67.5; H, 9.4.

The Na_2CO_3 washings were acidified with dilute HCl and yielded XIIa (1.25 g). It melted at 86 °C alone or on admixture with the sample described above.

Isomerization of the Unsaturated Acetates (Xa,b). Ethylenediamine (ca. 120 mL), dried with KOH and distilled over Na, was heated to 120 °C (oil bath temperature) under N_2. Freshly cut Li (1.5 g) was added in small bits with vigorous stirring. The liquid turned blue and after some time the color disappeared. When whole Li was added, the liquid acquired a pale yellow color with a small amount of a white suspended solid. The solution was further heated for 45 min to ensure complete dissolution. The unsaturated acetate mixture (2.5 g) was added in three installments whereupon the mixture turned light green. It was heated for 10 h at 115–120 °C. The contents were cooled in an ice bath and cold water gradually added till the initially formed white solid just dissolved. The organic material was extracted with ether and the ethereal extract washed with dilute HCl (6 N). The resulting product was distilled at 100 °C (1 mmHg) to afford a colorless material (1.5 g) which was reacetylated with Ac_2O (5 mL) and pyridine (5 mL). Distillation afforded the isomerized acetates (1.5 g): bp 100 °C (1 mmHg); ν_{max} 1730 cm^{-1}; NMR δ 2.0 (3 H, s), 4.1 (2 H, t, J = 7 Hz), 5.2 (½ vinylic proton).

Isomerization of the Unsaturated Alcohols (XIa,b). Unsaturated alcohols (5 g) were isomerized as described above, using *N*-lithioethylenediamine prepared from Li (2 g) and ethylenediamine (150 mL), at 115–120 °C for 15 h. It was worked up in the usual way to afford the isomerized unsaturated alcohols (2 g): bp 100 °C (1 mmHg); NMR δ 3.6 (2 H, t, J = 7 Hz), 5.2 (½ vinylic proton).

3-(2′,7′-Dimethylcycloheptenyl)propionaldehyde (XVb) and Bond Isomer (XVa). To dry CrO_3–pyridine complex from CrO_3 (12 g, 120 mmol) in CH_2Cl_2 (300 mL) was added at 10 °C the isomerized unsaturated alcohol mixture (3.6 g, 20 mmol) in CH_2Cl_2 (5 mL). After stirring for an additional 30 min at room temperature, the solution was decanted from the black residue and washed with NaOH solution (5%) and HCl (5%), and distillation of the residue afforded the aldehydes (XVa,b, 2.8 g), bp 115 °C (1 mmHg); ν_{max} 1724 cm^{-1}. Anal. Calcd for $C_{12}H_{20}O$: C, 79.9; H, 11.2. Found: C, 79.7; H, 11.1.

Methyl 3-(2′,7′-Dimethylcycloheptenyl)propionate (XIIIb) and Bond Isomer (XIIIa). The unsaturated aldehydes (XVa,b, 2.6 g, 14.2 mmol) were added with shaking to a suspension of Ag_2O in H_2O prepared from $AgNO_3$ (4.9 g, 18.3 mmol). After the solution was allowed to stand for 30 min, a black deposit was filtered off and the filtrate acidified with HCl (6 N). Workup afforded the crude acid mixture (2.4 g) and this was esterified with an excess of ethereal CH_2N_2 solution. Distillation afforded the unsaturated esters XIIIa,b: 2.2 g; bp 110 °C (0.2 mmHg); ν_{max} 1730 cm^{-1}. Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.2; H, 10.5. Found: C, 74.3; H, 10.5.

γ-Lactone of 3-(2′,7′-Dimethyl-*cis*-1′,2′-dihydroxycycloheptyl)propionic Acid (XVI) and δ-Lactone of 3-(2′,7′-Dimethyl-*cis*-1′,2′-dihydroxycycloheptyl)propionic Acid (XXI). To the unsaturated esters (XIIIa,b, 1.2 g) in ether (25 mL) was added OsO_4 (1 g) with stirring and the solution was left as such for 48 h. The residue, after removal of ether, was taken up in dry dioxane (25 mL) and H_2S passed for 10 min. Precipitated osmium sulfide was removed by filtration and from the filtrate dioxane was removed under suction. The residue was treated with NaOH (0.7 g) and MeOH (14 mL) and left overnight. Next day it was warmed at 60 °C for 2 h and cooled and the neutral fraction removed with ether. The aqueous alkaline solution was acidified with HCl and warmed on a steam bath for 30 min.

The acidic part was removed with dilute Na_2CO_3 solution (2%). The neutral part (500 mg) showed IR absorptions at 1760 and 1740 cm^{-1}. It was chromatographed over neutral alumina (18 g). Benzene–ether (50:1) eluted the γ-lactone XVI (360 mg) as a liquid, which was evaporatively distilled at 130 °C (0.1 mmHg): ν_{max} 3620, 1760 cm^{-1}; NMR δ 0.9 (3 H, d, J = 7 Hz), 1.3 (3 H, s), and 2.2 (1 H, s, exchangeable); M^+ m/e 212. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.9; H, 9.5. Found: C, 67.5; H, 9.4. Elution with benzene–ether (1:1) afforded the solid δ-lactone XXI (20 mg): mp 150 °C (EtOAc–light petroleum); ν_{max} 3620, 1740 cm^{-1}; NMR δ 0.95 (3 H, d, J = 7 Hz), 1.34 (3 H, s), and 2.2 (1 H, s, exchangeable). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.9; H, 9.4. Found: C, 67.6; H, 9.4.

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Registry No.—V, 61426-32-2; VI, 61426-33-3; VII, 61426-34-4; VIII, 61475-98-7; IX, 61426-35-5; Xa, 19923-89-8; Xb, 61426-36-6; XIa, 61426-37-7; XIb, 61426-38-8; XIIa, 61426-39-9; XIIb, 61426-40-2; XIIIa, 61426-41-3; XIIIb, 61426-42-4; XIV, 19946-75-9; XVa, 61426-43-5; IVb, 61426-44-6; XVI, 61426-45-7; XX, 61475-99-8; XXI, 61527-74-0; 2,7-dimethylcycloheptanone isomer a, 21631-95-8; 2,7-dimethylcycloheptanone isomer b, 21631-93-6; *cis*-2,7-dimethylcycloheptanone 2,4-dinitrophenylhydrazone, 21631-96-9; *trans*-2,7-dimethylcycloheptanone 2,4-dinitrophenylhydrazone, 21631-94-7; 2-methyl-2-ethoxycarbonylcycloheptanone, 20043-64-5; diethyl α-methylsuberate, 61426-46-8; 2-ethoxycarbonyl-2,7-dimethylcycloheptanone, 7272-18-6; allyl bromide, 106-95-6; Ac_2O, 108-24-7; CH_2N_2, 624-90-8.

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The Structure of Benulin, a New Pentacyclic Triterpene Hemiketal Isolated from *Bursera arida* (Burseraceae)

Florin Ionescu,[1] Shivanand D. Jolad, and Jack R. Cole*

College of Pharmacy, University of Arizona, Tucson, Arizona 85721

Satish K. Arora and Robert B. Bates

Department of Chemistry, University of Arizona, Tucson, Arizona 85721

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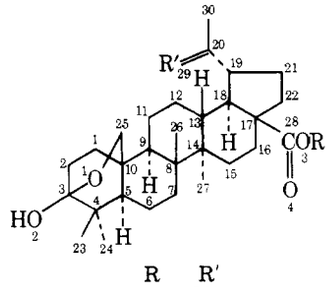
Investigation of the chloroform extract of *Bursera arida* (Burseraceae) resulted in the isolation of a new pentacyclic triterpene hemiketal which was named benulin. On the basis of biogenetic considerations and physical and chemical data, benulin was postulated to be 3α-hydroxy-3,25-epoxylup-20(29)-en-28-oic acid. This structure was confirmed by an x-ray study of benulin.

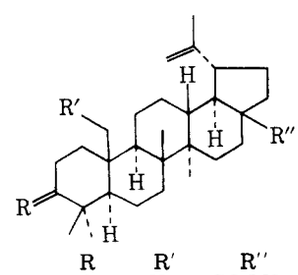
Fractionation of the chloroform extract of the stems, leaves, twigs, and bark of *Bursera arida* (Rose) Standl (Burseraceae)[2] yielded, in addition to β-sitosterol, naringenin, betulonic acid, and four new lignans, benulin, a new pentacyclic triterpene hemiketal. Benulin (I) is 3α-hydroxy-3,25-epoxylup-20(29)-en-28-oic acid.

Results and Discussion

Elemental analysis and molecular weight determination suggested the molecular formula $C_{30}H_{46}O_4$ for benulin. The general appearance of the IR and NMR spectra and the fragmentation pattern in the mass spectrum suggested a triterpene with a lupane skeleton. Spectral data (IR, NMR, mass) indicated the presence of a carboxyl and an isopropenyl group in benulin. Confirmation was established by the preparation of the methyl ester (Ia) and the dihydro (Ib) derivatives and their spectral data.



	R	R′
I	H	CH_2
Ia	Me	CH_2
Ib	H	Me



	R	R′	R″
II	O	H	COOH
IIa	O	OAc	COOH
IIb	H_2	OH	COOH
IIc	β-OH	OH	CH_2OH
IId	β-OAc	OAc	CH_2OAc

The presence of a hydroxyl group and hemiketal linkage was established by the acetylation of benulin, leading to keto