impure N-ethyl-*m*-hemipinimide, and evaporated to dryness. The residue was dissolved in 5 ml of dry ether, 5 ml of Skellysolve A was added, and the solution was concentrated slowly to give a yellow liquor and oily precipitate. The liquor was further diluted with Skellysolve A and allowed to concentrate slowly during the course of several days to give 10 mg of a crystalline precipitate, mp 75–85°, which was proved identical with authentic N-ethylhemipinimide, mp 87–90°, prepared from the corresponding acid (K and K Laboratories, Inc.), by comparison of their infrared spectra in potassium bromide.

Studies Leading to the Stereoselective Total Synthesis of *dl*-β-Eudesmol, *dl*-β-Selinene, *dl*-Costol, and Related Naturally Occurring Sesquiterpenes

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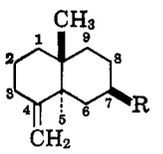
The key intermediate in these synthetic studies, *trans*-8-methylene-10-methyl-2-decalone (**7**), was prepared from 10-methyl-1(9)-octal-2-one (**1**) by a six-step sequence. The ketal derivative **2** of octalone **1** afforded the *cis*-fused hydroxy ketal **3** upon hydroboration and oxidation. The corresponding *cis*-decalone **4** was converted to the *trans* isomer **5** *via* acid- or base-catalyzed equilibration and the methylene derivative **6** was prepared from this ketone using methylenetriphenylphosphorane in dimethyl sulfoxide. This same methylene decalin (**6**) resulted when the *cis*-decalone **4** was similarly treated. Hydrolysis afforded the corresponding decalone **7**. The *trans* ring fusion of decalone **7** was confirmed through independent synthesis of its dihydro derivative **12** from *trans*-8,10-dimethyl-1(9)-octal-2-one (**8**) *via* hydrogenation of the related octalol **10** and oxidation of the resulting decalol **11**. Decalol **18**, prepared from decalone **7** using lithium aluminum hydride, was converted to the nitrile **20** through its *p*-toluenesulfonate derivative **19**. The related acid **21** was obtained through saponification of nitrile **20**. Addition of methyllithium to the methyl ester **22** of acid **21** afforded racemic β-eudesmol (**23**). Additional evidence for the stereochemical assignments of nitrile **20** and acid **21** was secured through a study of the synthesis and saponification of the isomers of *trans*-10-methyldecalin-2-nitrile, **26** and **30**, prepared from appropriate sulfonates of alcohols **24** and **28**. The synthesis of β-selinene was effected by the condensation of *trans*-2β-acetyl-8-methylene-10β-methyldecalin (**31**) with methylenetriphenylphosporane in dimethyl sulfoxide. Ketone **31**, which was obtained through addition of methyllithium to nitrile **20** and hydrolysis of the intermediate imine, also yielded β-eudesmol (**23**) upon treatment with methyllithium. Costol (**37**) was synthesized *via* reduction–elimination of the enolate of malonic ester **36** with lithium aluminum hydride. Ester **36** was stereoselectively prepared from the methanesulfonate derivative **35** of decalol **34** which was secured by formolysis of the *p*-toluenesulfonate **19** in moist N,N-dimethylformamide and saponification of the formate **33** thereby obtained. Costal (**39**) and costic acid (**40**), two naturally occurring relatives of costol, were prepared by successive oxidation of costol with manganese dioxide and silver oxide.

The eudesmane group of sesquiterpenes[2] confronts the student of organic synthesis with a variety of interesting problems. β-Eudesmol, an example of the simpler structural types to be found in this group, is noteworthy for its role in the stereochemical correlation of terpenes and steroids.[3] The carbon framework of β-eudesmol, including the C-4 exocyclic methylene grouping, reappears in a number of its close relatives such as β-selinene,[4] costol,[5] costal,[6] and costic acid.[7] Since these compounds differ only in the substitution pattern of their C-7 isopropyl side chains, we felt that all might conceivably be amenable to synthesis from the same intermediate. In this report we describe one such intermediate, *trans*-10-methyl-8-methylene-2-decalone (**7**), and illustrate its utility in the synthesis of racemic counterparts of the aforementioned sesquiterpenes.[8]

Chart I outlines the sequence employed for the synthesis of decalone **7**. The readily available bicyclic



β-eudesmol, R = $(CH_3)_2COH$
β-selinene, R = $CH_2{=}CCH_3$
costol, R = $CH_2{=}CCH_2OH$
costal, R = $CH_2{=}CCHO$
costic acid, R = $CH_2{=}CCO_2H$

ketone, 10-methyl-1(9)-octal-2-one (**1**)[9] afforded the ethylene ketal derivative **2** upon treatment with ethylene glycol in either refluxing benzene or toluene containing *p*-toluenesulfonic acid. Although we were unable to force this reaction to completion, relatively pure ketal **2** could be secured by crystallization of the crude product at low temperature. The material thus obtained gave rise to an unresolved triplet at 5.23 ppm (vinyl hydrogen) in its nmr spectrum in accordance with the expected double bond migration from the $\Delta^{1(9)}$ to the Δ^{8} position during ketalization.[10] Hydroboration, followed by oxidation of the resulting organoborane with alkaline hydrogen peroxide,[11] provided the means for converting unsaturated ketal **2** to hydroxyl ketal **3**. We expected the *cis*-fused hydroxy ketal **3** to predominate on steric grounds since the axial oxygen of the ketal grouping in **2** appears to effectively block the

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(2) Reviews: (a) stereochemical relationships; W. Cocker and T. B. H. McMurry, *Tetrahedron*, **8**, 181 (1960); (b) progress in synthesis; J. M. Mellor and S. Munavalli, *Quart. Rev.* (London), **18**, 270 (1964).

(3) B. Riniker, J. Kalvoda, D. Arigoni, A. Fürst, O. Jeger, A. M. Gold, and R. B. Woodward, *J. Am. Chem. Soc.*, **76**, 313 (1954).

(4) L. Ruzicka, and M. Stoll, *Helv. Chim. Acta*, **6**, 846 (1923).

(5) V. Benešová, V. Herout, and F. Sorm, *Collection Czech. Chem. Commun.*, **24**, 2365 (1959).

(6) S. Itô, K. Endo, H. Honma, and K. Ota, *Tetrahedron Letters*, **No. 42**, 3777 (1965).

(7) A. S. Bawdekar and G. R. Kelkar, *Tetrahedron*, **21**, 1521 (1965).

(8) A part of this work has been described in preliminary form: J. A. Marshall and M. T. Pike, *Tetrahedron Letters*, **No. 35**, 3107 (1965); J. A. Marshall and R. D Carroll, *ibid.*, **No. 47**, 4223 (1965).

(9) J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, **29**, 2501 (1964), and references cited therein.

(10) *Cf.* Q. R. Petersen and E. E. Sowers, *ibid.*, **29**, 1627 (1964).

(11) H. C. Brown, K. J. Murray, L. J. Murray, J. A. Snover, and G. Zweifel, *J. Am. Chem. Soc.*, **82**, 4233 (1960).

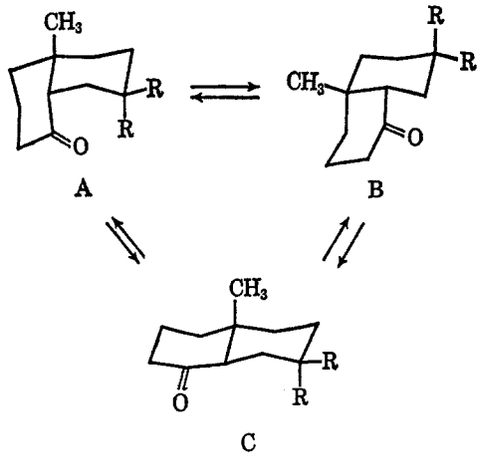
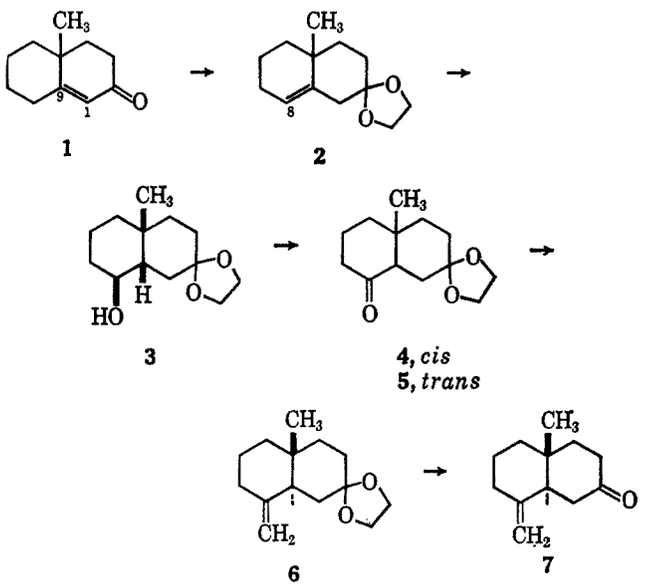


Figure 1.—Equilibration of 10-methyl-1-decalones.

CHART I



underside of the double bond. Sondheimer and coworkers[12] found this to be the case in the hydroboration of 5-cholesten-3-one ethylene ketal, a steroidal analog of **2**.

When treated with chromic acid under conditions carefully chosen to prevent decalone epimerization (*i.e.* **4** ⇆ **5**),[13] the crude mixture obtained from the hydroboration sequence yielded the *cis*-fused keto ketal **4** in 30% yield, isolated by direct crystallization. Concordant with expectation, keto ketal **4** afforded a mixture containing principally the *trans*-fused isomer **5** (*trans*/*cis* = 2) upon treatment with methanolic sodium methoxide. In refluxing toluene with *p*-toluenesulfonic acid as an equilibration catayst, we secured a 1:3 mixture of **4** and **5** from which the major component (**5**) could be isolated in 65% yield by direct crystallization at low temperature. The ratios of **4** to **5** were taken from the nmr spectra by evaluating the integration trace of the angular methyl peaks which appeared at differing chemical shifts for the two isomers. The relative positions of these peaks support our stereochemical assignments of keto ketals **4** and **5**.[14]

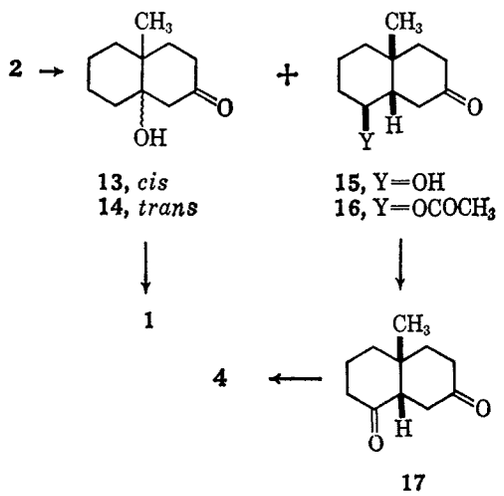
(12) M. Nussim, T. Mazur, and F. Sondheimer, *J. Org. Chem.*, **29**, 1120 (1964).

(13) *Cf.* J. A. Marshall, N. Cohen, and K. R. Arenson, *ibid.*, **30**, 762 (1965).

(14) K. L. Williamson, L. R. Sloan, T. Howell, and T. A. Spencer, *ibid.*, **31**, 436 (1966).

At this point it should be noted that the ketal grouping, in addition to functioning as a protecting group, plays an important role in assuring the preponderance of *trans*-decalone **5** at equilibrium. We were led to this expectation in our initial synthetic planning through conformational analysis of the 10-methyl-1-decalone system illustrated in Figure 1. In the parent compound (R = H) the *trans* isomer (C) possesses three skew butane interactions *vs.* four such interactions in conformer B of the *cis* isomer and three in conformer A. Conformer A also possesses *syn*-axial interactions between the carbonyl group and the axial hydrogens[15] at C-5 and C-7, but these are substantially less severe than a skew butane interaction.[16] Thus A and C represent stable conformers of 10-methyl-1-decalone (R = H) which should be nearly equally populated at equilibrium, a prediction which closely parallels the experimental finding.[17] With the *cis*-fused keto ketal **4**, conformer A becomes less stable owing to interactions between the axial ketal oxygen and the carbonyl group. This results in a net destabilization of the *cis* isomer **4** relative to the *trans* isomer **5**. Sondheimer and Wolfe[18] noted an analogous stability relationship for *cis*- and *trans*-7,7,10-trimethyl-1-decalone (Figure 1, R = CH_3) where the equilibrium mixture contained at least 90% of the *trans* isomer. Thus the 7,7-dimethyl grouping not unexpectedly exerts a greater destabilizing influence on the *cis* conformer A than the identically situated ethylene dioxy grouping.

An alternative route to keto ketal **4** which involved the selective ketalization of dione **17** was briefly explored. Although this study failed to provide a superior route to **4** it shed some light on the hydroboration step (**2** → **3**) and we therefore present some of the pertinent details. Hydrolysis of the crude hydroxy ketal **3** with concentrated hydrochloric acid in actone gave a mixture of alcoholic and ketonic (saturated and conjugated) materials as shown by the infrared absorption bands at 3.0, 5.85, and 5.95 μ. This mixture, upon oxidation with chromic acid, afforded the crystalline dione **17**, isolated in 30% over-all yield from ketal **2** by direct



(15) For a general treatment of similar conformational problems and an explanation of nomenclature, see E. L. Eliel, N. L. Allinger, S. G. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, Inc., New York, N. Y., 1965, pp 43, 231.

(16) *Cf.* E. L. Eliel, *et al.*,[15] p 114.

(17) F. Sondheimer and D. Rosenthal, *J. Am. Chem. Soc.*, **80**, 3995 (1958).

(18) F. Sondheimer and S. Wolfe, *Can. J. Chem.*, **37**, 1870 (1959).

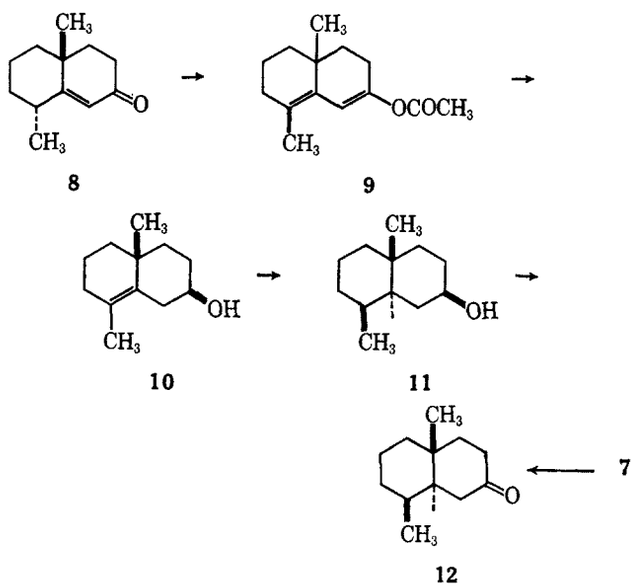
crystallization. Some additional dione along with a second crystalline substance, *cis*-9-hydroxy-10-methyl-2-decalone (**13**),[9] and octalone **1** could be obtained through chromatography of the mother liquor. Hydroxy ketone **13** most likely arises through anti-Markovnikov additon of diborane to unsaturated ketal **2**[19] followed by hydrolysis of the ketal grouping. Octalone **1** would then be formed through dehydration of this β-hydroxy ketone under the conditions employed for ketal hydrolysis. In fact, a 2:1 mixture of *cis*-hydroxy ketone **13** and the corresponding *trans*-isomer **14** when subjected to these conditions, gave octalone **1** in 40% yield along with a 2:1 mixture of unchanged **13** and **14**. This experiment supports the postulated genesis of octalone **1** and suggests that the *cis*-fused hydroxy ketal greatly predominates in the anti-Markovnikov hydroboration of unsaturated ketal **2**. According to our best estimate based upon infrared and nmr spectra, and yield of isolated products, the hydroboration of unsaturated ketal **2** gives 50% of the hydroxy ketal **3**, 10% of the anti-Markovnikov hydroboration product (the ketal derivative of ketol **13**), and 40% of ketal cleavage products. The cleavage of ethylene ketals during hydrobroation finds precedent in steroidal systems.[12]

Dione **17** afforded the *cis*-fused keto ketal **4** as the major product upon treatment with 1 equiv of ethylene glycol in refluxing benzene containing a small amount of *p*-toluenesulfonic acid. In refluxing toluene with the same catalyst to dione ratio, or in refluxing benzene with a larger quantity of acidic catalyst, we obtained a mixture of **4** and **5** in which the more stable *trans* isomer **5** predominated. In both cases these substances were contaminated by impurities judged to be bisketals and starting dione by examination of the infrared and nmr spectra. These impurities seriously hamperd the effective purification of **4** and **5**, as they could not be removed by chromatography, and they markedly lowered the efficiency of isolations *via* low-temperature crystallization. Consequently, the crystalline *trans*-fused keto ketal **5** could only be secured in about 18% yield starting from crystalline dione **17**.

Having devised a reasonably efficient route to keto ketal **5**, we turned our attention to the preparation of the corresponding methylene derivative **6**. Methylenetriphenylphosphorane in dimethyl sulfoxide[20] readily effected the desired conversion and the resulting product, when heated with aqueous hydrochloric acid in acetone, afforded decalone **7** as a low-melting but highly crystalline solid. We were surprised to find that the *cis*-decalone **4** likewise gave the *trans*-fused methylene derivative **6** upon treatment with the methylene phosphorane in dimethyl sulfoxide. Evidently, *cis*-decalone **4** epimerizes under these reaction conditions and the resulting *trans*-decalone **5** preferentially condenses with methylenetriphenylphosphorane. This result may stem from the greater steric hindrance connected with the carbonyl grouping in the *cis*- *vs.* *trans*-1-decalone isomers. Presumably, the large excess of dimethyl sulfoxide which is used as the solvent renders enolate formation reversible or, alternatively, a relatively small amount of enolate catalyzes the isomerization of *cis*-decalone **4**. Were this not the case, we should obtain a mixture of the keto ketals **4** and **5** from this reaction since the enolate derivatives, if formed irreversibly, would not be expected to condense with the phsphorane. Our results here contrast sharply with the findings of Corey and co-workers who observed no equlibration of epimerizable ketones under similar reaction conditions.[21]

Since both keto ketals **4** and **5** afforded the same methylene derivative we could no longer be certain of the stereochemistry of this substance. We favored the *trans* isomer **6** for the reason mentioned above, but sought more definite proof through an independent synthesis (Chart II) of *trans*-8β,10β-dimethyl-2-decalone (**12**), the hydrogenation product of decalone **7**. The starting material for this sequence, *trans*-8,10-dimethyl-1(9)-octal-2-one (**8**),[22] was converted to the unsaturated alcohol **10** *via* reduction of the dienol acetate **9** with sodium borohydride, as reported for steroidal conjugated ketones.[23] This alcohol gave decalol **11** upon catalytic hydrogenation. Previous studies have shown that hydrogen preferentially adds

CHART II



to the underside of similarly situated double bonds in related compounds,[24] and the stereochemistry of decalol **11** is assigned accordingly. Oxidation with chromic acid gave decalone **12** identical with that obtained through hydrogenation of decalone **7**,[24] as judged by comparison of the infrared and nmr spectra and the gas chromatographic retention times.

With the structure of decalone **7** firmly in hand and a ready supply of this ketone available, we began working toward the first of our chosen synthetic objectives, racemic β-eudesmol (**23**), as outlined on Chart III. Decalol **18** was obtained *via* reduction of decalone **7** with lithium aluminum hydride, a method long recognized as giving equatorial alcohols from unhindered

(19) *Cf.* H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962, p 120.

(20) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).

(21) E. J. Corey, R. B. Mitra, and H. Uda, *J. Am. Chem. Soc.*, **86**, 485 (1964).

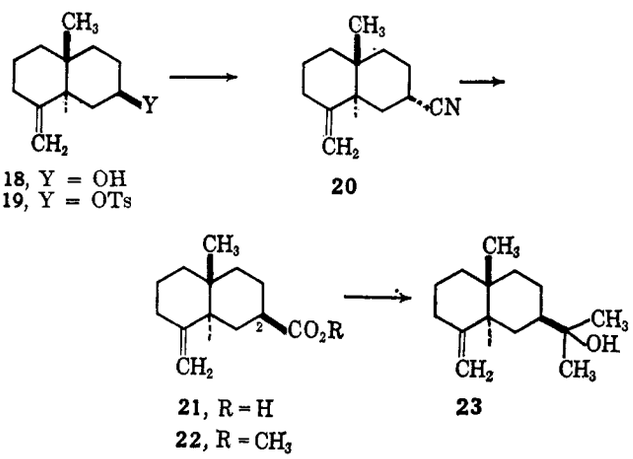
(22) J. A. Marshall and D. J. Schaeffer, *J. Org. Chem.*, **30**, 3642 (1965).

(23) W. G. Dauben and J. F. Eastham, *J. Am. Chem. Soc.*, **73**, 4463 (1951); B. Belleau and T. F. Gallagher, *ibid.*, **73**, 4458 (1951).

(24) *Cf.* F. J. McQuillin and J. D. Parrack, *J. Chem. Soc.*, 2973 (1956); J. A. Marshall, N. Cohen, and A. R. Hochstetler, *J. Am. Chem. Soc.*, **88**, 3408 (1966).

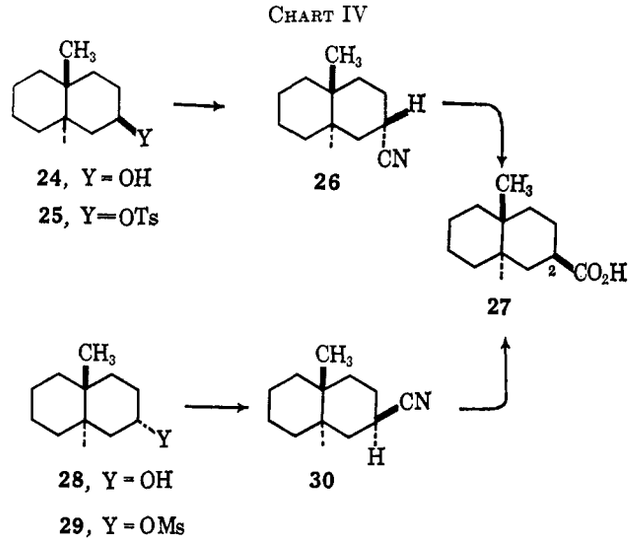
cyclohexanones[25] such as **7**. The corresponding *p*-toluenesulfonate derivative (**19**), when treated with sodium cyanide in N-methylpyrrolidone,[26] afforded nitrile **20** which, upon subsequent saponification using potassium hydroxide in ethylene glycol at 160° for 16 hr, yielded the crystalline carboxylic acid **21**.

CHART III



We assumed that nitrile **20** would equilibrate during the course of this step and give the more stable carboxylic epimer. Since our knowledge of the stereochemistry at C-2 in acid **21** rests upon the validity of our assumption, we sought additional clarification of this point through a study involving the stereochemically defined decalols **24** and **28**[27] (Chart IV).

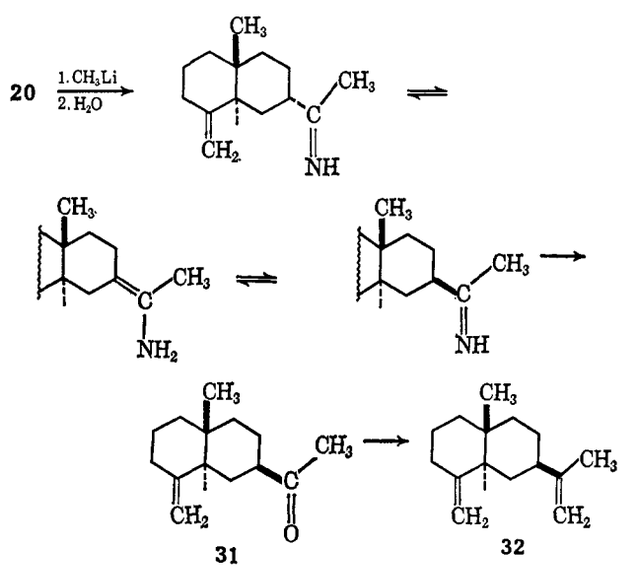
CHART IV



The equatorial *p*-toluenesulfonate **25** afforded a crystalline nitrile (**26**) upon treatment with sodium cyanide in N-methylpyrrolidone whereas the axial methanesulfonate **29** (the *p*-toluenesulfonate of decalol **28** could not be prepared in high yield) gave an oily nitrile (**30**) under comparable conditions. The nmr spectra shed considerable light on the stereochemical orientation of the cyano grouping in each of these isomeric nitriles. In the spectrum of nitrile **26**, the C-2 hydrogen gave rise to an envelope (unresolved triplet) at 2.98 ppm whose width at half-height (9 cps) suggested an equatorial conformation.[28] With nitrile **30**, the corresponding hydrogen was seen as a complex pattern between 2.6 and 2.1 ppm suggestive of an axial proton. These assignments agree with the expectation of stereochemical inversion in the reaction of sulfonates **25** and **29** with sodium cyanide. Both nitriles gave the same crystalline carboxylic acid (**27**) upon saponification under the conditions previously employed for nitrile **20**, thus showing that equilibration takes place during this reaction. Although the conformational preference for an equatorial *vs.* axial cyano cyclohexane is slight,[29] a considerable rate factor should separate the hydrolysis of such epimers owing to increasing steric bulk in the transition state.[30] This kinetic discrimination could easily lead to a substantial prepondernace of the equatorial carboxylic acids **21** and **27** from axial nitriles **20** and **26**. We could not determine whether the carboxylic acids themselves might be equilibrated (*via* a carboxylate enolate) under the saponification conditions. However, the above kinetic argument obviates the need for such information in predicting the stereochemical outcome for the saponification reaction.

Acid **21** was converted to the corresponding methyl ester **22** using ethereal diazomethane. This ester afforded racemic β-eudesmol (**23**), upon treatment with excess methyllithium followed by hydrolysis of the lithium salt.[31] The infrared spectra, gas chromatographic retention times, and tlc mobilities of synthetic and natural β-eudesmol corresponded exactly.

An alternative and more direct route to β-eudesmol involved the addition of methyllithium to nitrile **20** followed by hydrolysis of the resulting imine to give ketone **31**. We assign the indicated stereochemistry to this ketone on the basis of its failure to epimerize in

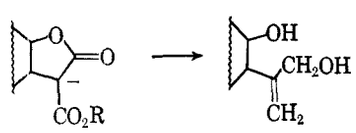


(25) D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953).
(26) *Cf.* H. B. Henbest and W. R. Jackson, *ibid.*, 954 (1962).
(27) R. H. Baker, L. S. Minckler, and A. S. Hussey, *J. Am. Chem. Soc.*, **81**, 2379 (1959).
(28) *Cf.* R. H. Bible Jr., "Interpretation of NMR Spectra," Plenum Press, New York, N. Y., 1965, p 35 ff.
(29) E. L. Eliel, et al.,[15] p 44. A sample taken from the reaction mixture before saponification was complete contained the axial and equatorial nitriles **26** and **30** in the ratio 3:2.
(30) See E. L. Eliel, et al.,[11] p 72, for a discussion of the hydrolysis of equatorial and axial cyclohexanecarboxylates.
(31) This method has been used previously in connection with a synthesis of γ-eudesmol: A. R. Pinder and R. A. Williams, *J. Chem. Soc.*, 2773 (1963).

methanolic sodium methoxide and its conversion to racemic β-eudesmol upon treatment with methyllithium. The stereochemical inversion which accompanies the transformation of nitrile **20** to ketone **31** no doubt takes place during work-up when the intermediate imine salt is treated with aqueous ammonium chloride. A facile imine–enamine interconversion could account for the remarkable ease with which this epimerization occurs.

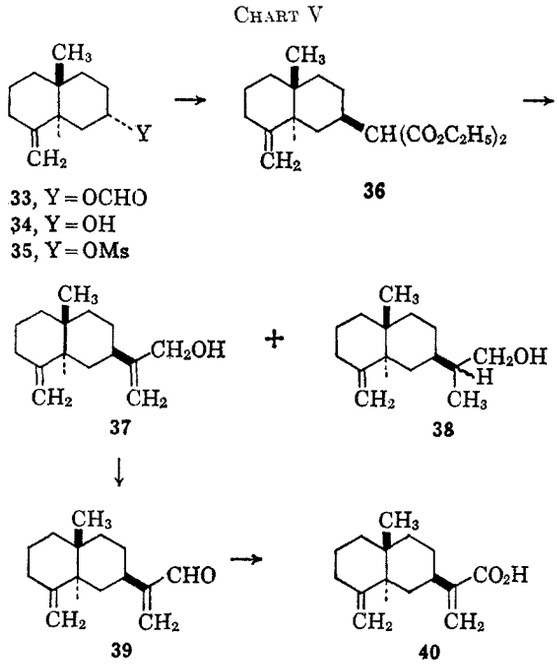
The attainment of ketone **31** afforded an excellent opportunity to complete a stereoselective synthesis of β-selinene (**32**). This goal was accomplished through treatment of ketone **31** with methylenetriphenylphosphorane in dimethyl sulfoxide.

The total synthesis of costol (**37**) required a stereoselective method for introducing the most unusual feature of this molecule, the C-7 propenol side chain, into ketone **7**. In connection with investigations aimed at the synthesis of α-methylene-γ-butyrolactones[32] we observed the reduction of sodio enolates of α-carboalkoxy-γ-butyrolactones with lithium aluminum hydride to give allylic alcohols as shown below. We



expected this method to proceed analogously in the present case to give racemic costol (**37**)[33] provided we could prepare malonic ester **36**. As can be seen from Chart V, this objective was simply reached through

CHART V



33, Y = OCHO
34, Y = OH
35, Y = OMs

36

37 + **38**

39 → **40**

alkylation of diethyl sodiomalonate with the methanesulfonate derivative **35** of alcohol **34**. The requisite axial alcohol **34** was obtained by heating a solution of toluenesulfonate **19** (Chart III) in wet N,N-dimethylformamide according to the procedure of Blickenstaff and Chang[34] and treating the formate **33** thus obtained with dilute base. Alcohol **34** differed from its epimer **18** as shown by mixture melting point depression, comparison of the infrared spectra, and gas chromatographic retention times.

The sodio derivative, prepared from decalylmalonate **36** using sodium hydride in refluxing 1,2-dimethoxyethane, was reduced with lithium aluminum hydride in the same solvent giving a 3:1 mixture of racemic costol (**37**) and dihydrocostol (**38**).[35] When this mixture of alcohols was stirred with activated manganese dioxide in chloroform, the costol component was selectively oxidized to costal (**39**) and the dihydrocostol was recovered unchanged.[36] These two compounds were readily separated by column elution chromatography. The racemic costal (**39**) obtained in this manner afforded racemic costol (**37**) upon reduction with etheral lithium aluminum hydride, and racemic costic acid (**40**) upon oxidation with silver oxide. The spectra of these synthetic materials and the published spectra[7] of the corresponding natural products were identical.

Experimental Section[37]

Melting points were taken on a Fisher-Johns hot stage. Nmr spectra were obtained with a Varian A-60 spectrometer. A Beckman IR-5 spectrophotometer was used for infrared spectra. Gas chromatography was accomplished with an F and M Model 720 instrument using helium as the carrier gas. Retention times are reported in minutes from the air peak. Combustion analyses were performed by Micro-Tech Laboratories, Skokie, Ill., and Miss H. Beck, Northwestern University.

2,2-Ethylenedioxy-10-methyl-8-octalin (**2**).—A mixture containing 23.3 g of 10-methyl-1(9)-octal-2-one (**1**),[9] 28.5 g of ethylene glycol, and 0.3 g of *p*-toluenesulfonic acid monohydrate in 300 ml of toluene was heated at reflux for 22 hr with continuous azeotropic removal of water and excess ethylene glycol by means of a Dean–Stark trap.[37b] The cooled mixture was washed with saturated brine, saturated aqueous sodium bicarbonate, and dried over anhydrous potassium carbonate and magnesium sulfate. The solvent was removed under reduced pressure and the residue was distilled affording 30 g of colorless ketal **2**, bp 77° (0.3 mm). The infrared spectrum of this material revealed a weak band at 5.98 μ (conj CO) arising from an estimated 5–10% of octalone **1**. A band of the same relative intensity was also present at 5.98 μ in the spectrum of the crude material prior to distillation. Similar results were obtained using benzene as the reaction solvent. The distilled material was diluted with several volumes of pentane and cooled to −30° whereupon a white solid was obtained which melts below room temperature. The mother liquor was removed at −30° through a sintered glass filter stick and the residue was recrystallized two more times by the same procedure giving 12.0 g (40%) of ketal **2**, mp *ca.* 5°, whose infrared spectrum showed no carbonyl bands; λ_{max}^{film} 6.00 (C=C), 7.11, 8.43, 9.10, 10.11, 10.52, 11.73, 12.44, and 14.40 μ; $\delta_{TMS}^{CCl_4}$ 5.23 (C=CH, unresolved triplet, width at half-height = 7 cps), 3.80 (OCH_2CH_2O), and 1.05 ppm (CH_3). This material was

(32) J. A. Marshall and N. Cohen, *J. Org. Chem.*, **30**, 3475 (1965).

(33) For an alternative method of constructing the propenol side chain see K. R. Varma and S. C. Bhattacharyya, *Tetrahedron*, **20**, 2927 (1964).

(34) R. T. Blickenstaff and F. C. Chang, *J. Am. Chem. Soc.*, **80**, 2906 (1958).

(35) The ratio of costol to dihydrocostol closely resembles the ratio of the analogous products obtained from diethyl sodiocyclohexylmalonate in the same manner. The mechanism of this reduction is currently under study and will be reported in a forthcoming publication.

(36) *Cf.* D. Herbst and C. Djerassi, *J. Am. Chem. Soc.*, **82**, 4337 (1960).

(37) (a) The prefix *dl* is omitted from the names of racemic substances. The prefixes α and β are used to denote relative stereochemistry. (b) The apparatus described by W. S. Johnson and W. P. Schneider [*Org. Syn.*, **30**, 18 (1950)] was used to maintain a nitrogen atmosphere. (c) The following sequence describes a typical isolation procedure. The reaction mixture was treated with water and thoroughly extracted with the specified solvent. The combined extracts were washed with saturated brine and dried over anhydrous magnesium sulfate and, in cases where the product was thought to be acid sensitive, anhydrous potassium carbonate was added. After drying, the solvent was removed from the filtered extracts under reduced pressure on a steam bath.

highly sensitive to atmospheric moisture and satisfactory analytical values could not be obtained.

Crude *cis*-2,2-Ethylenedioxy-10β-methyl-8β-decalol (3).[37a]—The procedure of Brown and co-workers[11] was employed to prepare a solution of diborane in tetrahydrofuran. To 12.0 g of ketal **2** in 125 ml of tetrahydrofuran at 0° was added 120 ml of 0.25 *M* diborane solution over a 30-min period.[37b] After an additional 30 min at 0° and 2.5 hr at room temperature, the mixture was cooled to 0° and water was cautiously added to destroy the boron hydrides. The cold solution was treated with 75 ml of 10% aqueous sodium hydroxide and 75 ml of 30% hydrogen peroxide solution was then slowly added to the well-stirred mixture. The product, 13 g of crude hydroxy ketal **3**, was isolated with ethyl acetate.[37c] The ketal grouping of this material seemed highly prone to hydrolize. A 200-mg sample gave 156 mg of colorless oil, bp 90–95° (bath temperature) at 0.02 mm, upon distillation. The spectra of this material suggested the presence of several impurities as evidenced by bands at 5.89 μ (CO) in the infrared spectrum and bands at 1.07 and 0.98 ppm (angular CH_3) in the nmr spectrum. No significant separation was achieved when this material was chromatographed on silica.

***cis*-2,2-Ethylenedioxy-10-methyl-8-decalone (4).**[37a] **A. Oxidation of the Crude Hydroxy Ketal 3.**—A 600-mg sample of the crude hydroxy ketal **3** in 5 ml of acetone at 0° was treated with 0.71 ml of standard chromic acid reagent.[38] After stirring at 0° for 10 min, the mixture was treated with 2-propanol to destroy the excess oxidant and a small amount of solid sodium bicarbonate was added to neutralize any excess acid. The mixture was filtered through Super Cel, the gummy solid was triturated with ethyl acetate, and the combined filtrates were concentrated under reduced pressure. The residue was taken up in ethyl acetate, washed with saturated brine and aqueous sodium bicarbonate, and dried, and the solvent was removed under reduced pressure. The residue was dissolved in hot hexane and seeded with authentic keto ketal **4** to give 313 mg (53%) of the same material as a white solid: $\lambda_{max}^{CHCl_3}$ 5.88 (CO), 7.61, 7.77, 8.52, 9.10, 9.71, 10.52, 10.65 and 11.08 μ; $\delta_{TMS}^{CCl_4}$ 3.88 (OCH_2CH_2O), 0.95 ppm (CH_3). The analytical sample, mp 77–78°, was secured after several recrystallizations from hexane.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.9; H, 9.0.

B. Ketalization of Dione 17.—A mixture containing 3.10 g of dione **17**, 1.17 g of ethylene glycol, and 25 mg of *p*-toluenesulfonic acid monohydrate in 300 ml of benzene was heated to reflux for 24 hr with continuous removal of water by means of a Dean–Stark trap.[37b] The mixture was cooled, washed with saturated aqueous sodium bicarbonate and brine, and dried over a mixture of anhydrous potassium carbonate and magnesium sulfate. The solvent was removed under reduced pressure to give 3.5 g (90%) of yellow oil whose infrared and nmr spectra closely matched those of the authentic keto ketal **4**, prepared according to part A. When this material was equilibrated using *p*-toluenesulfonic acid according to the procedure described below, the crystalline *trans* keto ketal **5** was obtained in 18% yield.

***trans*-2,2-Ethylenedioxy-10-methyl-8-decalone (5).**[37a] **A. Base-Catalyzed Equilibration of the *cis* Keto Ketal 4.**—A solution of 587 mg of keto ketal **4** in 15 ml of 5% methanolic sodium methoxide was stirred at room temperature for 16 hr.[37b] Saturated brine was added to the light brown reaction mixture and the product was isolated with ethyl acetate[37c] giving 535 mg of orange oil. Distillation afforded 336 mg (57%) of pale yellow oil, bp 90° (bath temperature) at 0.02 mm, estimated as a 2:1 mixture of *trans* and *cis* keto ketals **4** and **5** by evaluation of the integrated area of the peaks at 0.95 (CH_3 of **4**) and 0.80 ppm (CH_3 of **5**) in the nmr spectrum of the mixture.

B. Acid-Catalyzed Equilibration of the *cis* Keto Ketal 4.—Part of the toluene was distilled from a solution containing 5 mg of *p*-toluenesulfonic acid monohydrate in 50 ml of toluene in order to remove all traces of water. A 116-mg sample of the *cis* keto ketal **4** was added and the solution was stirred at reflux for 19 hr,[37b] cooled, and filtered through a pad of barium oxide. The solvent was distilled from the filtrate at reduced pressure and the residue, a 3:1 mixture of **5** and **4** based on the nmr spectrum, was crystalized from hexane at −30° giving 76 mg (65%) of a low-melting white solid. One recrystalization afforded 67 mg (57%) of keto ketal **5**: mp 35–38°; $\lambda_{max}^{CHCl_3}$ 5.87 (CO), 7.60, 7.70, 7.80, 7.91, 9.08, 9.70, 10.56, and 11.20 μ; $\delta_{TMS}^{CCl_4}$ 3.88 (OCH_2CH_2O) and 0.80 ppm (CH_3). The analytical sample exhibited mp 41–42° after two successive sublimations.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.8; H, 9.2.

C. From Dione 17.—A mixture containing 470 mg of dione **17**, 0.16 ml of ethylene glycol, and 25 mg of *p*-toluenesulfonic acid monohydrate in 25 ml of benzene was stirred at reflux for 22 hr[37b] with continuous removal of water *via* a Dean–Stark trap. The mixture was cooled and processed as described above to give 509 mg (87%) of colorless oil, bp 95–110° (bath temperature) at 0.2 mm, containing mainly the *trans* keto ketal **5** as evidenced by the nmr spectrum. Crystallization from ether–hexane at −25° afforded 110 mg (18%) of **5**, mp 42–43°. The infrared spectrum of this material was identical with that of the crystalline keto ketal prepared in part B.

***trans*-10-Methyl-8-methylene-2-decalone (7).**[37a] **A. From the *trans* Keto Ketal 5.**—The procedure of Corey, *et al.*,[20] was employed. To a stirred solution of 11.0 ml of 0.5 *M* dimethylsulfinylsodium[39] in dimethyl sulfoxide at 0° was added a solution of 2.05 g of methyltriphenylphosphonium bromide in 10 ml of dimethyl sulfoxide.[37b] The resulting orange-brown mixture was stirred for 20 min at room temperature and a solution of 375 mg of *trans*-decalone **5** in 5 ml of dimethyl sulfoxide was added dropwise. After 3.5 hr, the mixture was diluted with water and the product was isolated with ether.[37c] The crude mixture was chromatographed on silica to remove the triphenylphosphine oxide. Elution with benzene gave 310 mg (83%) of the methylene ketal **6**: λ_{max}^{film} 3.27, 6.08 (C=CH_2), 8.45, 9.08, 9.67, and 11.17 μ; $\delta_{TMS}^{CCl_4}$ 4.75, 4.45 (C=CH_2), 2.24 (OCH_2CH_2O), and 0.75 ppm (CH_3).

A mixture containing 2.06 g of ketal **6**, equivalent to the material described above, 5 ml of water, and 15 drops of concentrated hydrochloric acid in 50 ml of acetone was heated on a steam bath for 20 min,[37b] cooled, and extracted with ether. The combined extracts were washed with saturated brine, aqueous sodium bicarbonate, and dried. The solvent was distilled under reduced pressure leaving 1.76 g of low-melting solid which was recrystallized from hexane giving 0.73 g (44%) of solid methylene decalone, mp 45–51°. The analytical sample, mp 50.5–51°, was secured after two additional recrystallizations: λ_{max}^{KBr} 3.24 (C=CH_2), 5.85 (CO), 6.07 (C=CH_2), 7.84, 8.54, 11.09, and 11.23 μ; $\delta_{TMS}^{CCl_4}$ 4.87, 4.52 (C=CH_2) and 0.97 ppm (CH_3).

Anal. Calcd for $C_{12}H_{18}O$: C, 80.84; H, 10.18. Found: C, 80.7; H, 10.2.

B. From the *cis* Keto Ketal 4.—The procedure described above in part A was employed using 3.3 ml of 1.1 *M* dimethylsulfinylsodium, 1.45 g of methyltriphenylphosphonium bromide, and 280 mg of *cis* keto ketal **4** in 5.5 ml of dimethyl sulfoxide. The methylene ketal (280 mg), eluted from alumina with benzene, was identified as the *trans* isomer through infrared and nmr spectral comparison with the material prepared above in part A. Hydrolysis afforded 170 mg of crude decalone **7**. The gas chromatogram[40] showed peaks at 16.2 (1.5%), 18.8 (80% **7**, identified by peak enhancement with authentic material), 22.8 (3.5%), and 26.8 min (15.5%). The crude material was crystallized from hexane and the mother liquor was concentrated and subjected to preparative gas chromatography.[41] In this manner 105 mg of white solid was obtained whose infrared spectrum was identical with that of the *trans*-decalone **7**.

8,10β-Dimethyl-8-octal-2β-ol (10).[37a]—A solution of 509 mg of *trans*-8,10-dimethyl-1(9)-octal-2-one (**8**) in 5 ml of isopropenyl acetate containing 5 mg of *p*-toluenesulfonic acid monohydrate was heated at 100° for 24 hr[37b] while acetone was slowly collected through a short Vigreux column. An additional 5 ml of isopropenyl acetate was added and the procedure was repeated during 30 hr. The temperature was then increased to 165° and most of the remaining isopropenyl acetate was collected. The cooled mixture was filtered through a pad of barium oxide with the aid of benzene and the filtrate was distilled affording 612 mg (98%) of pale yellow enol acetate **9**: bp 105–110° (bath temperature) at 0.3 mm; λ_{max}^{film} 5.70 (CO), 6.00, 6.10 (C=C), 6.88, 6.98, 7.30, 8.20, 8.46, 8.86, 9.00, and 9.53 μ; $\delta_{TMS}^{CCl_4}$ 6.10 (H-1), 2.20 (CH_3CO), 1.67 (C-8 CH_3), and 1.03 ppm (C-10 CH_3).

(38) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

(39) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **84**, 866 (1962).

(40) A 13 ft × 0.25 in. Carbowax 20 M on 60–80 Diatoport S column was used at 185° with a helium flow rate of 87 cc/min.

(41) A 10 ft × 0.5 in. column of 20% Carbowax 20 M on 60–80 Chromasorb W was used at 203° with a helium flow of 250 cc/min.

To a 350-mg sample of the above enol acetate in 3.6 ml of absolute ethanol at 0° was added with stirring a solution of 420 mg of sodium borohydride in 5.5 ml of ethanol and 1.1 ml of water.[23] The mixture was allowed to stand at −7° for 50 hr, treated with 1.2 ml of 10% aqueous sodium hydroxide, diluted with saturated brine, and thoroughly extracted with hexane. The product was distilled giving 255 mg (88%) of colorless alcohol **10**: bp 93–98° (bath temperature) at 0.3 mm; λ_{max}^{film} 3.01 (OH), 6.88, 7.29, 9.38, 9.45, and 9.80 μ; $\delta_{TMS}^{CCl_4}$ 4.15 (OH), 3.0–2.5 (C*H*OH), 1.63 (C-8 CH_3), and 1.07 ppm (C-10 CH_3). The analytical sample was secured after two successive redistillations.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.95; H, 11.18. Found: C, 80.2; H, 11.4.

***trans*-8β,10β-Dimethyl-2-decalone (12).**[37a] **A. From Octalol 10.**—A 125-mg sample of octalol **10** was stirred with platinum (from 50 mg of platinum oxide) in 15 ml of acetic acid under one atmosphere of hydrogen for 20 min. The mixture was filtered through Super Cel with the aid of toluene and the acetic acid was removed from the filtrate under reduced pressure as the toluene azeotrope. The residual oil was distilled giving 98 mg (78%) of alcohol **11**: bp 95° (bath temperature) at 0.3 mm; λ_{max}^{film} 3.00 (OH), 9.47, and 9.70 μ.

The above alcohol was dissolved in 3 ml of acetone and stirred at 0° while 0.25 ml of standard chromic acid reagent[38] was added. The mixture was treated as described above for the preparation of keto ketal **4** from hydroxy ketal **3** and the crude ketonic material was distilled giving 87 mg (90%) of decalone **12**: bp 95° (bath temperature) at 0.3 mm; λ_{max}^{film} 5.85 (CO), 7.21, 8.10, 8.47, 8.69, 9.02, 9.44, and 10.62 μ; $\delta_{TMS}^{CCl_4}$ 1.13 (C-10 CH_3) and 0.95 ppm (C-8 CH_3, doublet; J = 7 cps). The gas chromatogram showed peaks at 4.8 (10%) and 5.6 min (90%, **12**).[42] The semicarbazone derivative, mp 198–199° from ethanol, was prepared for combustion analysis.

Anal. Calcd for $C_{13}H_{23}N_3O$: C, 65.80; H, 9.77; N, 17.71. Found: C, 65.8; H, 9.8; N, 17.5.

B. From Unsaturated Ketone 7.—A 200-mg sample of methylene decalone **7** in 60 ml of methanol was stirred with platinum (from 120 mg of platinum oxide) under one atmosphere of hydrogen until 25.2 ml of hydrogen had been taken up. The mixture was filtered through Super Cel with the aid of benzene and ether, and the filtrate was distilled giving 149 mg (75%) of ketone **12**, bp 95° (bath temperature) at 0.3 mm. The infrared and nmr spectra of this material exactly matched those of the material prepared in part A and the gas chromatographic retention times were also identical (peak enhancement). The semicarbazone derivative exhibited mp 199–200°, alone or upon admixture with the semicarbazone described in part A.

***cis*-10β-Methyl-8β-hydroxy-2-decalone (15).**[37a]—A 539-mg sample of the crude hydroxy ketal **3** in 20 ml of acetone containing 10 drops of concentrated hydrochloric acid was heated at reflux for 10 min,[37b] diluted with water, and extracted with ethyl acetate. The combined extracts were washed with saturated sodium bicarbonate and brine, and dried. The solvent was removed under reduced pressure giving 400 mg of yellow oil: λ_{max}^{film} 2.92 (OH), 5.85 (saturated ketone CO), 6.00 (conjugated ketone CO), and 6.18 μ (C=C). The intensity of the band at 2.92 μ suggested the presence of diols in this mixture. A 1.00-g sample of comparable material was heated at reflux with 1.0 g of Girard's T reagent,[43] 1 ml of glacial acetic acid, and 9 ml of 95% ethanol for 1.5 hr. The cooled mixture was diluted with 50 ml of water containing 0.63 g of sodium hydroxide and thoroughly extracted with ether. The combined extracts were dried and evaporated giving 0.47 g of alcoholic materials (strong bands at 2.9–3 and 9–10 μ in the infrared spectrum) contaminated with ketonic impurities (medium-to-weak bands at 5.85 and 5.98 μ).

The ketonic materials were liberated from their water-soluble hydrazones by treating the aqueous solution described above with 3 ml of concentrated hydrochloric acid.[37b] After 3 hr at room temperature, 0.50 g of material was isolated from the acidic mixture by extraction with ethyl acetate.[37c] This material was chromatographed on Florisil to give octalone **1** (0.06 g) and hydroxy ketone **15** (0.35 g, 22% based on unsaturated ketal **3**): λ_{max}^{film} 2.95 (OH), 5.86 (CO), 7.24, 8.31, 8.71, 9.38, 9.58, 9.72, 10.17, 10.40, and 10.80 μ. Subsequent experiments (see below) suggest that hydroxy ketone **13** is also present in these latter fractions.

(42) A 10 ft × 0.25 in. Carbowax 20 M on C-Pack column was used at 175°.

(43) *Cf.* A. Vogel, "Practical Organic Chemistry," Longmans, Green, and Co., Ltd., London, 1956, p 576.

The acetate derivative **16**, mp 97–98°, was prepared using sodium acetate in refluxing acetic anhydride: $\lambda_{max}^{CCl_4}$ 5.74 (ester CO), 5.81 (ketone CO), 7.22, 7.32, 8.06, 9.44, 9.56, 9.70, 10.29, and 10.90 μ; $\delta_{TMS}^{CCl_4}$ 4.51 [H-8, triplet of doublets; J (triplet) = 10 cps, J (doublet) = 4 cps], 2.00 CH_3CO, and 1.30 ppm (C-10 CH_3).

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.60; H, 8.99. Found: C, 69.3; H, 9.0.

***cis*-10-Methyl-2,8-decalindione (17).**[37a]—The crude hydroxy ketone **15** obtained as described above from 2.24 g of ketal **2**, was taken up in 15 ml of acetone, cooled to 0°, and treated with 3.0 ml of standard chromic acid reagent.[38] The product was isolated as described above for keto ketal **4** to give 1.06 g (51% based on ketal **2**) of oil which was crystallized from hexane to give 610 mg of dione **17**, mp 94–95°, and 160 mg, mp 75–85°: λ_{max}^{KBr} 5.84 (CO), 6.82, 6.95, 7.08, 7.32, 7.61, 8.18, 8.39, 8.82, 9.23, 9.58, 9.77, 10.36, 10.38, and 12.92 μ; $\delta_{TMS}^{CHCl_3}$ 1.33 ppm (CH_3). The analytical sample exhibited mp 95.5–96° from hexane.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.27; H, 8.95. Found: C, 73.1; H, 8.7.

The combined mother liquors from the above crystallization were chromatographed on 25 ml of Florisil. Ketol **13** (69 mg), identified by the infrared spectrum,[9] was eluted with 10% ether in benzene.

An additional 58 mg of dione **17** was eluted with 50% ether in ethyl acetate and 40 mg of octalone **1** was eluted with ethyl acetate.

Acid-Catalyzed Dehydration of a Mixture of the *cis*- and *trans*-Hydroxydecalones 13 and 14.—A mixture of 125 mg of *trans*-10-methyl-9-hydroxy-2-decalone (**14**) and 250 mg of *cis*-10-methyl-9-hydroxy-2-decalone (**13**) in 11 ml of acetone containing 2.2 ml of water and 0.2 ml of concentrated hydrochloric acid was heated at reflux for 20 min. The cooled mixture was diluted with water and the product was isolated with ether affording 330 mg of oily solid estimated to contain 40% of octalone **1**, 20% of the *trans*-decalone **14**, and 40% of the *cis*-decalone **13** by examination of its infrared spectrum; λ_{max}^{KBr} 2.92 (OH of **14**), 5.96 (CO of **1**), 9.50 (band of **13**) and 10.00 μ (band of **14**).

***trans*-8-Methylene-10β-methyl-2β-decalol (18).**[37a]—A solution of 665 mg of ketone **7** in 8 ml of ether was added to a stirred suspension of 250 mg of lithium aluminum hydride in 50 ml of dry ether. After 3 hr, 0.5 ml of water and 0.4 ml of 10% aqueous sodium hydroxide were carefully added, and the mixture was stirred overnight, and filtered through Super Cel. The solvent was distilled from the filtrate under reduced pressure to give 735 mg of oil which solidified on standing. Recrystallization from hexane afforded 555 mg (83%) of alcohol **18**: mp 64–65°; λ_{max}^{KBr} 3.00 (OH), 3.27 (C=CH_2), 6.06 (C=C), 8.51, 9.45, 9.62, 10.01, 10.34, 11.16, and 11.60 μ; $\delta_{TMS}^{CCl_4}$ 4.80, 4.54 (C=CH_2), 3.62 (C*H*OH), 3.14 (OH), and 0.77 ppm (CH_3). After two successive recrystallizations from hexane the analytical sample, mp 67–67.5°, was secured.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.95; H, 11.18. Found: C, 79.8; H, 11.1.

***trans*-8-Methylene-10β-methyl-2β-decalol *p*-Toluenesulfonate (19).**[37a]—To a well-stirred solution of 4.48 g of alcohol **18** in 250 ml of pyridine at 0° was added, portionwise, 5.23 g of *p*-toluenesulfonyl chloride.[37b] After 1 hr at 0° and 48 hr at room temperature, the mixture was diluted with 1 l. of ether, 700 ml of water, and thoroughly extracted. The combined extracts were washed successively with water, 3% aqueous sulfuric acid, water, saturated aqueous sodium bicarbonate, and saturated brine. The extracts were dried, the solvent was distilled under reduced pressure, and the residue, a yellow oil, was crystallized from hexane giving 6.53 g (78.5%) of white solid *p*-toluenesulfonate **19**: $\lambda_{max}^{CCl_4}$ 3.27 (C=CH_2), 6.08 (C=C), 6.24 (C=C), 8.40, 8.48, and 11.20 μ. A sample of this material was recrystallized twice from hexane to give the analytical sample, mp 81.5–82.5°.

Anal. Calcd for $C_{19}H_{26}O_3S$: C, 68.22; H, 7.83; S, 9.59. Found: C, 68.2; H, 7.8; S, 9.5.

***trans*-8-Methylene-10β-methyldecalin-2α-nitrile**[37a] **(20).**—The procedure of Henbest and Jackson[28] was employed. A solution of 4.0 g of *p*-toluenesulfonate **19** and 6.2 g of sodium cyanide in 325 ml of dry *N*-methylpyrrolidone was stirred at 90° for 21 hr.[37b] The cooled mixture was treated with ice-water and the product was isolated with pentane[37c] giving 2.33 g of solid. Recrystallization from hexane gave 1.46 g (64%) of nitrile **20**: mp 63–65°; λ_{max}^{KBr} 3.27 (C=CH_2), 4.49 (CN), 6.08 (C=C), 6.93, 10.02, 11.10, and 11.58 μ; $\delta_{TMS}^{CCl_4}$ 4.78, 4.42 (C=CH_2), 3.05 (CHCN, unresolved triplet, width at half-height = 10 cps), and

0.73 ppm (CH_3). The gas chromatogram[44] showed a single symmetrical peak at 17.6 min.

Anal. Calcd for $C_{13}H_{19}N$: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.2; H, 10.2; N, 7.5.

trans-**8-Methylene-10β-methyldecalin-2β-carboxylic Acid**[37a] (**21**).—A solution of 1.00 g of nitrile **20** and 3 g of potassium hydroxide in 40 ml of ethylene glycol was stirred at 160° for 16 hr.[37b] The cooled solution was diluted with water and washed with ether. The aqueous phase was acidified to pH 3.5 with concentrated hydrochloric acid and the liberated organic material was isolated with ether[37c] to give 0.71 g (65%) of solid acid **21**. One recrystallization from hexane afforded 0.41 g of white solid: mp 116–117°; λ_{max}^{KBr} 3.2–4.0 (acid OH), 5.89 (CO), 6.08 (C=C), 7.02, 7.68, 8.23, 8.47, 10.40, and 11.28 μ; $\delta_{TMS}^{CCl_4}$ 12.57 (COOH), 4.78, 4.52 ($C=CH_2$), and 0.75 ppm (CH_3). The analytical sample, mp 117–117.5°, was secured from this material after two additional recrystallizations from hexane.

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.95; H, 9.68. Found: C, 74.7; H, 9.9.

dl-**β-Eudesmol** (**23**). **A. From Ester 22.**—An ethereal solution of diazomethane[45] was added dropwise to a solution of 310 mg of acid **21** in 5 ml of ether until the yellow coloration persisted. After 30 min, glacial acetic acid was added dropwise to discharge this color and the solution was washed with water, dilute sodium hydroxide, and brine. The ethereal extracts were dried and distilled giving 249 mg (76%) of oily ester **22**, bp 115° (bath temperature) at 0.15 mm; λ_{max}^{film} 3.24 ($C=CH_2$), 5.74 (CO), 6.07 (C=C), 6.64, 8.58, 9.58, and 11.22 μ; $\delta_{TMS}^{CCl_4}$ 4.78, 4.55 ($C=CH_2$), 3.68 (CO_2CH_3), and 0.77 ppm (C-10 CH_3).

A 280-mg sample of equivalent material in 250 ml of anhydrous ether was treated with 7 ml of 1.6 *M* ethereal methyllithium.[46] After 4 hr at room temperature, the excess methyllithium was destroyed by the cautious addition of water and the mixture was washed with saturated brine and dried. The solvent was removed and the residue was distilled affording 220 mg (80%) of a colorless oil which solidified upon standing. Sublimation at 55° (13 mm) gave a fluffy white solid, mp 60–61°, identified as *dl*-β-eudesmol by noting the exact correspondance of the infrared spectrum with the spectrum of authentic β-eudesmol;[47] λ_{max}^{KBr} 3.02 (OH), 3.25, ($C=CH_2$), 6.09 (C=C), 7.25, 7.95, 8.22, 8.42, 8.82, 10.15, 10.45, 11.12, 11.32, and 11.72 μ; $\delta_{TMS}^{CCl_4}$ 4.78, 4.54 ($C=CH_2$) 2.72 (OH), 1.67 [$(C(OH)(CH_3)_2)$], and 0.72 ppm (C-10 CH_3). Sublimation at 55° (0.3 mm) afforded a more dense white solid, mp 68–69°, likewise identified as *dl*-β-eudesmol. The yield of these two polymorphic forms of **22** was 73%. The analytical sample, mp 68.5–69.5°, was obtained by resubliming the higher melting polymorph at 53° (0.3 mm).

Anal. Calcd for $C_{15}H_{26}O$: C, 81.00; H, 11.79. Found: C, 80.85; H, 11.7.

The gas chromatogram[48] showed a single peak at 16.3 min, the same retention time (peak enhancement) as naturally derived β-eudesmol. The tlc mobilities of both materials were likewise identical (R_f 0.3).

B. From Ketone 31.—The procedure outlined above in part A was followed using 160 mg of ketone **31** and 1.5 ml of 1.6 *M* methyllithium in 10 ml of ether. The material obtained in this manner (106 mg) was identical with that from part A.

trans-**10β-Methyldecalin-3α-nitrile**[37a] (**26**).—The procedure outlined above for nitrile **20** was followed using 300 mg of the *p*-toluenesulfonate **25**,[27] and 0.51 g of sodium cyanide in 50 ml of dry *N*-methylpyrrolidone at 90° for 20 hr. The resulting product was recrystallized from hexane affording a first crop of 68 mg, mp 60.5–61.5°, and a second crop of 47 mg, mp 54–58° (total yield 70%): λ_{max}^{KBr} 4.48 (CN), 6.93, 8.51, and 10.02 μ; $\delta_{TMS}^{CCl_4}$ 2.98 (CHCN, unresolved triplet; width at half-height = 9 cps) and 0.87 ppm (CH_3). The analytical sample, mp 60.5–61.5°, was secured after an additional recrystallization from hexane.

Anal. Calcd for $C_{12}H_{19}N$: C, 81.27; H, 10.80; N, 7.90. Found: C, 81.1; H, 10.7; N, 7.8.

trans-**10β-Methyldecalin-2β-carboxylic Acid**[37a] (**27**). **A. From Nitrile 26.**—A solution of 110 mg of nitrile **26** and 0.3 g of potassium hydroxide in 10 ml of ethylene glycol was heated to 170° for 18 hr.[37b] The acidic material was isolated as described above for acid **21** affording 74 mg (61%) of brown solid. Recrystallization from hexane yielded 25 mg of yellow solid, mp 107.5–108.5°; $\lambda_{max}^{CCl_4}$ 3.75 (acid OH), 5.85 (CO), 7.70, 8.01, 8.22, 8.50, and 10.03 μ; $\delta_{TMS}^{CCl_4}$ 12.12 (CO_2H) and 0.88 ppm (CH_3). The analytical sample exhibited mp 107.5–108° from hexane.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.41; H, 10.27. Found: C, 73.6; H, 10.5.

B. From Nitrile 30.—A 50-mg sample of nitrile **30** was stirred with 0.1 g of potassium hydroxide in 10 ml of ethylene glycol at 155° for 22 hr.[37b] The acidic material was isolated as described above for acid **21** affording 74 mg (45%) of solid acidic material which was filtered through 8 ml of silica with ether and recrystallized from hexane. Material, mp 107–108°, which gave no melting point depression when mixed with the acid obtained in part A was thereby secured.

trans-**10β-Methyldecalin-2β-nitrile**[37a] (**30**).—The methanesulfonate derivative **29** was prepared from decalol **28**[27] according to the procedure of Eschenmoser and Frey.[49] This derivative was obtained as an oil which could not be induced to crystallize and was therefore used directly. A 527-mg sample of **29** and 1.12 g of sodium cyanide in 50 ml of *N*-methylpyrrolidone was stirred at 90° for 25 hr.[37b] The product was isolated according to the procedure described above for nitrile **20** to give 242 mg of oil, bp 85° (bath temperature) at 0.02 mm. Nitrile **30** was purified *via* preparative gas chromatography:[50] λ_{max}^{film} 4.48 (CN), 6.09, 7.23, 10.01, 11.20, and 12.01 μ; $\delta_{TMS}^{CCl_4}$ 0.90 ppm (CH_3); $n^{27}D$ 1.4865. The analytical sample, bp 88° (bath temp) at 0.03 mm, was prepared by short-path distillation.

Anal. Calcd for $C_{12}H_{19}N$: C, 81.27; H, 10.80; N, 7.90. Found: C, 81.2; H, 10.95; N, 8.1.

trans-**2β-Acetyl-8-methylene-10β-methyldecalin**[37a] (**31**).—To a well-stirred solution of 250 mg of nitrile **20** in 20 ml of ether at 0° was added 2.5 ml of 1.6 *M* ethereal methyllithium.[37b] After 3 hr at 0°, the mixture was treated with 30 ml of saturated ammonium chloride and stirred vigorously for 2.5 hr at room temperature. The product was isolated with ether and distilled giving 247 mg (91%) of ketone **31**: bp 90° (bath temperature) at 0.2 mm; λ_{max}^{film} 3.26 ($C=CH_2$), 5.84 (CO), 6.08 (C=C), 7.93, 11.28, and 11.65 μ; $\delta_{TMS}^{CCl_4}$ 4.66, 4.40 ($C=CH_2$), 2.04 ($COCH_3$), and 0.72 ppm (C-10 CH_3). The gas chromatogram[51] showed two peaks at 18.3 (93%) and 15.2 min (7%). The composition of this material was unchanged by chromatography on basic alumina or by treatment with methanolic sodium methoxide at room temperature for 2 hr.

The semicarbazone derivative exhibited mp 189–190° after two recrystallizations from methanol.

Anal. Calcd for $C_{15}H_{25}N_3O$: C, 68.40; H, 9.57; N, 15.96. Found: C, 68.4; H, 9.5; N, 15.8.

dl-**β-Selinene** (**32**).—The procedure of Corey, *et al.*, was employed.[20] A solution of 0.28 g of methyltriphenylphosphonium bromide in 1.5 ml of dimethyl sulfoxide was added to 0.7 ml of 1.2 *M* dimethylsulfinylsodium[39] in dimethyl sulfoxide at 0°.[37b] The resulting yellow solution was stirred for 30 min at room temperature and a solution of 44 mg of methyl ketone **31** in 1 ml of dimethyl sulfoxide was added. After 4 hr, the mixture was diluted with water and extracted with pentane. The combined extracts were washed with 1:1 dimethyl sulfoxide–water, water, saturated brine, and dried over anhydrous magnesium sulfate. The crude residue, after evaporation of the solvent *in vacuo*, was filtered through 5 ml of alumina to remove traces of triphenylphosphine oxide. Elution with hexane gave 27 mg (63%) of a colorless oil identified as β-selinene (**32**) by the direct correspondence of the infrared and nmr spectra with the published spectra of natural β-selinene:[7,52] λ_{max}^{film} 3.28 ($C=CH_2$), 5.62, 6.09 (C=C), 6.88, 6.93, 7.26, 7.90, 8.28, 8.53, 8.68, 9.52, 10.10, 10.70, 11.25, and 12.67 μ; $\delta_{TMS}^{CCl_4}$ 4.63, 4.37 ($C=CH_2$), 1.72 ($=CCH_3$), and 0.72 ppm (C-10 CH_3). The analytical sample was prepared by preparative gas chromatography.[53] The chromatogram showed a single peak at 12.2 min.

(44) The Carbowax column[40] was used at 210° with a helium flow of 88 cc/mm.

(45) F. Arndt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p 165.

(46) Alpha Inorganics, Inc., Beverly, Mass.

(47) This spectrum was kindly provided by Dr. J. W. Rowe, Forest Products Laboratory, Madison, Wis.

(48) The Carbowax column[40] was employed at 210° with a helium flow rate of 88 cc/min.

(49) A. Eschenmoser and A. Frey, *Helv. Chim. Acta*, **35**, 1660 (1952).

(50) The 0.5-in. Carbowax column[41] was used at 200° with a helium flow rate of 250 cc/min.

(51) The Carbowax column[40] was employed at 210° with a helium flow rate of 69 cc/min.

(52) J. Pliva, V. Herout, B. Schneider, and F. Sorm, *Collection Czech. Chem. Commun.*, **18**, 500 (1953).

(53) The Carbowax column[40] was used at 150° with a helium flow rate of 80 cc/min.

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.7; H, 11.6.

***trans*-8-Methylene-10β-methyl-2α-decalol (34).**[37a]—The procedure of Blickenstaff and Chang[34] was applied. A solution of 5.0 g of the *p*-toluenesulfonate **19** in 95 ml of N,N-dimethylformamide containing 0.3 ml of water was maintained at 95° for 48 hr.[37b] The mixture was allowed to cool, diluted with water, and the product was isolated with ether[37c] to give 4.0 g of formate **33**; λ_{max}^{film} 3.27 (C=CH_2), 5.78 (CO), 6.06 (C=C), and 11.21 μ.

The above material was dissolved in 25 ml of ethanol containing 3 g of sodium hydroxide. After 5 hr, water was added and the product was isolated with ether[37c] giving 3.1 g of material which was chromatographed on 750 ml of Florisil. Elution with benzene gave 0.34 g of olefinic material which was not investigated further. Elution with 25% ether in benzene yielded 2.1 g of solid which was sublimed to give 1.8 g (64%) of alcohol **34**: λ_{max}^{KBr} 3.02 (OH), 3.27 (C=CH_2), 6.08 (C=C), 8.06, 8.19, 8.31, 8.68, 9.00, 9.59, 10.00, 10.24, 10.93, 11.27, 11.69, and 11.94 μ. The analytical sample, mp 66.5–67°, was secured by recrystallizing the sublimed solid from pentane. A 1:1 mixture of this decalol and decalol **18** exhibited mp 36–50°.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 80.2; H, 11.1.

***trans*-8-Methylene-10β-methyl-2α-decalyl Methanesulfonate (35).**[37a]—To a solution containing 1.3 g of decalol **34** in 13 ml of pyridine at 0° was added 0.94 g of methanesulfonyl chloride. The solution was allowed to stand at room temperature for 20 hr, water was added, and the mixture was thoroughly extracted with ether. The combined extracts were washed successively with water, cold 10% aqueous sulfuric acid, saturated aqueous sodium bicarbonate, saturated brine and dried over anhydrous magnesium sulfate. The solvent was distilled under reduced pressure and the solid residue was recrystallized from hexane giving 1.5 g (82%) of the methanesulfonate **35**: mp 57–58°; λ_{max}^{KBr} 3.23 (C=CH_2), 6.05 (C=C), 8.15, 8.44, 8.57, 8.69, 8.92, 10.20, 10.43, 11.00, 11.12, 11.63, and 12.07 μ.

An additional 0.2 g (11%), mp 54–58°, was obtained by concentrating the mother liquor. The analytical sample, mp 57.5–58°, was obtained from the first crop after one more recrystallization.

Anal. Calcd for $C_{13}H_{22}O_3S$: C, 60.42; H, 8.58; S, 12.40. Found: C, 60.6; H, 8.8; S, 12.5.

Diethyl (*trans*-8-Methylene-10β-methyl-2β-decalyl)malonate (36).[37a]—To a stirred suspension of sodium hydride (from 0.55 g of a 51.6% mineral oil dispersion) in 13 ml of 1,2-dimethoxyethane was added 2.0 g of diethyl malonate. Hydrogen was evolved almost immediately, and when this gas evolution stopped, 1.00 g of the decalyl methanesulfonate **35** was added and the mixture was stirred at reflux for 20 hr. Water was added to the cooled mixture and the product was isolated with ether,[37b] and chromatographed on 560 ml of Florisil to remove the mineral oil. The ester (0.93 g) was eluted with 2% ether in benzene and distilled affording 0.90 g (73%) of decalylmalonate **36**: bp 125° (bath temperature) at 0.3 mm; λ_{max}^{film} 3.24 (C=CH_2), 5.68–5.75 (CO), 6.06 (C=C), and 11.23 μ. Attempts at further purification were unsuccessful. Even material which had been chromatographed twice and undergone three successive careful evaporative distillations gave analytical values which were 0.7% low in carbon.

Reduction–Elimination of Decalylmalonate 36.—A mixture of 0.74 g of malonic ester **36** and 1.4 g of a 51.6% mineral oil dispersion of sodium hydride in 12 ml of 1,2-dimethoxyethane was stirred at reflux for 64 hr to ensure complete enolate formation. A 0.29-g portion of lithium aluminum hydride was added and the mixture was maintained at reflux with efficient stirring for an additional 2 hr. The mixture was allowed to cool, 2.0 ml of 10% aqueous sodium hydroxide was added, and stirring was continued for 1 hr. The granular salts were removed by filtration, the solvent was removed from the filtrate under reduced pressure, and the residue was chromatographed on 300 ml of Florisil to separate the mineral oil. Elution with 5% ether in benzene afforded 0.42 g (81%) of alcoholic material identified as a 3:1 mixture of costol (**37**) and dihydrocostol **38** by gas chromatography.[53]

***dl*-Costal (39).**—A 0.39-g sample of the 3:1 mixture of costol (**37**) and dihydrocostol (**38**) described above was dissolved in 70 ml of chloroform and 4.83 g of activated manganese dioxide[54] was added. The mixture was efficiently stirred for 2.5 hr at room temperature and filtered through a pad of Super Cel with the aid of benzene and ether. The filtrate was concentrated under reduced pressure affording 0.37 g of yellow oil which was chromatographed on 100 ml of Florisil. Elution with benzene afforded 0.23 g of costal (**39**) which was distilled to give 0.21 g (63%): bp 110° (bath temperature) at 0.3 mm; λ_{max}^{film} 3.23 (C=CH_2), 4.70 (CHO), 5.90 (CO), 6.06, 6.14 (C=CH_2), 7.23, 8.00, 8.24, 8.46, 8.66, 10.58, 10.91, and 11.23 μ; $\delta_{TMS}^{CCl_4}$ 10.33 (CHO), 6.17, 5.87 (CH_2=CCHO), 4.65, 4.35 (C-4=CH_2), and 0.90 ppm (C-10 CH_3).

The later benzene fractions yielded a mixture of costal (**39**) and dihydrocostol (**39**). No attempts were made to purify this latter substance (undoubtedly a mixture of diastereoisomers), but its structure follows from the following observations: (1) a strong band at 3.0 μ in the infrared spectrum; (2) peaks at 3.6–3.4 (CH_2OH), 0.88 (CH_3CH, doublet, J = 6 cps), and 0.70 ppm (C-10 CH_3) in the nmr spectrum; (3) its resistance to oxidation by manganese dioxide.

A product analogous to **38** is obtained in comparable yield *via* reduction of diethyl sodiocyclohexylmalonate with lithium aluminum hydride under the same conditions.[55]

***dl*-Costol (37).**—A solution of 123 mg of *dl*-costal (**39**) and 83 mg of lithium aluminum hydride in 5 ml of ether was stirred at room temperature for 30 min, treated with 0.1 ml of 10% aqueous sodium hydroxide and, after stirring for an additional hour, the resulting mixture was filtered through a pad of Super Cel. The solvent was removed from the filtrate under reduced pressure and the residue was distilled giving 114 mg (93%) of *dl*-costol: bp 130° (bath temperature) at 0.3 mm; λ_{max}^{film} 3.00 (OH), 3.23 (C=CH_2), 6.06 (C=C), 6.91, 7.07, 7.21, 7.88, 8.45, 8.64, 9.03, 9.71, 10.07, 10.57, 10.65, 11.22, and 11.59 μ; $\delta_{TMS}^{CCl_4}$ 4.95, 4.83 (CH_2=CCH_2OH), 4.65, 4.40 (C-4=CH_2), 4.01 (CH_2OH), and 0.73 ppm (C-10 CH_3).

The infrared and nmr spectra were identical with those of natural costol.[7] A sample was redistilled for analysis.

Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.5; H, 11.0.

***dl*-Costic Acid (40).**—To a well-stirred solution of 80 mg of *dl*-costal (**39**), and 120 mg of silver nitrate in 4 ml of 1:1 ethanol–water was added dropwise a solution of 0.12 g of sodium hydroxide in 5.4 ml of water. After 12 hr, the mixture was filtered through a pad of Super Cel and the filtrate was washed with ether. The aqueous phase was acidified to pH 3 with concentrated hydrochloric acid and the product was isolated with benzene[37c] giving 77 mg (88%) of solid costic acid (**40**). This material, recrystallized three times from hexane, provided the analytical sample: mp 115–116°; λ_{max}^{KBr} 3.25 (C=CH_2), 5.90 (CO), 6.06, 6.14 (C=C), 7.22, 7.64, 7.90, 8.12, 8.44, 8.59, 9.08, 9.58, 10.45, 10.60, 11.23, 14.32, and 15.26 μ.

Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.8; H, 9.7.

The infrared spectrum was identical with the published spectrum of natural costic acid.[7]

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(54) Beacon Chemical Co., Inc., Cambridge, Mass.

(55) Unpublished observations of Niels H. Andersen.